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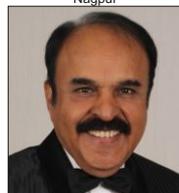
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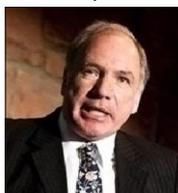
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[Progressive iron overload leads to liver fibrosis is a well-known complication in TDT
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This is not a new endeavor however there we tried to see the effect of other factors
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[In late 2019, an epidemic of Novel Corona Virus infection later named SARS-CoV2 hit China followed by rapid spread of infections across the World. Notwithstanding Government mandated measures like lockdown, rigorous testing, universal masking and COVID-19 screening camps, it is important for hospitals to be prepared to face the pandemic.]

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**PROF. TAMONAS
CHAUDHURI**
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Editorial

Why we should write....

“**S**hruti” the art of memorizing knowledge and passing it over from one generation to the next was the only medium of transfer of information from one person to another. However as such information gets communicated from one person to another to yet another or from one generation to another, the chance of distortion, error and modification of original data increases manifolds. Thus a piece of knowledge or wisdom which could have become a huge source of development for the future generation could become extinct or totally mutated into a mutilated form. Human civilization could still be struggling in solving their basics needs instead of progressing and developing as each generation would have to start every time from square one. We would still be struggling to fly an airplane or propel a ship across continents as we would not have an accumulated knowledge of the previous generation to bank upon. Let us further delve into this topic and later explore the relevancy of writing in context to our medical field.

“I never once failed at making a light bulb. I just found out 99 ways not to make one.” This famous statement from Thomas Alva Edison, the inventor of electric bulb shows clearly that history documents not only success but errors too which when passed on to the next generations will shield them from repeated flaws that can hinder progress. Writing thus is like the gift of gab to a writer who hones up his skill of writing on the anvil of practice and perfection. Writing can be therapeutic too. It can be a way to vent all the trapped frustrations taxing your mind into a far less volatile form, paper or screen. You can jot down your anger, fear, worry and stress. Writing can serve as a form of cathartic stress relief where you finally get to say what you can't say out loud, in real life. Writing to me is a

process of excavation of one's mind where the writer unearths his brewing ideas fermenting at the back of his mind and coding them on paper. As goes the saying – a pen is mightier than a sword and thus as a sword needs to be honed up regularly to maintain its cutting edge similarly a writer should write regularly to maintain as well as upgrade his writing skills. Writing regularly develops your analytical and rational skills. Working through your problems with a piece of paper encourages you to think things through clearly, in both linear (sequential) and non-linear (creative) ways. The best solutions come from a mix of both logical and creative thinking. Many people tend to panic and react emotionally to their problems, but if you're used to solving them by processing each component of the problem in writing, you'll develop a better approach and skill set. You'll at least pause to think through the situation before hitting the panic button next time something comes up! Discontentment, disillusionment, and unhappiness often come from forgetting why we're doing something (or, on a different track, not having a good reason for living a certain way) and it is important to keep those simple reasons at the forefront of your mind or you run the risk of letting your life become a series of boring, menial actions. It's not only important to remind yourself of your motives for your current actions; it's important to monitor your actions to see if they align with your life goals so that you can change them. Sometimes, the only way to keep such a close monitor on your actions and goals is to write about them every day.

Now comes the key question – ***Why should the medical professionals write?*** The Yale Internal Medicine Residency Writers Workshop was created in 2003 to provide a creative outlet for residents in internal medicine where Dr. Anna B. Reisman, teaches basic skills of writing. "Writing makes people better doctors because it increases their ability to be good observers," Reisman said. "They start to pay attention to details. If they're writing about a patient, we encourage them to notice not only what the patient

looks like, but ask, what are the sounds around the patient? What are the smells in the patient's room?" These skills help doctors notice more things about their patients, which helps boost empathy and diagnostic ability. "Learning the craft of writing requires that you learn how to reflect the perspective of others," Reisman said. "That's obviously a huge part of being a doctor." James Stubenrauch, Senior Fellow at the Center for Health, Media and Policy at Hunter College in the City University of New York (CUNY), co-taught the first narrative writing course to students in the Hunter-Bellevue School of Nursing. Developing a daily writing practice, he said, helps nurses combat the burnout, exhaustion, fatigue and stress that comes with dealing with death and suffering. It also empowers them to speak up and take greater roles in decision-making. "For me personally, writing has been a way to understand myself and to think through experiences," Reisman explained. "If I'm writing an essay about an experience, trying to get it right forces me to really look at it deeply in a way that I might not do if I'm just running through it in my head. And when we're teaching residents, they start to understand that also."¹

But can Doctors write? Literature and Medicine is as far apart from each other as earth is from the sun or a galaxy is from another galaxy you may conclude but have you heard of these names - **Anton Chekhov, John Keats, Arthur Conan Doyle, William Carlos Williams, A J Cronin, W Somerset Maugham**. They are famous writers immortalized by their writings but do you know each and every one of them was physicians too! Who can forget the famous Bengali writer **Dr. Nihar Ranjan Gupta** the Indian counter part of Arthur Conan Doyle. Yes, but all of the above have enriched literature but can writing enhance medical progress? A Big Yes.

Documented evidences of doctor's interaction with their patients, their logical thought process in solving a certain critical cases et. al when documented can serve as a vital source of reference for other doctors in

future to turn back to and refer benefitting both the patients and the physicians.

“The physician treats with words; within the physician-patient social system, the patient is moved by fears and other sentiments, and these are modified by the physician’s words and phrases. Physicians dispense not only medicines but words that influence medicines or, all by themselves, that affect the patient more than the medicine” – DR MORGAN MARTIN². Now if words only can have such magical powers, written texts of well known doctors documenting their experiences with patients and their adventurous paths towards success could be as interesting as a sleuth story high in literal value as well as extremely valuable as records of treatment.

The induction of novice residents can be done with a case report. Faculty should realize that while a case report may not be a significant addition to their list of publications, for the student, it is the first but difficult step that helps them embark on a journey into the world of scientific writing³. Scientific writing is a learning process, and one masters this skill through experience⁴.

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Original Article

Clinical Spectrum and Outcomes of Non-lupus Crescentic Glomerulonephritis : An Experience from Eastern India

Kanai Lal Karmakar¹, Rajendra Pandey²

Aims : To evaluate the clinical profile, histomorphology and clinical outcome of patients with Crescentic Glomerulonephritis (except Lupus) treated with pulse intravenous Cyclophosphamide using European Vasculitis Study Group (EUVAS) protocol.

Materials and Methods : Prospective observational single center study over a period of one and half year. Relevant clinical, laboratory and histological data were recorded. End points of study: death, completion of 6 month of follow up or end stage renal disease, whichever is earlier.

Results : Total 1023 renal biopsies were performed during the study period. 4.40% (n=45) had Crescentic Glomerulonephritis (CrGN) of which 3.42% (n=35) were non-Lupus and 0.98% (n=10) were Lupus Nephritis. Amongst the non-Lupus 91% (n=32) were pauci-immune & rest were Anti-GBM (AGBM) & IgA Nephropathy (IgAN). 68.75% (n=22) were ANCA positive and 10 (31.25%) were ANCA negative. 54.55% (n=12) c-ANCA positive and 45.45% (n=10) were p-ANCA positive. Average age was in 21 to 60 years with Male: Female ratio was 1:2.2. Maximum crescents were in Anti-GBM (93%) followed by ANCA group (65%). At presentation 80% (n=28) were oligoanuric & 82.86% (n=29) patients required dialysis. 68.57% (n=24) patients responded to EUVAS regimen while 31.42% (n=11) did not respond. 20% (n=7) remained dialysis (HD) dependent and 37.14% (n=13) non-HD Dependent. ANCA positive responded better to EUVAS protocol than ANCA negative and worst outcome noted in AGBM and IgAN.

Conclusion : Non Lupus CrGN treated by EUVAS protocol has an initial response rate of 66%. No histological or clinical parameter was significantly associated with response to therapy. Sepsis was the most common cause of death.

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Key words : Crescentic, Glomerulonephritis, Lupus.

Rapidly Progressive Glomerulonephritis (RPGN) is a severe form of Nephritic Syndrome characterized by the rapid loss of renal function, accompanied by proteinuria, glomerular hematuria and often, oliguria^{1,2}. Histologically, RPGN is usually associated with Crescentic Glomerulonephritis (CrGN) defined as presence of crescents in >50% of glomeruli on renal biopsy. In this study we have focused on non-Lupus CrGN. Prior to 1970s the outcomes for most of CrGN cases were dismal. Subsequently, cyclophosphamide and steroids have dramatically improved the remission rates³. Early diagnosis and treatment can significantly alter the course of the disease and may prevent irreversible loss of renal function. European Vasculitis Study Group (EUVAS) has provided a robust evidence for pulse cyclophosphamide therapy (EUVAS CYCLOPS protocol) and have led to consensus guidelines ie,

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Editor's Comment :

- Acute Renal Failure is a Medical Emergency and evaluation and management should be started at earliest possibility to prevent Renal death.
- There should be high degree of suspicion of Rapidly Progressive Renal Failure (RPGN) to all patients requiring dialysis when the disease duration less than 3 months.
- Renal Biopsy should be offered and to be done to all RPGN cases to see what is actually going on inside the Kidneys for better Renal survivability.

European League Against Rheumatism (EULAR) recommendations for treatment of Antineutrophil Cytoplasm Antibody (ANCA)-Associated Vasculitis (AAV) which is the most common non-Lupus CrGN^{1,3}. The evidence for pulse cyclophosphamide in other form of non-Lupus CrGN is less well established. The prevalence, serotype frequencies and clinico-pathologic phenotypes in AAV are influenced by racial/ethnic and geographic factors⁴. Despite the effectiveness of pulse cyclophosphamide therapy, the adverse effects of cyclophosphamide, particularly infections are a serious concern. These in turn may be affected by the socio-economic status and may vary across different populations. We planned this

study with the aim of evaluating the clinical profile, histomorphology and outcome of Crescentic Glomerulonephritis (except that due to Lupus) treated with European Vasculitis Study Group (EUVAS) intravenous cyclophosphamide protocol in patients presenting to our tertiary care institute.

MATERIALS AND METHODS

This is a prospective observational single centre study conducted at Institute of Postgraduate Medical Education & Research (IPGME&R), Kolkata, one of the largest tertiary care centers of Eastern India from January 2012 to December 2013. Patients of any age group diagnosed with Crescentic Glomerulonephritis (histologically) due to any etiology other than Lupus were included in the study. Informed and written consent of patient and that of the legal guardians in case of minors of the patient was taken before enrollment. Patients who refused or could not be given EULAR protocol, those who were not willing to participate and those who refused renal biopsy were excluded from the study.

Clinical, laboratory data and details of renal biopsy findings were recorded. Patients will be evaluated at presentation regarding: Clinical data including age, sex, skin or throat infection, blood pressure, systemic manifestations such as skin rash, arthritis, serositis, edema, manifestations of uremia, oliguria, gross hematuria and history of medications.

As a protocol laboratory parameters including urinalysis, serum creatinine, urea, sodium, potassium calcium, phosphorus, uric acid, complete blood count, plasma proteins, albumin, cholesterol, Anti-Streptolysin O (ASO), Anti-Nuclear Antibody (ANA), complement 3 (C3), anti-double stranded Nuclear Antibody (anti ds-DNA) and 24 hour urinary protein excretion. Anti-Neutrophil Cytoplasmic Antibody (ANCA) by ELISA and immunofluorescence and anti-Glomerular Basement Membrane (anti-GBM) were done for all the patients presenting as RPGN. Renal biopsy was considered for all RPGN patients. Only those who satisfied the inclusion criteria were included in the study. Subsequent investigations including Renal Function Test (RFT), complete hemogram, urine analysis and other investigations as and when needed were done at each follow up visit weekly after discharge for one month, then twice a month for 3 months and monthly thereafter. Renal biopsy was done in strict surgical aseptic procedure with real time Ultrasonography (USG) guided method after obtaining written informed consent. The protocol for renal biopsy procedure and assessment has been described in

supplementary data and supplementary Table 1 respectively. The protocol of treatment, modifications as per renal function, age and leucopenia (as mentioned in supplementary Table 2) and follow up is specified in supplementary data. The definition used for RPGN, CrGN, treatment responses and relapse have been given in supplementary data. The patients were followed up till attainment of end stage renal failure (requiring renal replacement therapy for 3 months), death or last follow-up at December, 2013, whichever was earlier.

Results are presented as means with standard Deviation (SD) for normally distributed data, or medians with percentiles for non-normally distributions. Nominally distributed continuous variables were compared using t-test. Categorical variables are compared using chi-square tests. All statistical tests will be two-sided with a P-value of <0.05 taken to indicate statistical significance. Independent variables affecting outcome have been analyzed using multivariate analysis.

RESULTS

A total of 1023 patients underwent renal biopsy during the study period. Among these 92(8.99%) patients had histological diagnosis of Glomerulonephritis with Crescents and 45 (4.40%) had Crescentic Glomerulonephritis (CrGN). Of these 45, 22.22% had lupus CrGN and 77.78% had non-lupus CrGN. The ratio of males: females for non-Lupus CrGN was 1:2.1. 91% of non Lupus CrGN were Pauci-Immune CrGN (PICrGN) while Antiglomerular basement membrane antibody disease (Anti-GBM) and Immunoglobulin A Nephropathy (IgAN) comprised 6% and 3% of all non-Lupus CrGN. One patient with Anti-GBM disease also had pANCA positivity. This patient

Table 1 — Age-wise distribution and baseline laboratory features of different types of non lupus Crescentic Glomerulonephritis

Age	Pauci-immune CrGN*	Anti-GBM CrGN*	IgAN#
Age groups :			
All (N=35)	91%	6%	3%
Age 1 to 20 years (N=6)	83%	0%	17%
Age 21 to 60 years (N=26)	92%	8%	0%
Age 61 to 100 years (N=3)	100%	0%	0%
Average age in years	38.41±14.834	33.50±4.95	17
Male: female	1:2.2	1:1	
Average Serum Creatinine (mg/dL)	5.08±3.664	12.94±2.475	8.62
Average Proteinuria (g/24 hours)	2.84±1.614	0.98±0.489	1.35
*CrGN : Crescentic Glomerulonephritis, # IgAN : Immunoglobulin A Nephropathy			

Table 2 — Clinical profile of different non lupus Crescentic glomerulonephritis

Characteristic	AGBM	ANCA+	ANCA-	IgAN	P
Male	1(%)	7(%)	3(%)	0(%)	0.852
Female	1(%)	15(%)	7(%)	1(%)	
Age (in years)	33.5±4.95	36.05±14.624	43.6±14.676	17±0	0.263
Duration of symptoms (in weeks)	3.5±0.707	4.14±1.49	3.9±1.792	8±0.0	0.106
Oliguria	2 (100%)	17(77%)	8(80%)	1(100%)	0.837
Gross Hematuria	0	1(5%)	0	0	0.895
Fever	1 (50%)	17(77%)	6(60%)	1(100%)	0.602
Seizures, Encephalopathy	2 (100%)	2(9%)	0	0	0.001
Rash	0	5(23%)	1(10%)	0	0.691
Arthralgias	1 (50%)	2(9%)	1(10%)	0	0.361
Hypertension	0	4(18%)	2(20%)	0	0.874
Creatinine (mg/dl)	12.94 ± 2.475	4.507 ± 2.534	6.324 ± 5.550	8.62	0.263
Nephrotic range Proteinuria(no.)	0 ± 0	0.23 ± 0.249	0.29 ± 0.296	0 ± 0	0.429

The average follows up was 8±1.25 months. 42.86% of patients died during therapy and 57.14% survived with the therapy during follow-up period.

The outcomes in the form of dialysis dependence (HD Dep), no dialysis dependence (non-HD) and death has been shown in Fig 1. We analysed the association of various clinical and biopsy

parameters with response/resistance in non lupus CrGN as shown in Table 6 but none were found to be statistically significant. The cumulative clinical response and outcomes at the end of follow up are shown in Table 7.

has been included in Anti-GBM group for discussion henceforth. The age wise distribution of non lupus CrGN and the baseline laboratory parameters in each of the biopsy diagnoses has been shown in Table 1. Among pauci-immune group 68.75% were ANCA positive and 31.25% were ANCA negative. The clinical characteristics of patients with non lupus CrGN has been shown in Table 2. The average delay in diagnosis was 3.5±0.70 weeks in AGBM group, 4.14±1.49 weeks in ANCA positive group and 3.90±1.792 weeks in ANCA negative group and 8 weeks in IgAN. Organ systems involvement in various types of non Lupus CrGN has been shown in Table 3. The histological findings in the various non Lupus CrGN has been shown in Table 4.

Table 9 shows the proportionate distribution of cellular, fibrocellular and fibrous crescents in PICrGN patients at diagnosis.

In 82.86% (n=29) patients required dialysis at presentation. 74.29% (n=26) were treated plasmapheresis. The therapeutic response to the IV Cyclophosphamide protocol has been shown in Table 5. Complete or partial remission has been clubbed together as total response. The patients who did not achieve either form of remission have been considered as resistant. 68.57% patients in our study responded to EULAR regimen but about 1/3rd of patients did not respond to therapy.

Table 3 — Organ systems involvement in various types of non lupus CrGN

Organ System Involvement	Number of Patients	% of Patients	AGBM	ANCA+	ANCA-	IgAN
Total Number of Patient	35		2	22	10	1
Renal	35	100%	100%	100%	100%	100%
Pulmonary	12	34.3%	2(100%)	5(22.7%)	4(40%)	1(100%)
Upper Respiratory Tract	4	11.42%	1(50%)	1(4.5%)	2(20%)	0
Musculoskeletal	4	11.4%	1(50%)	2(9.1%)	1(10%)	0
Neurologic	4	11.4%	2(100%)	2(9.1%)	0	0
Gastrointestinal	2	5.7%	0	1(4.5%)	0	1(100%)
Cutaneous	6	17.1%	0	5(22.7%)	1(10%)	0
Ocular	1	2.8%	0	1(4.5%)	0	0
Fever	25	71.4%	2(100%)	17(77.3%)	5(50%)	1(100%)
Otic	22	62.8%	1(50%)	14(63.6%)	6(60%)	1(100%)

Table 4 — Histological findings in different categories of non lupus Crescentic Glomerulonephritis

	AGBM	ANCA+	ANCA-	IgAN	P
No of glomeruli in the biopsy	22.5 ± 10.61	19.55 ± 9.16	18.7 ± 9.09	14 ± 0	0.888
Globally sclerosed glomeruli	1 ± 1.41	2 ± 3.42	4.5 ± 5.74	6 ± 0	0.351
% Glomeruli with crescents	93.33 ± 9.43	65.05 ± 34.57	63.53 ± 48.17	100 ± 0	0.620
% Glomeruli with BM thickening	0(0)	0(0)	2(20%)	0(0)	0.151
% Glomeruli with mesangial cellularity	0(0)	6(27%)	3(30%)	0(0)	0.762
% Glomeruli with mesangial matrix expansion	0(0)	3(14%)	2(20%)	0(0)	0.856
% Interstitial fibrosis/ tubular atrophy	0	7.5±14.45	5.0±8.81	10±0	0.835
Presence of ATN	0(0)	3(14%)	1(10%)	0(0)	0.916
Presence of vasculopathy	0(0)	5(23%)	4(40%)	1(100%)	0.230

Table 5 — Response of different types of non lupus Crescentic Glomerulonephritis using EULAR protocol

	Patients Treated	Total response	Resistant
AGBM	2	0 (%)	2 (100%)
ACNA+	22	16 (72.73%)	6 (27.27%)
ANCA-	10	7 (70%)	3 (30%)
IgAN	1	1 (100%)	0 (0%)
Total	35	24 (68.57%)	11 (31.43%)

Table 6 — Association of various parameters with response to treatment

	Responders	Resistant	P
Age in years	39.62 ± 17.24	38.29 ± 15.71	0.867
Female gender	10(76.9%)	5(71.4%)	0.787
Serum Creatinine at presentation	4.13±3.013	6.51±4.326	0.091
Globally sclerosed (GS) glomeruli	11.53 ± 15.69	28.24 ± 31.09	0.123
Percent of glomeruli with crescents	59.79 ± 38.65	54.68 ± 38.86	0.782
Glomerular infiltrate	7(53.8%)	3(42.9%)	0.639
Mesangial cellularity	3(23.1%)	1(14.3%)	0.639
Mesangial matrix expansion	3(23.1%)	1(14.3%)	0.639
Interstitial fibrosis/ tubular atrophy	1(7.7%)	2(28.6%)	0.212
Acute tubular necrosis	1(7.7%)	2(28.6%)	0.212
Vasculopathy	4(30.8%)	1(14.3%)	0.417

Table 7 — Cumulative Outcomes in non lupus Crescentic Glomerulonephritis at the end of follow up

Patients Treated	Remission (at 6 months)	Relapse (cumulative, at the end of 6 months)	ESRD (defined at 3 months)	Death (cumulative, at the end of 6 months)
AGBM	2	0	2(100%)	2(100%)
ANCA+	22	10(45.46%)	12(54.56%)	8(36.36%)
ANCA-	10	3(30%)	6(60%)	4(40%)
IgAN	1	0	1()	1(100%)
Total	35	13(37.14%)	21(60%)	15(42.86%)
P value	0.450	0.462	0.450	0.220

cumulative outcomes though numerically cANCA responded slightly better. Cause of death in different types of non lupus CrGN have been shown in Table 8. Sepsis was the most common cause of death. All the patients in AGBM and IgAN group died shortly before completion of therapeutic course. Table 9 shows comparison of clinical and laboratory parameters at baseline and at end of cyclophosphamide induction therapy in the PICrGN groups. There is significant improvement in clinical parameters like urine output, renal function tests and markers of inflammation. Fig 2 shows renal survival in non lupus crescentic glomerulonephritis patients.

Table 8 — Cause of death in different types of non lupus Crescentic Glomerulonephritis

	AGBM	IgAN	ANCA +	ANCA -	Total
Septicemia	2 (100%)	1 (100%)	4 (50%)	1 (25%)	8(53.33%)
Cardiac	0	0	3 (37.5%)	1 (25%)	4(26.67%)
Others	0	0	1 (12.5%)	2 (50%)	3(20%)
Total	2	1	8	4	15

DISCUSSION

The reported incidence of CrGN has been variable, ranging from 2 to 10% in studies from Europe, America as well as from Asia⁵⁻⁸. Studies from other parts of India have reported an incidence of 2 to 5%⁹⁻¹². Previous study from our Institute showed incidence of 7.5%¹³. We found a similar incidence of CrGN. Though the previous study from our institute found male: female ratio of 1:1.3, in this study we found female predominance with ratio 1:2.1 despite excluding Lupus CrGN. Some other studies have also reported a female pre-ponderance^{5,6}. The proportion of lupus and non-lupus CrGN was about 20% and 80% respectively, comparable to that other Indian studies ie, 20 to 30% and 80 to 70% respectively^{5,6,8}. Some studies from our country have not found a significant number of ANCA negative pauci immune GN contributing to PICrGN^{5,6}, however, we found serologically, only about 60% had ANCA positivity and rest were negative for both cANCA and pANCA, similar to some other larger series/studies¹⁴⁻¹⁶. These group of patients have been found to have negative ANCA serology despite repeated testing.

The mean age of patients in our study in PICrGN group was lesser in our study compared to that reported from other countries^{10,17-19}. A study reported ANCA negative PICrGN patients to be significantly younger than ANCA positive patients²⁰. Other studies from India also found PICrGN in younger

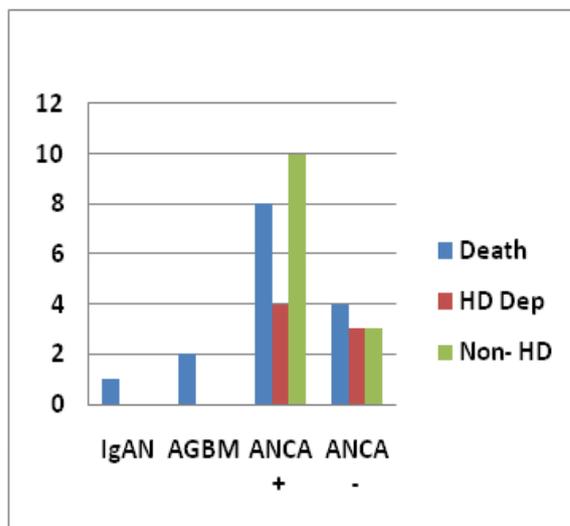


Fig 1 — Patient outcomes (death, HD Dep= hemodialysis dependent, Non-HD= not dialysis dependent) at the end of induction in IgAN (Immunoglobulin A nephropathy), AGBM (Anti glomerular basement membrane disease), ANCA + (positive) and ANCA - (negative) patients

Table 9 — Clinical and laboratory changes in pauci-immune Crescentic Glomerulonephritis before and after induction therapy using EUVAS regimen

Clinical	p-ANCA positive			c-ANCA positive			ANCA negative		
	Before	After	p	Before	After	P	Before	After	P
Urine volume (ml)	1067±539.75	1195±1223.94	0.709	1237.5±511.74	991.67±1145.11	0.452	855±520.39	730±1060.45	0.695
Creatinine at biopsy (mg/dl)	4.04±1.87	1.74±1.87	0.017	4.9±2.71	1.54±2.02	0.002	6.32±5.55	2.25±2.78	0.105
Urea at biopsy (mg/dl)	105.2±50.92	44.3±38.31	0.012	115.58±59.38	36.25±45.5	0.004	118.6±68.69	53±64.84	0.105
CRP (mg/l)	24.7±7.62	13.1±5.13	0.010	21.58±4.58	15.25±7.76	0.019	25.2±5.69	17±7.36	0.049
ESR (mm/1 h)	67.3±13.33	38±16.26	0.002	76.75±18.6	48.17±21.12	0.002	83.11±15.41	43.2±13.76	<0.001
24 h urinary Protein excretion(g)	3.12±1.34	0.28±0.27	<0.001	2.87±1.55	0.18±0.23	<0.001	2.54±2.01	0.29±0.3	0.006

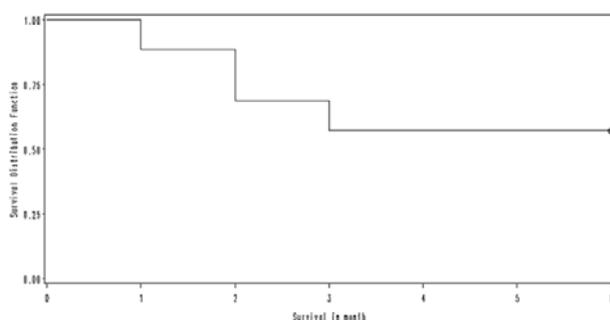


Fig 2 — Renal survival in non lupus Crescentic Glomerulonephritis patients on cyclophosphamide therapy

patients similar to our study 5²¹. Whether these findings are related to role of ethnicity in the pathogenesis of ANCA remains speculative.

Serum creatinine at presentation was highest in Anti GBM followed by IgAN and PICrGN in that order. This is consistent with natural history of Anti-GBM disease as it is often aggressive presenting with severe renal dysfunction compared to PICrGN¹. The most common clinical presentation was oliguria. Fever was common constitutional symptom. Hypertension was observed in about 20% of patients. Pulmonary involvement was seen in 1/3rd of patients and upper respiratory tract involvement was seen in approximately 17% of all patients. Respiratory involvement was seen in both ANCA positive and ANCA negative patients. Central Nervous System (CNS) involvement was found in both patients with Anti-GBM disease and in 9% of ANCA positive patients. CNS involvement is uncommon but has been reported earlier in Anti-GBM disease²²⁻²⁴. The pathogenesis of this phenomenon is unclear. Of the PICrGN patients, ocular, nervous system and gastrointestinal involvement was only seen in ANCA positive and not in ANCA negative group. One patient with Anti-GBM disease with pANCA positivity had otic and nasal involvement. Some studies have reported lesser extra-renal involvement in ANCA negative

patients^{16,25} while others have noted significant extra renal involvement in ANCA negative patients as well²⁶. Whether this is partly due to false negative/low titres of ANCA antibody due to inaccuracies of ANCA testing²⁷ or if truly it is reflective of ANCA negativity being a part of the spectrum of small vessel pauci immune vasculitides continuum is difficult to establish definitively.

Histologically, percentage of crescents were higher in Anti-GBM patients than in PICrGN patients. This is consistent with previously published literature²⁸. There was only 1 patient with IgA CrGN (100% of IgAN) hence the % of crescents in Anti-GBM disease as compared to the other groups was not statistically significant. Other reported biopsy parameters were similar across all groups.

About 66% patients achieved some form of remission (complete and partial) on therapy. The total response rates in ANCA vasculitis patients treated with pulse cyclophosphamide in previous studies was about 80%^{29,30}. However, these trials were not exclusively done in severe (crescentic) ANCA vasculitis. The trials done in severe ANCA vasculitis found a total response rate of about 60%³¹. A trial that compared rituximab versus cyclophosphamide in severe AAV found improvement in Glomerular Filtration Rate (GFR) of about 20ml/min/1.73 m². Thus, despite a significant rate of response most patients with severe ANCA vasculitis continued to have GFR less than 60ml/min/1.73 m². We also found at the end of follow up 60% had ESRD and about 15% had remission but had chronic kidney disease. Rituximab, the newer agent used in induction has been also found non inferior to cyclo-phosphamide²⁸. Hence, the therapy for ANCA vasculitis though has improved immensely, it is far from satisfactory. None of the clinical and histological parameters (glomerular, tubulo-interstitial or vascular) included in our study were significantly associated with response to treatment. Some studies have found histological parameters to be predictive of

outcomes^{32,33}. Our study was confined to CrGN alone which itself is severe form of injury; this could have been the reason why we did not find significant association of histology with outcomes.

Most patients who were resistant to therapy died during the study. Amongst the patients who did respond to therapy about 16% died and only 37% of patients maintained remission and stable kidney function. Sepsis was the most common cause of death followed by cardiac causes. One of the reasons for high incidence of sepsis was that most patients presented with dialysis requiring renal failure and needed non tunnelled dialysis catheter insertion which has high risk of catheter related bloodstream infection. The socio-economic background and nutrition status of patients may also have impact on susceptibility to infections. Measures to prevent infection ie, antibiotic prophylaxis, monitoring for leukopenia, counselling regarding measures to maintain personal hygiene meticulously, consideration of switching to tunnelled venous dialysis catheter from non tunnelled catheter in that requiring dialysis for prolonged duration may be improve outcome. At baseline none of the patients had overt cardiac involvement. The terminal event was cardiac in some patients. Whether this was due to vasculitis perse or secondary to other complications could not be definitively ascertained. Other Indian studies have also reported a less than satisfactory outcome in PICrGN^{14,34}. Limitations of study are relatively small sample size and shorter follow up.

CONCLUSION

Non lupus CrGN treated by EUVAS protocol has an initial response rate of 66%. But the number of patients who survived and had sustained remission was about 37%. No histological or clinical parameter was significantly associated with response to therapy. There is significant morbidity and mortality associated with resistance to cyclophosphamide therapy as well as its adverse effects in those responsive to cyclophosphamide. Sepsis was the most common cause of death. Measures to prevent infection may improve outcomes in non-Lupus Crescentic Glomerulonephritis.

Limitation : Limitations that the study was carried out in a single referral tertiary Hospital

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Conflict of interest : There was no conflict of interest

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Original Article

Laparoscopic Retro-rectus Onlay Mesh Repair (RROM) for Ventral Abdominal Wall Hernias – Is It the New Gold Standard ?

Kalpesh Jani¹, Samir Contractor²

In this paper, we describe the evolution of the radical new surgery for ventral abdominal hernias, developed by us, known as laparoscopic Retro-Rectus Onlay Mesh Repair (RROM). This represents a retrospective review of the cumulative data for the surgical procedure since it was initially conceptualized in 2007 upto March 2021.

A total of 244 patients underwent laparoscopic repair by this technique, consisting of 140 umbilical hernias, 78 incisional hernias and 26 divarication of recti. Females predominated, comprising 61% of our patients. Of the total, 196 patients underwent laparoscopic RROM repair alone while in 48 cases, either unilateral or bilateral Transversus Abdominis Release (TAR) was added. In 9.2% cases, an additional concomitant surgery was performed, majority being unilateral Total Extra-Peritoneal (TEP) for groin hernias. Other concomitant surgeries included bilateral TEP repair for groin hernias, cholecystectomy and tubal division, all performed laparoscopically.

Nearly 64% patients completed 2 years of follow-up. Clinical seroma detection rate was 11%, none requiring intervention. Two patients developed divarication of recti in the postoperative period and none developed mesh infection or had recurrence.

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Key words : Retro-rectus onlay mesh (RROM), hernia, laparoscopy, extraperitoneal repair.

Midline ventral hernias constitute approximately 20% of all abdominal wall hernias; they may be primary or secondary¹.

Most, if not all, ventral hernias require surgery as they tend to enlarge over time and may develop complications such as incarceration, obstruction or strangulation resulting in considerable morbidity and mortality².

Introduction of prosthetic repairs have substantially reduced recurrence rates when compared to primary tissue approximation and are indicated in all but the smallest of ventral hernias^{3,4}.

Since the first case of laparoscopic incisional hernia repair with synthetic mesh was reported in 1993⁵, based on the open technique pioneered by the Rives-Stoppa operation^{6,7}, it has evolved globally in recent years and offers numerous advantages over the conventional open approach, including decreased postoperative pain, length of hospital stay, and recurrences⁸. The Intra-peritoneal Onlay Mesh (s-IPOM) or its modification IPOM-Plus have come to be considered as the 'gold standard' for laparoscopic management of ventral abdominal hernia⁹. However, there are two major drawbacks to this technique, viz, cost and intraperitoneal placement of mesh. We have

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Editor's Comment :

- The RROM approach safely combines the advantages of the laparoscopic intra-peritoneal repair (IPOM) and the extra-peritoneal repair (e-TEP) for ventral abdominal hernias.
- It allows intraperitoneal dissection and reduction of hernia contents under vision. At the same time, the mesh is placed in the extra-peritoneal space, circumventing any complications that can arise from the placement of a large foreign object in the peritoneal cavity.
- Moreover, due to the lack of requirement of any special type of mesh or fixation apparatus, the cost of the surgery is drastically reduced.

developed and reported on a new laparoscopic approach to ventral abdominal hernia, circumventing both these disadvantages¹⁰. In this paper, we trace the evolution of our new technique of laparoscopic Retro-Rectus Onlay Mesh Repair (RROM) and present a retrospective analysis of our cumulative data.

MATERIAL AND METHODS

The procedure was initially conceptualized in 2007 and gradually adopted into practice. This is a retrospective analysis of all the cases of midline ventral abdominal wall hernias operated using the RROM approach from 2007 to 2020.

Though the technique was conceptualized in 2007, initially it was only offered to highly selected patients as it was a radically new approach to laparoscopic repair of ventral abdominal wall hernias. It was only by the end of 2016 that RROM replaced IPOM as our procedure of choice and was offered to all patients. Initially, the RROM was done only for small, reducible

umbilical hernias. As our experience and confidence grew, it was offered to all ventral midline abdominal wall hernias, including incisional hernias, upto a maximum transverse defect size of 8 cms. Upto a maximum transverse defect size of 4 cms., RROM repair is done alone. For defects 4-8 cms in size, intraoperative assessment is done whether the posterior rectus sheath can be closed without tension and Transversus Abdominis Release (TAR) is added either on one or both sides as needed. Beyond 8cms defect size, usually open repair is offered. In addition to this, RROM repair was also done in patients with divarication of recti.

The main steps of the procedure are already described elsewhere¹⁰. To briefly recap the same:

(1) The patient is placed in a supine position with nasogastric tube in situ. The surgical team stands near the head of the patient on either side while the monitor is placed at the foot end of the patient.

(2) Pneumoperitoneum is created by Veres needle insertion at Palmer's point. Trocars are inserted as depicted in Fig 1.

(3) Reduction of hernia contents and adhesiolysis, if needed.

(4) Transverse incision on the posterior rectus sheaths, extending from one linea semilunaris to the other, 7 cm cranial to the cranial edge of hernia defect.

(5) Dissection of space between recti muscles and posterior rectus sheaths.

(6) Division of the posterior rectus sheath on both sides, about 2 mm from midline.

(7) Reduction or division of the hernia sac.

(8) The extent of dissection is: The median limit of the dissection is the where the posterior rectus sheath turns ventrally to form the linea alba. The lateral limit of the dissection is the point where one sees the lateral neurovascular bundles, which have to be preserved. The caudal limit of dissection is 7 cms caudal to the caudal border of the defect or the pubic symphysis, whichever is more cranial.

(9) Measurement of defect and selecting appropriately sized mesh to allow 5 cms overlap over the edges of the defect in all directions.

(10) Closure of any ventral defect, if larger than 1 cm. using 1-0 polydioxanone barbed suture running stitch.

(11) Deploying the mesh. We prefer self-fixating

polypropylene mesh (the mesh has a fine layer of barbs on one surface, which is placed facing the recti muscles). Three midline tranfixating polydioxanone sutures are placed and tied. The mesh is spread out and gently compressed against the posterior aspect of the recti muscles to enable self-fixation. There is no need for additional tackers/sutures to fix the mesh (Fig 2).

(12) The divided edges of the posterior rectus sheath are repaired using 1-0 polydioxanone barbed suture running stitch.

(13) Finally, the transverse incision in the posterior aspect of the rectus sheath is sutured using 1-0 polydioxanone barbed suture running stitch.

The nasogastric tube is removed before extubation. All patients are mobilised in four hours and liquids are started. Soft diet is commence on the next day. The patient is discharged by 24-48 hours after surgery, depending on his or her comfort level.

Patients are also given an abdominal support belt to wear.

Typically, patients are called for follow-up 7 days after surgery, and subsequently after one month and three months. Thereafter, they are advised to visit yearly or if fresh complaints develop.

For epigastric hernia, the technique is slightly different. The patient is placed in a modified lithotomy position, the surgeon stands between the legs of the patient and the camera assistant is on the right side of the patient with the monitor at the head end. Under guidance of a 5 mm laparoscope initially placed at the Palmer's point, four trocars are put in the lower quadrants as mirror image of Fig 1.

RESULTS

The laparoscopic RROM repair was done in a total of 244 patients. For the purposes of simplicity, 14 cases of epigastric hernias are included along with umbilical hernias as the technique and outcomes are identical. Between 2007 to 2016, it was done very selectively in 30 patients as the technique was

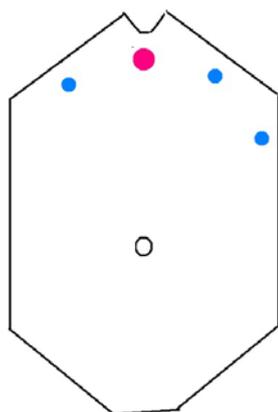


Fig 1 — Port positions



Fig 2 — Retrorectus space has been created, fascial defect closed, self-fixating mesh deployed and left half of it has been opened

finessed. The remaining 214 patients were operated between 2016 to March 2021. The distribution of cases is summarized in Table 1. Out of the 78 cases that underwent the laparoscopic RROM repair, unilateral or bilateral Transversus Aponeurosis Release (TAR) was done in 26 cases, as it was also done in 22 cases operated for divarication. The distribution of type of surgeries performed is summarized in Table 2.

Females predominated in our data, comprising 61% of our sample. While we were selective in the initial years (upto 2016) in offering this surgery to patients with BMI less than 25 kg/m², subsequently it was offered to all patients considered fit for laparoscopic repair and the data reflects this. Same holds true for other factors like Diabetes Mellitus (DM), smoking and Chronic Obstructive Pulmonary Disease (COPD). The demographic details of the sample are given in Table 3.

Concomitant surgery was performed in 23 patients (9.2%). The commonest surgery was unilateral groin hernia repair (TEP) in 12 (4.9%), followed by cholecystectomy in 8 (3.3%), bilateral groin hernia repair (TEP) in 3 (1.2%) and tubal division for family planning in 1 (0.4%) patients.

The operating time varied depending on the type of surgery as well as whether any additional surgery was performed at the same time. The data for ventral abdominal hernia repair alone is detailed in Table 4. Additional procedures increased the mean operative time by 12 minutes, 18 minutes, 22 minutes and 38 minutes for tubal division, cholecystectomy, unilateral groin hernia repair and bilateral groin hernia repairs respectively.

Out of the 244 patients, 156 patients (63.9%)

	Indication			Total
	Umbilical hernia (%)	Incisional hernia (%)	Divarication (%)	
Total	140 (57.3%)	78 (32.0%)	26 (10.7%)	244

Type of surgery	Indication			Total
	Umbilical Hernia (%)	Incisional hernia (%)	Divarication of recti (%)	
Laparoscopic RROM	140(57.4%)	52(21.3%)	4(1.6%)	196 (80.3%)
Laparoscopic RROM + TAR	0	26 (10.7%)	22 (9%)	48 (19.7%)

Parameter	Number
Total number of patients	244
Male : Female	95 : 149
Mean BMI (Range) kg/m ²	26.1 (23-42)
DM	45 (18.9%)
Smokers	19 (7.8%)
COPD	7 (2.9%)

Surgery	Operative timings in minutes (Range)
Laparoscopic RROM	74 (62-145)
Laparoscopic RROM	106 (75-176)
Laparoscopic RROM + TAR	125 (86-210)

completed at least two years follow-up. Clinical seroma was detected in 27 patients (11.1%). All the patients responded to conservative management and reassurance. Two cases developed divarication of recti in the postoperative period, one of which required surgical correction, which was done by the open conventional technique. None of the patients had chronic postoperative surgical site pain or developed recurrence or mesh infection.

DISCUSSION

Incisional hernia is the most common complication following laparotomy and is still representing a challenge to surgeons due to high recurrence rate and morbidity¹¹.

Over the last two decades, LIHR has steadily gained recognition as an alternative to open procedures because of several purported advantages, including the lower incidence of surgical-site infection¹². While the s-IPOM technique is simpler to perform, the IPOM-Plus modification, in which the fascial defect is sutured closed, is advocated by many as it seems to reduce the incidence of adverse hernia-related events including recurrence, seroma formation, and mesh bulging¹³. However, in both s-IPOM and IPOM-Plus, since the mesh is to be placed intraperitoneally, a specialized composite mesh has been used to minimize adhesions between the mesh and the intraperitoneal contents. Composite meshes are expensive. While a 15 X 15 cm composite mesh costs between 25000-32000 INR, the self-fixating polypropylene mesh that we used in most of our cases costs approximately 4500 INR.¹⁴ Additionally, the mesh is usually fixed in s-IPOM/IPOM-Plus with absorbable tackers, which cost almost as much as the mesh itself. This is not required in the RROM approach since the mesh is sandwiched between the posterior rectus sheath and the recti muscles, not requiring any additional fixation apart from the barbs built on its surface. Moreover, intraperitoneal placement of mesh leaves a foreign body inside which may have long-term consequences including delayed presentation with adhesions, bowel obstruction, fistulization and increased morbidity during subsequent explorations¹⁵. Finally, it has been found that when the mesh is placed in the retro-rectus plane (sub-lay) position, as in the RROM approach, the outcomes are superior than when the mesh is in the inlay or bridging position (s-IPOM) or underlay

position (IPOM-Plus)¹⁶.

During our initial experience, we performed only RROM approach for selective small umbilical hernias. As our experience grew, we included patients with incisional hernias without domain loss and then, with domain loss upto 8 cms. In the latter cases, we perform unilateral or bilateral Transversus Abdominis Release (TAR) as described by Novitsky *et al*¹⁷. Similar approach has also been supported for IPOM-Plus¹⁸.

Females outnumbered males in our data since almost all the incisional hernias, except two, were in female patients following either lower abdominal caesarean section or open hysterectomy. Our risk-averse selection bias was also evident in the early part of our series as far as BMI and co-morbidities like chronic obstructive pulmonary disease (COPD) were concerned. However, after 2018, we have included patients with BMI upto 42 kg/m² and those with controlled COPD as well as smokers and diabetics.

The RROM approach is also well-suited in patients developing recurrence after open repair, as is evident from the 14 (5.7%) cases in our series. Twenty-three patients (9.2%) in our series underwent concurrent surgery, with safe outcomes. This has been demonstrated to be safe by others as well in the case of s-IPOM/IPOM-Plus^{19,20}.

Seroma formation impacts negatively on patients' aesthetic outcomes and causes discomfort, pain, and/or infection. The incidence rate of seroma formation following IHR is unknown, as its presence varies significantly between series of studies²¹. The reason behind the differences in the reported incidence of seroma in various studies is the methodology of the diagnostic criteria used by different authors. In one comparative study of IPOM-Plus and sIPOM, the incidence of seroma was 5.6% vs 27.8%, but in another study, it was 11.4% versus 4.3%^{22,23}, this could indicate that the effectiveness of IPOM-Plus is questionable in terms of reducing seroma formation. We have logged in clinically detectable seroma, on examination of the patients, as recordable entity and found this to be the case in 11.1% of our cases. However, all the patients responded to conservative management and, in all the cases, complete resorption of the seroma occurred, latest by 12 weeks. Two patients in our series developed divarication of the recti in the post-operative period. This was due to iatrogenic damage to the linea alba while dividing the medial end of the posterior rectus sheath. An immediate course correction by leaving at least 2 mm of the posterior rectus sheath medially ensured that there was no recurrence of this complication.

Various other researchers have described other

endoscopic approaches to the same space and placement of the mesh in the retro-rectus plane like the e-TEP, MILOS, EMILOS, TARM²⁴⁻²⁷. However, we feel that the RROM approach is superior as it is technically easier, allows intraperitoneal adhesiolysis under vision as it is a transperitoneal approach, does not require any specialized equipment and same approach can be used for adding unilateral or bilateral TAR.

Mesh bulging, believed to be the out-pouching of the bridging portion of the mesh in s-IPOM protruding into the hernial sac as a result of intra-abdominal pressure is classified as pseudo-recurrence, but may contribute to significant patient dissatisfaction. The incidence of mesh bulging after sIPOM has been reported to be as high as 17.4%²⁸. Since both the anterior and posterior fascial defects are sutured close in the RROM approach, we did not encounter any incidence of mesh bulging in our series.

Chronic pain after hernia repair is always a significant issue after ventral hernia repair, seen in upto 39% of patients, purportedly due to the transfascial fixating sutures or tackers^{29,30}. In the RROM approach, the mesh is not fixed by any devices except by the three orienting sutures in the midline, which is essentially devoid of any nerves. It is held in place initially by the barbs on its outer surface due to its unique design. As the pneumoperitoneum is evacuated, the space collapses and the mesh is held in place between the posterior rectus sheaths and the recti muscles. Avoidance of any transfascial sutures laterally may have contributed to the absence of chronic post-operative pain in our series. Apart from the 3 in the midline. Also there is no need for fixation of the mesh with the tacker because the mesh itself is self fixating.

Our study had several limitations, including the fact that it is a retrospective review. Also, since it documents the evolution of a new technique, there was a significant learning curve involved for us as well. The operative time as well as certain complications like post-operative divarication of recti because of iatrogenic damage to the linea alba reflect this progression. Moreover, the patients were highly selective, especially in the early part of the evolution. But as we gained more experience and confidence in the technique, our case selection became much more liberal, including cases with higher BMIs, co-morbidities like diabetes mellitus and COPD, Smokers and Incisional Hernias with domain loss upto 8 cms., with comparable results.

We feel that the RROM approach truly reflects the philosophy of MAS (minimal access surgery) for the masses as it is a safe approach, giving equivalent outcomes as compared to the IPOM techniques at significantly lower costs. In our opinion, this technique

of RROM is suitable to become the gold standard in the management of ventral abdominal wall hernias. Further research in the form of direct comparison with s-IPOM/IPOM-Plus through a randomized clinical trial or a cohort study may help to establish its true worth.

Limitations of the study : This is the result from a single center, the surgeries being performed by an expert surgeon who was also the innovator of this technique. There may be a significant learning curve associated with the technique as it requires extensive intra-corporeal suturing. Moreover, lack of familiarity with the new perspective may lead the novice surgeon to damage the linea alba, resulting in postoperative dehiscence of the recti (recti diastases). Randomised controlled trials may be helpful in establishing the true worth of the technique. At the same time, cost-effectiveness studies would help to determine whether this technique is economically beneficial.

Conflict of Interest : Both the authors declare that there is no conflict of interest whatsoever.

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Original Article

Perception of Undergraduate Medical Students about the Current Medical Curriculum in India

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Introduction : Indian Medical Education System is currently on the verge of a transformation after the National Medical Commission (NMC) Bill was passed in August 2019. Objective of this study was to assess the perception of undergraduate Students about the current medical curriculum and their knowledge about NMC suggestions.

Material and Methods : A web-based cross-sectional Google forms questionnaire was distributed to medical students across India and the data gathered was analyzed.

Results : Only 54.5% of students were aware of NMC suggestions like Problem-Based Learning (PBL) and Team-Based Learning (TBL). Majority of the students felt that the present curriculum is more teacher-centric and relies on memorizing rather than concept building. They feel that traditional curriculum provides only knowledge-based learning, but not competency-based learning and should be supplemented with problem-based learning simulation technology, and research methodology. Majority of respondents prefer a combination of formative and summative assessment and want a more supervised and structured internship.

Conclusions : The NMC suggestions are welcomed as being more student-centric with inclusion of PBL/TBL, simulation training, research methodology, and a competency-based module for learning. Students also indicated their preference for a combination of formative plus summative assessments.

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Key words : Curriculum, Education, Medical, Undergraduate, Evaluation, Problem-solving, Teaching methods, Problem-based learning, Team-based learning.

The Indian Medical Education System is one of the largest in the world and is currently on the verge of transformation after the National Medical Commission (NMC) Bill was passed in August 2019. Traditionally, medical education has been a combination of didactic lectures in the classroom and hands-on training in the clinical/lab setting. This was widely perceived as the teacher-centric teaching with students acquiring knowledge passively without using their inquisitiveness and doesn't translate into empathetic practical application in the health care delivery system of India^{1,2}. Currently Undergraduate Medical Students tend to devote lots of time for preparation of Postgraduate Entrance Examinations which is completely multiple

Editor's Comment :

- Majority of the students felt that the present Curriculum is more teacher-centric, and relies on memorizing rather than concept building.
- They feel that traditional curriculum provides only knowledge-based learning, but not competency-based learning and should be supplemented with problem-based learning, simulation technology, and research methodology.
- Students also indicated their preference for a combination of formative plus summative assessments, better structured and supervised Internship and uniformity amongst different Medical Colleges.

choice question based and doesn't sync at all with the Undergraduate teaching and examination pattern³. Additionally, a widening gap was perceived between the societal health needs and the Medical Education provided. All these combined led to major reforms in the NMC bill in the form of Competency Based Undergraduate Medical Curriculum/ Education (CBMC/E)^{4,5}. Objective of this study was to assess the perception of Undergraduate students about the current medical curriculum and their knowledge about NMC suggestions.

MATERIAL AND METHODS

A web-based cross-sectional Google forms questionnaire was sent *via* WhatsApp and Email to Identified Medical Students across India. The

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questionnaire was kept open for responses from 1st February 2021 to 30th April 2021. The term 'Medical Student' here included – 1st, 2nd, 3rd Professional MBBS students and Interns. Each student was allowed to complete the questionnaire only once. All respondents were informed about the objectives of the study and consent was obtained. The questionnaire included demographic questions, qualitative questions and multiple-choice questions (Table 1). The questions featured the ability to select only one answer based on Likert's Scale (1-3, strongly disagree to strongly agree). Apart from demographics, the questionnaire focused on student's perception about the current curriculum, impact of learning methods and evaluation of students about the Internship with an intersection of background of their awareness about reforms made by NMC recently.

It was a prospective observational study without any intervention; therefore Institutional Ethics Committee waiver was not required.

The study responses were collected and managed using the Google forms electronic tool. The data analysis was done using SPSS® version 16. The categorical variables were expressed as numbers and percentages.

RESULTS

The questionnaire was sent to 700 Medical Students across India; 362 completed it, a response rate of 51.71%. The male to female ratio was 1: 1.1. The majority of the responders (56%) were in the age group of 18-20 years. The highest numbers of the respondents (51.93%) were First Professional Medical Students followed by Second Professional Students (16.57%) and the least number of responses was from the Final Year Students (12.15%). The ratio of Private and Government Medical College students was 1:1.2. Responses to questionnaire are shown in Table 1.

Awareness of NMC Guidelines, PBL and TBL was found in just over half of the respondents; and even smaller numbers felt that Current Curriculum is well framed for PBL (43%) and TBL (46%).

Only half of the students felt that the Curriculum is more teacher-centric rather than student-centric; updated as per the current needs and Medical Ethics and Behavioral Sciences are touched upon adequately. 60.22% of students feel that the curriculum encourages memorizing rather than concept building and a majority of the students (87.29%) feel that the Curriculum should be Hybrid including both didactic lectures and PBL. The majority of the students (85.64%) think that research methodology and simulation technology

should be a part of the Medical Curriculum. Only one-third of students think the Current Curriculum provides enough opportunity for competency-based learning over knowledge-based learning and there is not enough opportunity for emergency learning.

The majority of the students (61.87%) want a change in the current evaluation system used in the examination and felt that the evaluation system should be more objective. Almost half of the students (54.14%) prefer assessment by both formative and summative methods.

The majority of the students (80.66%) felt that disparities amongst colleges like infrastructure, availability of clinical material, etc affect the learning opportunities. Around 60% of students think that the Internship is poorly supervised/ structured, and adversely affects their preparation for National Eligibility-cum-Entrance Test (NEET) (Table 1).

DISCUSSION

"I never try to teach my students anything. I only try to create an environment where they can learn".

— **Albert Einstein**

Our survey revealed Undergraduate Medical Students' perceptions about their Current Curriculum and NMC bill's suggestions. Only half of them were aware of the NMC bill but majority were in favor of student-centric educational reforms like inclusion of PBL, TBL, research methodology, simulation technology and competency-based learning in their Curriculum. Similar reforms were favored by the majority for current evaluation system used in the examination (preference for more objective type questions) and Internship (preference for better structure and more supervision).

Traditional Curriculum's stagnation and dependence on 'teacher-centric' didactic teaching does not allow students to develop their personal critical decisional framework. This has resulted in majority of our respondents' dissatisfaction with the current curriculum and its inability to effectively use student-centric techniques of learning, like PBL and TBL. More structured and also more interactive teaching is the need of the hour for the current generation of medical Students⁶. It is now well-known that student-centric learning encourages better retention of knowledge, critical thinking, concept building, metacognition and collaboration and leadership skills in addition to self-evaluation and peer feedback⁷⁻⁹. However, majority of respondents agreed that tutors' didactic teachings remain important for initial knowledge-based learning and a hybrid model combining it with PBL/ TBL would

Table 1 — The summary of the responses of the questionnaire

Question	Unaware(1)		Unaware(2)		Aware (3)	
	n	%	n	%	n	%
Are you aware of new NMC guidelines? (Inclusion of foundation course, increased clinical exposure, introduction of case scenarios for classroom discussion/case-based learning, mandatory list of skills, objective assessment?)	36	9.94	132	36.46	194	53.59
Are you aware of problem-based learning (PBL, eg Case and scenario discussion)?	56	15.46	104	28.72	202	55.80
Are you aware of team based learning (TBL)? (Small group teaching methods, goal oriented, self-directed learning where teacher is a facilitator)	54	14.91	108	29.83	200	55.24
		Strongly disagree (1)		Strongly disagree (2)		Strongly agree (3)
Is UG curriculum updated as per current needs? (with respect to theoretical content, practical training and integrated teaching)	68	18.78	110	30.39	184	50.83
Is the curriculum more teacher-centric rather than student-centric?	90	24.86	92	25.41	180	49.72
Are medical ethics and behavioural sciences (soft skills) touched upon adequately?	88	24.31	80	22.10	194	53.59
Is the curriculum more for memorizing rather than concept building?	58	16.02	86	23.76	218	60.22
Is it well framed for group learning (group discussion and activities)?	106	29.28	88	24.31	168	46.41
Is the current curriculum well framed for problem-based learning?	98	27.07	108	29.83	156	43.09
Does the current curriculum provide enough opportunity for competency-based learning over knowledge-based learning?	112	30.94	114	31.49	136	37.57
Does the current curriculum provide enough opportunity for emergency learning?	160	44.20	90	24.86	110	30.39
Do you think simulated patients and simulation technology should be a part of the medical curriculum?	8	2.21	44	12.15	310	85.64
Do you think research methodology should be included in the curriculum for teaching and application?	20	5.52	72	19.89	270	74.59
Are you satisfied with the current evaluation system used in examination (Theory, internal assessment, external assessment (long, short cases, table viva)?	108	29.83	116	32.04	138	38.12
Is there a need to restructure the current evaluation system with reference to CBT, objective assessment, OSCE-objective structured clinical exams?	40	11.05	98	27.09	224	61.88
Do you think disparities amongst colleges like infrastructure, communication opportunities, public dealing, availability of clinical material, etc affect the learning opportunities?	14	3.87	56	15.47	292	80.66
Do you think internship is poorly supervised and structured, and need reforms?	20	5.52	118	32.60	224	61.88
Do you think involvement in internship adversely affect your preparation for NEET?	60	16.57	84	23.20	218	60.22
How do you think the curriculum should be?		Didactic lecture-based		Problem-based learning		Hybrid
	4	1.10	42	11.60	316	87.29
Which form of assessment you would prefer?		Formative		Summative		Both
	92	25.41	74	20.44	196	54.14

give the best results for competency-based learning¹⁰. Similarly, combining the best of PBL and TBL can optimize student learning; as both are complimentary^{11,12}.

The importance of sowing the seeds of Ethics in Undergraduate Medical Education to create 'Good Virtuous Doctors' is well known. NMC's suggestions on teaching students how to apply ethical knowledge and critical thinking to real cases in clinical practice and shaping future doctors' right character is a great idea and ~ 50% of respondents favored more focus on this issue¹³. Similarly, importance of including Behavioral Sciences in their curriculum is appreciated by the respondents. Medicine was, is and will remain a 'Social' Science and pride of place of applied Social Science in Medicine is now axiomatic¹⁴.

Incorporation of research methodology in curriculum, as desired by ~86% respondents, is known to have positive learning experiences. These include Ethics, Evidence Based Medicine; Protocol Writing; Data Processing; Dissemination of findings and Results; and their use in informing a health promotion intervention¹⁵. A similar number favored the use of simulation in their curriculum. Simulation bridges the gap between theory and practice, provides realistic standardized experiences

to learners in a controlled environment without exposing patients to harm and technological advances can enhance traditional basic science content¹⁶. Several low-cost solutions are available or can be improvised and these can open up an entirely new World of Learning to the Medical Student of the 21st century¹⁷.

Evaluation system used in the examination is a matter of concern and ~62% students are in favor of more objective system. Evidence shows that multiple choice questions and short answer questions correlate better with the clinical performance of students than multiple essay questions¹⁸⁻²⁰. However, a middle path of a combination of formative and summative evaluation was preferred by ~54% students.

Students are aware that the Internship period, if not used productively, is a missed opportunity; hence a majority of them want a better structured and Supervised Internship. This sentiment is in sync with evidence showing that clear objectives, self-directed learning and regular feedback will have a positive impact on this transition of Medical Student to a Full-Fledged Doctor with better understanding of tackling Emergency Situations²¹⁻²⁴.

Every teaching technique, ideally, incorporates a feedback but having sought this feedback now the onus of changing according to NMC's reforms and these feedbacks is on the teachers. It must be remembered that all benefits of reforms like PBL, TBL, multiple choice questions etc. will depend upon developing and implementing appropriate user-friendly coursework and questions; a task which has been effectively performed by the teachers²⁵⁻²⁷. Additionally, NMC has to ensure mitigation of disparities amongst different medical colleges like infrastructure, availability of clinical material etc. which affect the quality of learning opportunities.

Limitations of our study include a relatively small number of responses and a majority of respondents being students from the first professional. The later might be the reason of relatively low awareness of NMC's reforms. The other limitation of the study is that assessors were not sure about students were familiar with the pedagogic terms such as Formative", "Summative", "Simulation Technology", and "research methodology. More senior students and interns were, apparently, preoccupied with busier schedule of online teachings and COVID duties respectively. Another shortcoming is absence of questions on two examinations: the current National Eligibility-cum-Entrance Test for Postgraduation and the proposed National Exit Test, common final year undergraduate

Medical Examination. Both these questions were excluded because of inherent difficulties in analyzing qualitative responses to open ended questions like these in an online survey. However, ours is the first study of its kind which has sought such a feedback form undergraduate Medical Students on two important topics like current Curriculum and NMC's suggested reforms. It shows the way forward to realize the full potential of Undergraduate Medical Curriculum in India.

CONCLUSIONS

More student-centric approach with inclusion of PBL/TBL, simulation training, research methodology, and a competency-based module for learning should be applied. Students also indicated their preference for a combination of formative plus summative assessments.

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Original Article

Analysis of Hematological and Biochemical Parameters as Diagnostic Test for Malaria in Patient with Acute Febrile Illness

Deepti Sharma¹, Avdhesh Singh Solanki², Mirdulata Prajapati³

Introduction : Malaria is one of the important causes of Febrile Illness in the World. We analysed the Hematological and Biochemical parameters in patients of Acute Febrile Illness.

Material and Methods : This study was carried out at GMC Kota, Rajasthan in Department of General Medicine. We included 200 patients of Acute Febrile Illness from April, 2018 to January 2020. Diagnosis of malaria was confirmed by both thin and thick film smear. Hematological and Biochemical parameters were done in all patients.

Results : Total 200 patients were included in which 100 were Malaria negative and 100 were malaria positive cases in which P Vivax (55%) were more than P falciparum (38%), 7% of cases were positive for both. Anaemia was present in 69% of cases, Leukopenia in 26% of cases, Thrombocytopenia in 78% of cases, Hyperbilirubinemia in 74% of cases, SGOT was raised in 70% of cases, SGPT was also raised in 62% of cases, S LDH was increased in 86% of cases, RDW-CV was increased in 28% of cases.

Conclusion : Our study indicate that Anaemia, Leukopenia, Thrombocytopenia, increased S LDH, Hyperbilirubinemia, SGOT/SGPT >1.5 and RDW-CV may be useful tool in diagnosis of Malaria.

[J Indian Med Assoc 2021; 119(9): 32-4]

Key words : Malaria, Hematological, Biochemical, Febrile illness.

Malaria is a protozoan disease transmitted by bite of infected female Anopheles mosquitoes. It is transmitted in 91 countries containing 3 billion people and causes approximately 1200 death each day¹. Six species of genus plasmodium cause nearly all malarial infection these are P falciparum, P vivax, 2-morphological identical species of P.ovale, P malariae & in Southeast Asia Monkey Malaria parasite P knowlesi². The clinical diagnosis of Malaria is challenging because of non-specific nature of signs & symptoms, which overlaps considerably with other Febrile Illnesses common in Tropical region. Hematological and Biochemical changes enable the Clinician to establish an effective & early therapeutic intervention in order to prevent the occurrence of major complications. Hematological abnormalities that have been reported to invariably accompany with Malaria infection include –Anaemia, Leukopenia and Leukocytosis (In some cases) and Thrombocytopenia³.

Common Biochemical alterations are-Hyperbilirubinemia, increased level of SGOT, SGPT and S LDH.

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Editor's Comment :

- Hematological and Biochemical Parameters help us to diagnose malaria in endemic zone.
- Anaemia, Thrombocytopenia, SGOT>SGPT & Indirect bilirubin > Direct bilirubin are the Indirect evidence for Starting anti-malarial treatment.

So the present study was carried out to analyse and statistically evaluate Hematological and Biochemical changes in patient of acute febrile illness with Malaria positive and Malaria negative report and wheather they could guide Physician to institute specific Anti-malarial Treatment.

MATERIAL AND METHODS

Our study was carried out on patients admitted with Acute Febrile Illness in the Department of General Medicine, GMC Kota, Rajasthan from April 2018 to January 2020. Total 200 patients were included in which 100 were Malaria positive and 100 were malaria negative. Written consent was taken for all patients to participate in the study. Hematological and biochemical investigations were done for all patients. Diagnosis of Malaria was confirmed by both thin and thick blood smear.

RESULTS

In Malaria positive (case) group females (56%) were more than males (44%) whereas in Malaria negative [control] group male > female ie, 54% & 46%. Most commonly involved age group was 18-30 years in both case & control group. Anaemia was seen in 69% of

cases & 55% of controls Leukopenia in 26% of cases and 4% of controls, Thrombocytopenia in 78% of cases and 35% of controls, Hyperbilirubinemia in 74% of cases and 59% of controls, indirect bilirubin was more than direct bilirubin, SGOT was raised in 70% of cases and 50% of controls, SGPT was raised in 62% of cases and 51% of controls, SGOT was more raised than SGPT, S LDH was raised in 86% of cases and 65% of controls, RDW-CV was raised in 28% of cases and 10% of controls, Splenomegaly was seen in 50% of cases and 15% of controls, Hepatosplenomegaly in 9% of cases and 2% of controls. Most common associated symptom with fever in case group was chills and rigors- in 64% of cases, vomiting in 58% of cases, headache in 44% of cases. 55% cases were positive for *P vivax*, 38% cases for *P falciparum* and 7% cases for both.

Parameters	Cases (%)	Controls (%)
Anaemia	69%	55%
Leukopenia	26%	4%
Thrombocytopenia	78%	35%
Raised Total Bilirubin	74%	59%
Raised Direct Bilirubin	72%	54%
Raised Ind. Bilirubin	60%	36%
Raised SGOT	70%	50%
Raised SGPT	62%	51%
Raised S LDH	86%	65%
Raised RDW-CV	28%	10%
Chills and Rigors	64%	58%
Vomiting	58%	60%
Headache	44%	16%
Unconsciousness	18%	12%
Splenomegaly	50%	15%
Hepatosplenomegaly	9%	2%
<i>P vivax</i> positive	55%	-
<i>P falciparum</i> positive	38%	-
Both positive	7%	-

DISCUSSION

In our study females were more in number than males ie, 56% females & 44% male. Our study correlates with Ashwini Kumar Nigam *et al*⁴ who found 52% females and 48% males.

In our study maximum number of positive cases were in the age range of 18-30 years ie, 48%. Similar results were found in the study done by Prashant Khurayia *et al*⁵ with 43% cases in this age range.

Mean Hemoglobin level of case group was 9.90±2.96 gm/dl and of control group was 10.33±2.09 gm/dl and the difference was statistically non-significant (p-value 0.23). Similar results were found in the study done by Mohammed Al-Salahy *et al*⁶ with

mean Hemoglobin level of case group & control group was 9.4±0.28gm/dl and 10.02±0.42 gm/dl and the difference was statistically non-significant with p-value 0.082.

Mean TLC of the case group was 7.14±4.49 and of control group was 9.03±3.26 and the difference was statistically significant with p-value of 0.0008. Similar results were seen in study of Zeeba Shamim Jairajpuri *et al*⁷ with mean TLC 4.9±2.62 in case group and 7.1±3.6 in control group with significant p-value of 0.001.

Mean platelet count of case group was 126.98±105.05 (10³/cu mm) and of control group was 186.65±71.31 (10³/cu mm) and the difference was statistically significant with p-value of 0.0001. Similar results were found by Mohamed Al-Salahy *et al*⁶, with mean platelet count 116.6±7.03 and 353.4±18.72 in case and control group respectively and the difference was statistically significant with p-value of 0.0001.

Mean Total bilirubin of case group was 2.23±2.51 mg% and of control group was 1.57±0.96 mg% and the difference was statistically significant with p-value of 0.01. Our study correlates with Sudha Jha *et al*⁸, who found mean Total bilirubin of case group 1.63±2.27 mg% and of control group 0.67±0.08 mg% and this difference was statistically significant (p-value 0.001).

Mean direct bilirubin level of case group was 0.89±1.14 mg% and of control group was 0.49±0.47 mg% and the difference was statistically significant with p-value of 0.001. Similar results were found by Gagan Deep *et al*⁹ with Mean direct bilirubin level of 0.48±0.43 mg% in case group and 0.13±0.031 mg% in control group with significant p-value of 0.0001.

Mean indirect bilirubin level in case group was 1.24±1.45 mg% and of control group was 1.08±0.77 mg% but the difference was statistically non-significant with p-value of 0.11. Similar results were found by Ratendra Bisht *et al*¹⁰ who found Mean indirect bilirubin level in case group 1.65±2.67mg%.

Mean SGOT level of case group was 81.05±75.91 (IU/L) and of control group was 64.84±43.32 [IU/L] but difference was statistically non-significant with the p-value of 0.06. Similar results were found by Rajesh Deshwal *et al*¹¹, who found Mean SGOT level 83.92±43.71IU/L.

Mean SGPT level of case group was 65.35±64.18 (IU/L) and of control group was 51.67±32.70 (IU/L) and the difference was statistically significant with the p-value of 0.05. Similar results were found by Dr T Anil Kumar *et al*¹² who found Mean SGPT level 64.4±2.6 IU/L in case group and 18.2±1.3 IU/L in control group with significant p-value of 0.05.

Mean of SGOT was more than Mean of SGPT in case group as well as in control group.

Mean S LDH level of case group was 1196.3 ± 994.34 (IU/L) and of control group was 832.77 ± 489.73 (IU/L) and the difference was statistically significant with the p-value of 0.001. Similar results were found by Mohammad Ali Pir *et al*¹³ who found Mean S.LDH 1276.41 ± 263.2 IU/L in case group and 266.06 ± 22.5 IU/L with statistically significant p-value of 0.0001.

Mean RDW-CV of case group was $16.37 \pm 3.97\%$ and of control group was $14.33 \pm 1.38\%$ and difference was statistically significant with p-value of 0.0001. Only one such type study was found which was done by Zeeba Shamim Jairajpuri *et al*⁷ with Mean RDW-CV of case group $16.4 \pm 4\%$ and of control group $15.2 \pm 1.23\%$ and difference was statistically significant with p-value of 0.001.

USG findings were as- splenomegaly in 50% cases and in 15% controls, Hepato- splenomegaly in 9% cases and in 2% controls. Our study correlates with study done by Ashwini Kumar Nigam *et al*⁴ who found USG findings as- splenomegaly in 52% cases and in 14% controls, Hepatosplenomegaly in 7% cases and in 4% controls.

Fever was present in 100% of cases and controls, chills & rigors in 64% cases and in 58% controls, vomiting in 58% cases and in 60% controls, headache in 44% cases and in 16% controls, unconsciousness in 18% cases and in 12% controls. Our study well correlates with study done by Ketaki Motram Surve *et al*¹⁴ who found fever in 100% of cases, chills & rigors in 52% cases and in 46% controls, vomiting in 51% cases and in 49% controls, headache in 36% cases and in 22% controls, unconsciousness in 15% cases and in 6% controls. 55% cases were positive for P vivax, 38% cases for P falciparum and 7% cases for both. Similar results were found by Dr Kalavathi GP *et al*¹⁵ who found 57.14% cases positive for P vivax, 37.14% cases for P falciparum and 5.72% cases for both.

CONCLUSION

Overall the Hematological and Biochemical aspects of Malaria constitute a very interesting area. We observed that Hematological changes such as Anaemia, Leukopenia, Thrombocytopenia and Red Cell Distribution Width, Biochemical changes like-Hyperbilirubinemia, indirect bilirubin more than direct

bilirubin, SGOT/SGPT ratio >1 (almost 1.5 time), Raised S LDH level & splenomegaly showed a statistically significant correlation with malarial infection. So these parameters can provide a diagnostic clue in a patient with acute Febrile illness in Malaria endemic areas thus increasing the probability of correctly diagnosing malaria and enhancing prompt initiation of Anti-malarial treatment. Because of limitation of resources and trained health personnel in much of the Malaria infested areas, presumptive clinical diagnosis seems a relevant option.

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Original Article

The Utility of Transient Elastography (Fibro-Scan) as an Indicator of Hepatic Iron Overload in Transfusion Dependent Thalassemia Patients (TDT) from a Tertiary Care Hospital from Eastern India

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Background : Progressive iron overload leads to liver fibrosis is a well-known complication in TDT patients. This study was done to evaluate the liver iron load in correlation to Serum Ferritin. This is not a new endeavor however there we tried to see the effect of other factors besides iron overload in the progression of liver fibrosis with a non-invasive test.

Material and methods : A retrospective cross-sectional study from December 2018-December 2019 on sixty (n=60) transfusion dependent thalassemia patients who were on regular iron chelation underwent liver function and Serum Ferritin by the automated analyzer and liver stiffness measured by transient elastography. The severity of fibrosis by TE is graded as ≤ 7.9 kPa; Significant (F2) >7.9 - 10.3 kPa; Severe (F3) >10.3 - 12.0 kPa; cirrhosis (F4) >12.0 kPa as per previous studies.

Results : Out of a total of 60 TDT patients with primary diagnosis Hb E- β thalassemia, median age 15 years (11-25 years), mean transfusion requirement 12.9 ± 3.68 Units/year and median ferritin was 1933ng/ml. There were 13 patients with anti-HCV positive, two were HIV Seropositive and one Hepatitis B Positive. On fibroscan, there were 43.34%(n=26), 13.34%(n=8), 6.66%(n=4), 36.66%(n=22), patients with Mild, Significant, Severe and Cirrhosis Fibrosis respectively. The correlation between the grade of fibrosis and ferritin level was found to be statistically insignificant. Out of 13 HCV Seropositive, 7(53.8%) were found to have liver stiffness of >12.0 kPa (cirrhosis), with a median ferritin value of 2291ng/ml.

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Key words : Fibroscan, Ferritin, Liver Stiffness, Thalassemia.

The Transfusion Dependent Thalassemia (TDT) patient requires a regular blood transfusion for growth and survival from a very early age. With regular blood transfusion and ineffective erythropoiesis, there is the gradual and continuous iron accumulation in TDT patients at a rate of approximately 0.3-0.6 mg/Kg/day¹. As human lacks the efficient mechanism to excrete excess iron, the management of iron overload requires regular Chelation Therapy to remove excess iron². The

Editor's Comment :

- Fibroscan is a non-invasive test to detect liver stiffness.
- Iron overload is common in TDT patients and the major brunt of injury is in the liver.
- Monitoring of serial serum ferritin level along with fibro scan (TE) might help us to diagnose the early stage of liver fibrosis.
- The correlation between the grade of fibrosis and ferritin level was found to be statistically insignificant in our study.
- HCV seropositive patients have higher liver stiffness at their corresponding serum ferritin levels.

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Serum Ferritin concentration is the most commonly used test to estimate iron overload in TDT patient³. The quantification of Liver iron by using Liver Biopsy (LIC) is still the gold standard to diagnose iron overload which is an invasive and painful procedure. Magnetic Resonance Imaging (MRI) using R2 or T2* techniques is another non-invasive and accurate evaluation of liver iron overload but it is not cost-effective and also not universally available⁴. Transient Elastography (Fibroscan) is used for the assessment of Liver Stiffness in patients with chronic liver disease. It is non-invasive, can be performed in the out-patient clinic with immediate results and good reproducibility⁵. Here we tried to see the correlation of Liver Stiffness with Serum Ferritin Levels in transfusion dependent

Thalassemia patients in the tertiary centre of Eastern India.

MATERIAL AND METHODS

Design : This is a cross-sectional, single centre, retrospective study conducted at Nil Ratan Sircar Medical College and hospital, Kolkata, in the period from December 2018 and December 2019. Ethical clearance for the study was taken from the Institutional Ethical Committee. Informed and written consent was taken from all the patients/guardians, after discussing in his/her language.

Patients : A total of sixty (n=60) Transfusion Dependent Thalassemia patients were enrolled, who were on regular blood transfusion support and attendees of the Thalassemia Clinic of our tertiary centre. All patients were diagnosed with high performance Liquid Chromatography (Bio Rad Variant III) and mutation study (if required). There were fifty-eight (n=58) Hb E-Beta Thalassemia and two (n=2) Beta Thalassemia patients. All patients were on regular blood transfusion within 5 years of life at intervals of 3-5 weeks with pre transfusion Hb kept as ≥ 9 gm/dl. Patients enrolled were on regular iron chelators once Serum Ferritin increased >1000 ng/ml.

Inclusion Criteria : All the TDT patients ≤ 10 years of age who were on regular iron chelation

Exclusion criteria : Patients with decompensated Cardiac Insufficiency, Chronic Kidney Disease Decompensated Liver Cirrhosis, pregnancy, and age younger than 10 years were excluded from the study.

Evaluation : All the included patients were subjected to thorough history taking and complete clinical examination with a series of investigations that are routinely performed, including Complete Blood Counts, Liver Function Tests; Hepatitis B Surface Antigen, Circulating Anti-HCV Antibodies, were tested using Enzyme Immunoassay Kits. Patients who were sero-reactive for anti HCV were undergone HCV RNA levels using RT PCR.

All the patients recruited were subjected to:

(1) **Serum Ferritin Level** determined using standard Laboratory Standards, using an Access Ferritin Kit in the Chemiluminescence Immunoassay analyzer (Beckman Coulter Access2). An average of two Ferritin levels of a patient was taken for analysis.

(2) **Transient Elastography** (Fibroscan) was carried out by experienced examiner in all patients, within the same week of Ferritin estimation. Liver Stiffness measurement Fibroscan (Echosens fibroscan 430 mini) was based on one dimensional TE that uses both ultrasound (5MHz) and low-frequency (50 Hz)

elastic waves. Liver Stiffness results were expressed in kilopascal (kPa) by the software.

The severity of Fibrosis by TE is graded as ≤ 7.9 kPa; Significant (F2) $>7.9-10.3$ kPa; Severe (F3) $>10.3-12.0$ kPa; Cirrhosis (F4) >12.0 kPa as per previous studies⁶.

Statistical analysis : The data was entered in MS EXCEL spread sheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. The patient's background characteristics and laboratory investigation data were expressed as mean and SD. Qualitative variables were correlated using the Chi-Square test and quantitative variables were compared using the t-test. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 60 TDT patients were enrolled in the study during the period December 2018-December 2019. The median age of the patients in the study was 15 years (11-25 years) with the male predominance (M: F-1.5:1). The median age of the receiving first blood transfusion was 2.5 years and the mean transfusion requirement in the cohort was 12.9 units per year. All patients were on regular iron chelators as per standard Guidelines¹. There were 13 (21.67%) patients who were HCV seropositive and 2 (3.34%) patients were HIV seropositive and were on treatment as per the standard care. Table 1 shows the clinical characteristics of all the patients. The mean Serum Ferritin level was 2174 ng/ml with an SD of 897.2 ng/ml (IQR = 1595.1-2557.7 ng/ml).

On Fibroscan, there were 26 (43.34%), 08(13.34%), 04(6.66%) and 22(36.66%) patients with Mild, Significant, Severe and Cirrhosis fibrosis grade respectively.

The significant fibrosis grade (F2-3) were seen in 12(20%) of patients while cirrhotic (F4) was seen in 22(36.66%) of patients. There were 26 patients

Table 1 — Various clinical characteristics

Characteristics	Results
Age in years (mean \pm SD)	15.4 \pm 4.65 years
Median age in years	15 (6-25) years
Gender	
Male (%)	60 %
Female (%)	40%
Age of first transfusion (mean \pm SD)	3.35 \pm 2.97 years
Median age of the first transfusion (years)	2.5 years
Transfusion requirement Units/year (Mean \pm SD)	12.9 \pm 3.68 Units/year
Serum Ferritin ng/ml (mean \pm SD)	2174.138 \pm 897.2 ng/ml
Anti HCV seropositive (%)	13 (21.67%)
HBsAg positive (%)	1 (1.67 %)
HIV seropositive (%)	2 (3.34%)

(43.34%), who were having mild/no fibrosis as assessed by TE. The mean±SD Ferritin level between the different grade of Fibrosis mild (F1), moderate (F2), severe (F3) and cirrhotic (F4) were 1910.8±677.8 ng/ml, 2069.42±610.2 ng/ml, 1865.9±652.9 ng/ml, 2443.1±930.4 ng/ml respectively. Tables 2 & 3 Summarizes the distribution of various grades of liver stiffness with mean Ferritin levels. The correlation (r=0.08) between Ferritin levels and the grade of fibrosis were statistically insignificant (p-value >0.05).

Out of 13 HCV seropositive, 7 were found to have Fibro Scan of >12.0PKa (cirrhosis), with the mean ferritin level of 2443.1±930.4 ng/ml and 3 out of 13 (23.07%) patients had the mild grade of Fibrosis with a mean Ferritin level of 2013.5±1009 ng/ml. There was a statistically insignificant difference (p-value>0.05) between mean Ferritin levels and Fibrosis grades (r=-0.2) in HCV sero-reactive TDT patients in the study.

In two groups HCV reactive and HCV free group there was no significant difference in the mean Ferritin levels (p-value >0.05) or mean Liver Stiffness was seen between two groups (p-value >0.05) (Table 4).

Fig 1 shows the linear regression graph of Ferritin levels (ng/ml) with respective TE value in TDT patients with concurrent HCV seropositivity.

DISCUSSION

Iron overload and its consequences are the main concern in the management of TDT patients, requiring frequent monitoring and timely intervention to prevent irreversible damage to the Liver and other organs of the body. Our study was an attempt to analyse the iron overload state in TDT patients as there is limited

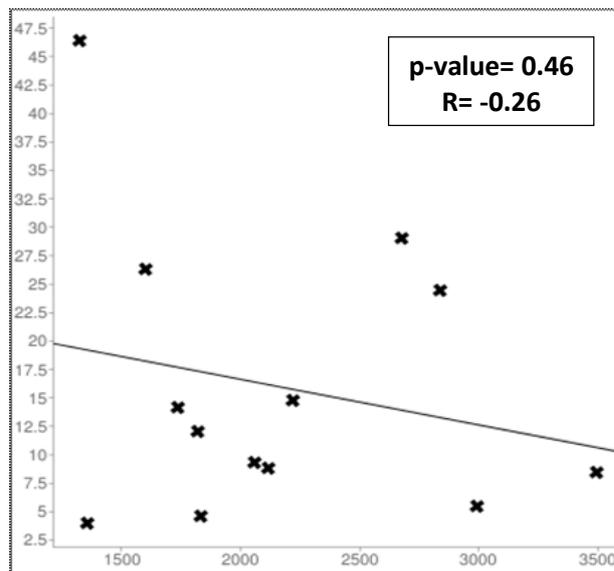


Fig 1 — Linear regression curve between mean serum ferritin levels and fibrosis grade (Pka) in HCV seropositive TDT patients

data regarding hepatic iron overload in Hb-E beta-thalassemia from the Eastern part of India⁷. The median age in our study cohort was 15 years (11-25 years) almost equivalent to that in other studies^{8,9}. There was a male predominance in our study with M:F-1.5:1 which might not represent the general population because of small sample size¹⁰, however it didn't found to influence the iron overload status as main factors involved in liver iron overload in TDT patients is regular blood transfusion with ineffective Erythropoiesis¹¹.

In our study, the mean Liver Stiffness Measurements (LSM) was found significantly increase with 22(36.66%) of patients having LSM >12Kpa and 34 (56.66%) patients showed LSMs >7.9 kPa, which is a cut-off value for significant fibrosis¹².

There is a definite higher risk of HCV infection due to repeated blood transfusion in TDT patients.

In our study, there is a statistically significant in the mean LSM in HCV infected and HCV free TDT patients 15.99Kpa and 10.62Kpa respectively, however, mean ferritin of 2158.36ng/ml and 2086.52 ng/ml statistically insignificant (Table 4). In the series of Di Marco, *et al* the TM patients free of HCV infection showed a mean LSM of 5.2 kPa in Thalassemia major patients and found in their study that Liver Stiffness is proportional to liver fibrosis and not on Liver Iron status¹³.

No statistically significant difference in LSM score between HCV infected and HCV free TDT patients (p value->0.05) or with different Serum Ferritin levels were

Table 2 — Distribution of TE grading and Ferritin Levels

Characteristics	F1 (≤7.9Kpa)	F2 (>7.9-10.3Kpa)	F3 (>10.3-12 Kpa)	F4 (>12Kpa)
No of patients	26	8	4	22
Patients (%)	43.34 %	13.34 %	6.66 %	36.66 %
Median ferritin (ng/ml)	1843.96	1925.01	2022.46	2291.96
Mean ferritin±SD (ng/ml)	1910.8±677.8	2069.42±610.2	1865.9±652.9	2443.1±930.4
HCV Seropositive	3	3	0	7

Table 3 — Different Ferritin levels and LSM score

Ferritin Level (ng/ml)	No of Patients (%) (n)	Mean LSM score (Pka)
>1000-≤2000	33 (55%)	10.66
>2000-≤3000	20 (33.34%)	11.8
>3000	07 (11.66%)	17.58

Table 4 — Mean serum Ferritin Levels and LSM score in HCV infected and HCV free

	HCV Infected (n=13)	HCV Free (n=44)	p-value
Ferritin Level	2158.36ng/ml	2086.52 ng/ml	>0.05
Mean LSM score (pka)	15.99	10.62	

found in these two groups (Table 4), indicating that Liver Stiffness is independent of iron overload¹³.

Assessment of Liver Fibrosis stage and LIC in TDT patients is most crucial for the long-term prediction of liver-related adverse outcomes. Although Liver Biopsy remains the gold standard in assessing hepatic injury^{14,15} the Coagulopathy associated or the concomitant HCV infection, biopsy related complications can be problematic. These and several previous studies¹⁶⁻¹⁸ had shown that TE has promising results as the non-invasive diagnostic tool with moderate to high accuracy for the assessment of Liver Fibrosis in HCV-infected and HCV free TDT patients.

This study is unique in providing data on the utility of TE in assessing Liver Stiffness in TDT patients of the Eastern part of India.

Limitations of our Study :

The limitations of our study include being a cross-sectional study with a small sample size influence of other factors on the Liver Stiffness cannot be ascertained. Secondly, we did not compare the results of the non-invasive assessment of Liver Fibrosis to the gold standard (liver biopsy). Therefore, a prospective study with a large number of TDT patients and especially on paediatric patients (<10years) is required to understand the utility and effectiveness of TE as a diagnostic tool for the early diagnosis of hepatic iron load and its related longterm adverse outcomes.

Conclusion :

Iron overload is common in TDT patients and the major brunt of injury is in the liver. Fibroscan is a non-invasive test to detect liver stiffness. Monitoring of serial serum ferritin level along with Fibro Scan (TE) might help us to diagnose the early stage of liver fibrosis. HCV Seropositive patients were found to have higher liver stiffness at their corresponding Serum Ferritin levels. The correlation between the grade of fibrosis and ferritin level was found to be statistically insignificant in our study because of smaller sample size.

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— Hony Editor

Review Article

Unified by COVID-19 : Healthcare Lessons Learned from USA, China and India

Mitali Sengupta¹, Arijit Roy², S B Raha³, Satyajit Chakrabarti⁴, Indraneel Mukhopadhyay⁵

Healthcare disparities and delivery system limitations create health inequities. They constantly challenge the conventional healthcare models across the globe. With the healthcare fallouts surrounding the recent COVID-19 pandemic, most countries worldwide have borne the brunt.

To understand the healthcare policies and practices in the light of COVID-19 situation, three countries representing high income, upper middle and lower middle income as per World Bank classification have been studied and their fiscal reforms, policy changes and effective response strategies are analyzed.

Though the healthcare economics of USA, China and India are distinct and divergent, yet the issues and challenges surrounding health and sociological perspectives have significant common ground for further analysis. This paper plausibly analyzes the existing healthcare expenditure, policies and practices of USA, China and India in combating COVID-19 pandemic.

While it is impossible to design a single global comprehensive model to cater to the whole world, collaborative efforts would lead to enhanced resources utilization in public health efforts, revamping economy, care of the vulnerable, regional and global cooperation to fight the menace of not only the current pandemic but also in future.

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Key words : Healthcare, Expenditure, COVID- 19 pandemic, USA, China, India.

Health and wellbeing are the key pillars of a sustainable nation. There is a strong relationship between health and social development. Poor health is a concomitant force for under-development and poverty¹.

The healthcare inequities are diverse, multi-factorial and complex that challenge healthcare personnel, policymakers and experts. Common factors include healthcare accessibility issues, physician scarcity, treatment modalities and outcome disparities across varied community settings². These differences are largely due to key drivers associated with healthcare costs, access and availability of healthcare services. The situation is aggravated by catastrophic Out Of Pocket (OOP) expenditure and limited availability of emergency services³.

Current challenges surrounding COVID-19 has unified the entire world. Every country irrespective of

Editor's Comment :

- Healthcare is a multifactorial, complex process involving financial, technical, administrative and geopolitical factors which varies across countries and their economical capacities.
- COVID-19 pandemic unified nations and tested the health capacities of USA, India and China across different parameters.
- Urgent Need to relook and shape public health policies, infrastructure and capital inflow into healthcare.
- Learning from the past and implementing for the future. Convergence of technical know-how, local and global cooperation, sustaining economy and preparing for resurgent future.

its financial power or demography is fighting against COVID-19 pandemic. International lockdown and sealing of national borders have been in place to curb this global menace. Every nation is working with their knowledge, resources and experience to deal with the situation, yet the trend of positive cases is on the rise and mortality ratios have increased manifold. One major limitation is the inability of conventional vaccines to specifically treat COVID-19. A few vaccines have been developed recently after clinical trials though their efficacy is under review⁴.

This paper has attempted to address the healthcare dynamics in the following manner. The initial sections highlight the conventional healthcare policies and practices of the three representative countries - USA, China and India belonging to high income, upper middle

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and lower middle income nations⁶. The health practices and COVID-19 associated expenditure have been analyzed and strategies for possible mitigation of such crises in future have also been recommended.

Healthcare expenditure, Policies and Practices- USA, China and India :

The healthcare policies and practices are unique and tailored for the population they serve. A brief discussion of each is as follows. Table 1 highlights the healthcare statistics for the different countries.

USA

The US healthcare system follow a mixed approach with approximately 92% of population having some coverage and nearly 8% without any insurance (2019)⁶. Apart from Medicare and Medicaid, employer sponsored insurance also cover a significant proportion and two third of Medicaid beneficiaries are part of organizations with managed care⁷. The Affordable Care Act (2010) has seen significant Government financing in healthcare with enhanced coverage worth 20 million⁸. Public spending, in 2017, have accounted for 45% of healthcare spending with 8% GDP and about 28% is represented by federal spending. Children Health Insurance Programs (CHIP) are funded by federal government to states and many states charge premiums for the same⁹.

In 2019, private healthcare insurance accounted for about one third of total healthcare expenditure. Approximately 68% of Americans had private health insurance while 34.1% had public health insurance⁶. Majority of this is employer sponsored (55.4%) while a minor population (11%) opted for profit or non-profit providers. It has been reported that the healthcare costs borne by regular households is similar in proportion to that of the Federal Government (2018:28%). 10% of the total healthcare expenditure

is Out Of Pocket (OOP), approximately 40% is invested towards dental care and about 14% on medicines¹⁰.

An important feature of the US healthcare system is the provision to obtain care during emergency where hospitals are required to provide treatment irrespective of their paying capabilities or insurance status, race and/or origin. Eventually, a lot of expense in healthcare is borne by private health establishments that remain uncompensated or turn charitable.

CHINA

The Chinese healthcare reforms aimed to establish universal healthcare system that is safe, convenient, effective and affordable for everyone. The basic medical insurance system covers about 95% of the total Chinese population. The national healthcare security administration was established in 2018 for managing different medical insurance programs¹¹. China spent 6.6% GDP on healthcare, 28% financed by local and Central Government, 44% public or private insurance and social donations and 28% is financed through Out Of Pocket (OOP)¹².

The healthcare costs and associated payments are linked to different insurance types that are owned by the patients. Those, that have other corporate medical insurance or commercial plans, the bill amount paid by the patients normally vary as per the coverage of the healthcare options within their medical insurance. For rural and urban areas, any catastrophic healthcare expenditure that cannot be borne by individuals through insurance or Out Of Pocket (OOP) are partly covered by social donations and local government.

Another novel initiative 'Healthy China 2030 plan' aims to deal with conventional diseases and accessibility issues for ageing population¹³. This plan emphasized on lifestyle improvement, health service options and sustainable growth of health industry with doorstep healthcare delivery provisions by year 2020.

INDIA

The Indian constitution obliges 'Right to health' for every citizen. Being a part of universal healthcare coverage, Government health services are free. Unfortunately, the public hospitals across the country are severely underfunded. Numerous healthcare programs in the past attempted to reduce this burden of catastrophic health expenditure, especially for people belonging to

Table 1 — Health Care expenditure of USA, China and India			
Population and health care statistics of USA, China and India			
	USA	China	India
Total population (2018)	327,167,434	1,393,000,000	1,325,000,000
Gross national income per capita (PPP international \$, 2018)	63,690	18,170	7,680
Life expectancy at birth total (years, 2017)	78.539	76.47	69.165
Current health expenditure per capita, PPP (current international \$) (2017)	10,246.139	841.115	253.322
Current health expenditure (% of GDP)(2017)	17.061	5.151	3.535
Domestic general government health expenditure (% of current health expenditure) (2017)	50.158	56.673	27.132

(Source : <https://data.worldbank.org>)

lower socio-income groups thus addressing their vulnerable situation. The Rastriya Swastha Bima Yojna (RSBY) in 2008 that subsumed to Pradhan Mantri Jan Arogya Yojna (PMJAY) covered only 40% of people who are economically downtrodden and later extended to mine and plantation workers¹⁴. Apart from Central Government Health Scheme (CGHS) the Employee State Insurance Scheme (ESI) is the only scheme where both employers and employees contribute towards health insurance. The Out Of Pocket (OOP) expenditure, thus, remained considerably significant.

The Ministry of Health and Family Welfare (MOHFW) with Federal ministry Established Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homeopathy (AYUSH) in 2014 as an alternative practice for delivery. Since, the healthcare GDP contribution is merely 1.28% on healthcare facilities, which is significantly lower than USA (17.07%) and China (4.98%), quality healthcare for all is a distant dream¹⁵. Only a handful of population has private insurance and low public health expenditure facilitates a higher number of non-insured people. They bear expenditure at the cost of household expenses whenever needed thereby severely affecting the standard of living.

COVID-19 infections and healthcare response :

Public healthcare financing varies across nations. The onset of COVID-19 dismantled the existing healthcare machinery and created an urgent need to rethink and redesign conventional protocols and strategies. Most importantly, it was clear that COVID-19 pandemic could not be insulated by proportionate increase in healthcare expenditure¹⁶.

USA

In USA, the Government was initially reluctant with fewer restrictions. Since wearing mask, social distancing and dissemination of public information was slow, it created disarray and misinformation amongst people. The jingoist nationalism further termed the virus as “Chinese made” that blocked trade relations and technical collaborations though the actual implication of the pandemic couldn't be assessed at this stage.

Preliminarily, in response to COVID-19 outbreak, inconsistent travel bans were introduced by allowing travel from Europe while banning those from China¹⁷. The fiscal reforms initiated by the US Government involved massive financing through various acts like Paycheck Protection Program and Healthcare Enhancement Act, Coronavirus Aid, Relief and Economic Security Act, Coronavirus Preparedness and Response Supplemental Appropriations Act and

Families First Coronavirus Response Act¹⁸. These provisions covered paid sick leaves, food and unemployment benefits for the affected healthcare personnel. It also assured International financial assistance and coverage for student loans.

CHINA

China was the epicenter of COVID-19 and incurred multidimensional losses especially in finance, infrastructure, emergency response, healthcare. Morbidity and mortality figures were highest between 31st December 2019 and 29th February 2020, however the daily incidence was less than other Nations¹⁹. COVID-19 outbreak led to immediate containment of cities, strict lockdown, ceasing large scale mobility, stringent testing protocols, social distancing and mandatory two-week quarantine²⁰.

Rapid dissemination of correct health information through electronic, print and local social media made people well versed with hygiene protocols, mask usage and disinfection. They were also encouraged to self-report infections. Free COVID-19 testing, monitoring of pricing for essential commodities including food and channelization of resources through Non-government and Charitable Institutions helped to a great extent¹⁷. Fiscal reforms included announcement of estimated RMB 2.6 trillion (2.5% of GDP), out of which approximately 50% of the promised amount has already been implemented¹⁸.

In response to COVID-19, China initiated key strategic decisions. Increased spending on epidemic control and prevention, upscaling of medical equipment production, accelerated disbursement of unemployment insurance with inclusion of migrant workers, relieve from taxation and waiving of social security obligations were initiated.

INDIA

With a daily upsurge of active cases and rapid increase in death figures, the Indian economy suffered a terrible demand shock in the wake of COVID-19 pandemic. The Government immediately restricted travel, movements and invoked the Epidemic Disease Act. Like China, lessons of social distancing, hand hygiene, contact tracing, quarantine and surveillance was enforced. Aarogya Setu app was launched by government to dispense health related information, compliance and regulate contact tracing of infected people. Another positive outcome was the rapid establishment of viral molecular testing protocols such as Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR), Cartridge Based Nucleic Acid Amplification Test (CBNAAT) etc. Additionally, rapid approval from

regulatory authorities like NABL were also solicited.

Teleconsultations formed the backbone of communication reducing the rural-urban divide. To encourage the same, Indian Council of Medical Research (ICMR) has issued updated rules and guidelines for teleconsultations with periodic amendments as per needs²¹.

The fiscal measures announced by the Government included a stimulus package valued at 0.85% of the GDP¹⁸. The prime elements were food, cooking gas and cash transfers to underprivileged, insurance coverage for healthcare personnel, wage support to low wage workers and in many cases, easing the criteria for receiving unemployment benefits. Previously, the government had announced 150 billion rupees (approximately 0.1% of GDP), for enhancing healthcare infrastructure that included strengthening of COVID-19 testing facilities, provision for PPE, supply of isolation beds, ventilators and increase ICU facilities across healthcare institutions²².

CONCLUSION

The emergence of COVID-19 has severely affected countries and their economies. Healthcare policies and preferences of USA, China and India are being tested for their resilience and capacity to withstand maximum possible turmoil. It has broken the classical myth regarding healthcare investment that wealth alone cannot be the only solution to restore the country from COVID-19 pandemic. Adversity being a powerful teacher, there is an urgent need to relook and shape public health policies, infuse capital flow in protecting lives and livelihood, amendment of allocation guidelines towards healthcare infrastructure for enhanced production of PPE, ICU beds and ventilators.

The variation in sizes, healthcare policies and overall preparedness of these three countries is broad remainder that 'one size does not fit all', yet there is a need to identify common goals, fallacies and equitable participation in specific areas. This unification of nations aided by a pandemic has grossly revealed our common inadequacies despite having segregations in the economic forefront.

Our study is a concerted effort to understand the approaches of these three representative economies-USA, China, India and their COVID -19 pandemic response. In our analysis we have put forward certain mitigation strategies, based on mutual cooperation and greater need to identify common goals and resolve other insufficiencies.

POSSIBLE MITIGATION STRATEGIES

Care of the vulnerable population :

COVID-19 has displaced the native local population, migrant workers and also the refugees that took shelter in other countries. In India, there is a huge population of migrant laborers who were left stranded, bereft of transportation, food provisions and livelihood. Similar incidents have also been echoed across China and African Nations.

In presence of economic and social disparities, differentiation based on urban and rural population should not be encouraged. As learnt from previous epidemics of Ebola and H1N1 influenza, the combination of resource diversion, shortage of medical supplies, closure of health facilities and lack of trained medical staff overwhelmed the various operational health systems across these nations, overburdening them more so in humanitarian context²³. Such restrictions can further, exacerbate resource distribution between rural, urban and other informal settlements. Additionally, people with comorbid conditions such as cardiovascular diseases, diabetes, tuberculosis and HIV infections are at increased risk of complications and death²³. Special attention, must be paid to pregnant mothers, children, elderly and immunocompromised people.

Protection and workplace safety of frontline healthcare workers is paramount. Unforeseen stress, long working hours and lack of vital essentials like PPE and other items have resulted in depression, burnout, insomnia and Post-Traumatic Stress Disorder (PTSD) amongst frontline healthcare workers. They also faced other psycho-social issues like increased risk of infection, quarantine, isolation, social distancing, negative societal vibes like stigma, depersonalization and lack of support from co-workers and organizations along with financial stress which further elevated role conflict²⁴. Early detection, risk communication, effective containment strategies and multinational collaboration where found to be effective during the 2009 H1N1 pandemic and needs to be replicated during the present crisis.

Surveillance activity concerning local, marginalized and displaced population needs to be balanced with public health measures, outbreak readiness, social distancing, crowd management, increased testing facilities and access to hospitals with adequate beds and ICU support. As quarantine is challenging, efforts must be made to ensure basic needs, food security and supportive services are maintained. Respective Governments, Private Sectors and Non-government

organizations, must act together to ensure a coordinated system of information sharing, data analysis, surveillance and effective roll out of measures in order to ensure protection and sustainability of vulnerable population.

Enhanced Resources in public health efforts :

While humanity braced itself against the deadly COVID-19 infection, an important question still remains unanswered: What have we learnt from previous pandemics and how well are we prepared to respond and effectively control disease spread? The answer(s) sadly remain ensconced within pages of voluminous texts, published articles and workshop summaries.

An important observation noted during COVID-19 outbreak is that developed economies having better health facilities had higher mortalities. Also other underlying comorbid conditions and lifestyle diseases contributed towards poor recovery outcomes.

Higher infectivity and transmission rates were reported across the nations, especially from the urban population with higher percentage of positive cases. Different factors like poorly designed policies, lack of political willingness, non-judicious resource management, significant chronic diseases and limited implementations are believed to be contributory towards the pandemic²⁵. However, this time, public health and community stakes have ensured that implementation of some previous suggestions are carried out.

Early detection of outbreak focused on integration of existing knowledge and strengthening of private, public and non-government participation. As this study involve countries with large population sizes, stakeholders need to approve effective, efficient and sustainable approaches keeping in mind their national capacities and existing legal framework.

In this digital era, an effective unbiased local and global coordinated system of information and data analysis will dramatically enhance the ability to contain microbial threats. A slew of epidemiological data and evidence based material on COVID-19 and multiple mathematical models and predictive analytics have kept researchers busy. While they are paramount, the actual exercise would be to get them validated and benchmarked in public health domain. The onus is to get a working predictive model as per requirement²⁶.

Regional and Global Cooperation :

To promote regional and global cooperation, 'whole of Government – whole of society' approach has been adopted but it lacks International response. Disparities in practices to contain COVID-19 pandemic are visible

in adoption of containment and lock down measures across different countries.

Regional and International cooperation is absolute towards establishment of an intelligent healthcare system based upon outcome, enhanced production capabilities, planning, forecasting and decision analysis of infectious diseases that will control future pandemics.

Current response to COVID-19 pandemic has clearly pointed out the difficulties amongst various nations. In the absence of sufficient cooperation, there were equipment poaching, export bans, travel restrictions and bidding wars. Several countries have pursued independent research programs in an attempt to polarize vaccine production and promote 'Vaccine Nationalism' Policy²⁷. Insufficient economic cooperation also ensured that poorer nations were mainly left to fend for themselves. Populist nationalism amongst countries have made the attitude of 'My Country First' become a global movement with 'America First' 'China First' and 'India First' initiatives²⁷. Such initiatives have undermined the overall willingness to cooperate with other countries thereby restricting the responses to deal with COVID-19 pandemic on a global scale.

Revamping economy and stabilizing financial markets :

Living through the most challenging times, we are forced to think about several basic questions- How to save lives and livelihood? What financial decisions should be taken by Governments? How to evaluate the risks associated with prolonged lockdown? How to maintain income security, food supplies, save financial institutions and safeguard the future generations and perhaps to find the best possible directions?

The answers to all these questions require integration of ideas and thoughts, financial experts, Government and policy makers; which is outside the purview of this paper. We however endeavor to seek a mutual platform to reduce the financial baggage in this pandemic.

With the rapid onset of COVID-19, protecting the livelihoods of people is the foremost challenge. Supporting the hardest hit, ie, informal workers, laborers in India, the working class population of China, single mothers, nurses and Asian Americans in USA has been challenging till date. Leaders and Government alike should determine the level of support that each population segment requires and ensure appropriate channels of distribution.

Income support and conditional cash programs like PMJDY, MNRGA in Indian context shall support millions²⁸. Also the ambit of coverage needs to be broadened and should be inclusive of pregnant mothers, child laborers, homeless and the elderly. Digitized payments through consolidation of databases could be helpful.

Post COVID, monetary expansion will be required to salvage industrial production, infusion of funds and growth of stock market. In this regard, the role of Central Banks and other financial policy making bodies will be crucial in determining the best possible strategies and long-term successes. USA and China with their deeper capital markets can secure loans. They can use their financial strength and institutional investors to reduce the pressure on public finance. In India, stimulus package has been flagged off to restore financial balance and accelerate recovery. However, since the different Indian States have variable geographical size, percentage of infected people and urban-rural differences, it requires tailor-made policies as per need²⁹.

Better funding and enhanced healthcare infrastructure strategies are being worked out at the government and local level¹⁷. Governments may also relax their taxation and other regulatory regimes to help businesses and their growth. Sectors such as food, agriculture, housing, power will require credit backstops, bankruptcy protection and liquidity support.

Digitization is the new mantra. China, already known as a globally acclaimed digital leader before COVID-19 happened, is facing competition from US and India who are catching up fast. In a traditional economy, areas of physical interactions are rapidly transiting to the digital mode and has accelerated both Business to Business (B2B) and Business to Customer (B2C) application channels. While Indian Government has already given a mandate in terms of augmenting digital platforms through increased use of wallet payments, online banking and electronic transfer of funds and monetary benefits given to the poorest of the poor, limited technical knowhow will continue to promote fear and reluctance amongst users.

Different countries hit by pandemic have witnessed growth fluctuations, certain industries like aviation, tourism and hospitality have been dealt with a body blow. Positive growth figures were witnessed in pharmaceuticals, biotech, healthcare supplies medical technologies, consumer durables and utilities. Emergence of telemedicine, education technology, elderly care has already made headlines across different countries. The role of private sector and

technology companies have become more significant with regard to their socio-economic contributions and emergence of powerful institutions that have donated millions to recovery efforts.

As is the case with Chinese economy, two thirds of its revenue have come from private sector. In case of India, recommendations of a robust Private Public Partnership (PPP) and legislations to provide strong legal and procedural support have come from various stakeholders.

The pandemic is a global tragedy and it is the right time to introduce inclusive economic reforms concerning fiscal, labor, environmental and social contexts. While digitalization, supply chain management, e-retailing will lead the way, global and national agenda driven by the principles of diminishing inequality, reducing poverty, protecting environment by ensuring financial inclusiveness and provision of better and more efficient public and social services needs to be figured out urgently by Governments, companies and Social Organizations.

Future Directions and the Road ahead

An important learning lesson from COVID highlighted the fact that mere investment in healthcare does not suffice all dimensions. Sustainable and intelligent healthcare policies with a healthy lifestyle, may reduce the risk of disease and co-morbidity. In urban areas, there is ease of availability and accessibility of drugs, diagnostic tools and treatment protocols where as in rural areas, low population density and better environment quality reduce chances of disease transmission²⁵.

Teleconsultation has proved to be an effective tool for patients and physicians alike³⁰. During COVID-19, telemedicine along with other various specialties like tele-ophthalmology, tele radiology has helped in providing treatment to patients located in varied geographical areas. This has diminished the burden on hospitals and reduced patient exposure to the virus. The scope and regulations of teleconsultation are exhaustive and are undergoing amendments as per the needs of changing scenario.

The response to COVID-19 pandemic has benefitted from the use of Artificial Intelligence (AI) and different mathematical models focusing on mitigation strategies keeping in mind the limited economic resources and socially disruptive factors. This has also helped in evaluating policies in a novel and rapidly evolving epidemiological circumstances²⁶. The use of data for forecasting and validating epidemiological changes coupled with their corresponding results should be available in public repositories for present and future

reference.

The emergence of newer treatment regimens for COVID-19 pandemic has enabled the convergence of applied sciences like biotechnology, immunology, virology to be synced with translational sciences and clinical research. Such an example was witnessed in the field of drug repurposing wherein existing antiviral, antimalarial and immunomodulatory drugs were used in treatment of COVID-19 pandemic³¹. The examples of Hydroxychloroquine and Ivermectin are relevant to the context. International cooperation for clinical trials across heterogeneous population shall be instrumental in understanding the pathophysiology of COVID-19.

Use of data sciences through standardizing and integrating demographic information coupled with DNA sequencing could be helpful but might need regulatory compliance to gain positive outcomes and maximum usage in public domain. The road ahead is essentially a 'federated learning' process in which telemedicine, novel AI techniques, biological and clinical research will ensure maximum therapeutic benefits for real world complex disease such as COVID-19.

Limitations :

The current study bears a few limitations. Firstly, it took into account the scenario and health policy details of USA, China and India as representative nations across different income levels. However, the practical healthcare challenges faced by different countries belonging to the same income level might not be different and thus all the recommendations may not yield optimal results. Secondly, this paper has considered data from authentic secondary sources. Detailed analysis considering primary empirical data might be beneficial to provide a holistic overview of the current pandemic challenges.

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Acronyms Used —

RT-PCR : Reverse Transcriptase Polymerase chain reaction

CBNAAT: Cartridge- based nucleic acid amplification test

NABL: National Accreditation Board for Testing and Calibration Laboratories

PPE: Personal Protective Equipment

ICU: Intensive care unit

PMJDY: Pradhan Mantri Jan-DhanYojana

MNREGA: Mahatma Gandhi National Rural

Employment Guarantee Act

GDP: Gross domestic product

B2B: Business to business

B2C: Business to Customer

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Review Article

Post Herpetic Abdominal Pseudohernia (PHAP)

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Post Herpetic Abdominal Pseudohernia is defined as the temporary paresis/paralysis of the segmental nerve/s of the abdomen resulting in a limited, mostly temporary, protrusion of the affected abdominal musculature giving rise to the phenomenon of "Pseudo Abdominal Hernia" known commonly as Post Herpetic Abdominal Pseudohernia (PHAP). It is important to consider HZ as a cause of unilateral segmental paralysis of the abdominal muscles, which resembles an abdominal wall hernia and is necessary for making a correct diagnosis so that unnecessary investigations and interventions can be avoided. The literature seems to be silent about patients needing surgical treatment for "Pseudohernia". Managing the bulge with a corset, pain management and weight loss are the recommended treatment.

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Key words : Herpes Zoster (HZ), Varicella Zoster Virus (VZV), Post Herpetic Abdominal Pseudohernia (PHAP), Post Herpetic Neuralgia (PHN), Acute Zoster Pain (AZP), Ramsay Hunt Syndrome (RHS).

Herpes Zoster (HZ) is a transient disease caused by reactivation of latent neurotropic (DNA) Varicella Zoster virus (VZV) in spinal or cranial sensory ganglia. It may affect one or several adjacent dorsal roots. The virus, after initial infection at a young age, remains inactive for years to decades without causing any clinical problems.

The HZ (Fig 1) is characterised by a painful erythematous rash in the affected dermatome/s. Approximately, 20-30% of people will get HZ in their life time^{1,2}. HZ is characterised by clustered maculopapular and vesicular lesions along a dermatome³.

Risk factors include advancing age and a compromised Cell Mediated Immunity (CMI). Early diagnosis and treatment with antivirals shortens the severity and duration of the disease and its complications like Post Herpetic Neuralgia (PHN) etc.

The incidence of PHN, which is defined as persistent pain three months after the onset of HZ rash, has been reported to be 10-20%⁴. This pain can, however, last for several years. The pain, in acute stage, is associated with fatigue, insomnia and

Editor's Comment :

- Post Herpetic Abdominal Pseudohernias should be diagnosed clinically, differential diagnosis with true hernia is essential by means of clinical and imaging techniques.
- Literature seems to be silent about requiring surgical treatment.
- Being an abdominal wall bulge without fascial defect and no true hernial sac, no risk of incarceration is present.
- Wearing a corset, weight loss and pain management are the treatment required.
- All the same we emphasize upon long term follow up of such cases till the pseudohernia completely disappears.
- The non-Herpetic neurological hernias, may however, complicate and require surgery.

decreased social activities rendering the patient morbid and negative. Sensory loss and allodynia have been reported to be hallmark sign of PHN⁵.

Pathophysiology :

Pathogenesis remains uncertain⁶. Generally after resolution of the primary infection with VZV, the virus remains latent in the Dorsal Root Ganglia and the Cranial Sensory Ganglia. When the CMI decreases, the virus replicates in the ganglia and subsequently spreads along the peripheral nerves to the skin leading to painful erythematous rash in the respective dermatome/s. Usually, the rash resolves in 7-10 days.

Replication of latent VZV in the sensory ganglia leads to the inflammatory neural damage resulting in Acute Zoster Pain (AZP) and Post Herpetic Neuralgia (PHN), an entity which remains the most common and nagging complication of the disease.

Spread of infection and inflammation from dorsal horn to the anterior horn results in motor complications causing temporary paresis of the segmental nerves. Motor deficit occurs in 1-5% of patients⁷ giving rise to

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somatic and visceral complications.

Zaladonis *et al* postulated that about 5% of all patients of HZ will develop some form of Zoster Paresis/ Muscle Zoster⁸. The commonest somatic manifestation is Ramsay Hunt Syndrome (RHS) - a rare neurological disorder characterised by paralysis of the facial nerve and a rash affecting the ear/mouth resulting in hearing loss, tinnitus, disturbances of balance and of lachrymal and nasal secretions in addition to some sensory abnormalities of hearing and taste (Geniculate ganglion involvement)⁹. Segmental paralysis of limbs, diaphragm and abdominal musculature may also occur. Visceral manifestations may involve GI tract and urinary bladder etc. resulting in pseudo-obstruction, voiding problems etc. In approximately 20% of cases, constipation and false bowel obstruction will occur owing to decreased intestinal motility from autonomic neuropathy¹⁰.

The temporary paresis/paralysis of the segmental nerve/s of the abdomen results in a limited, mostly temporary, protrusion of the affected abdominal musculature giving rise to the phenomenon of "Pseudo Abdominal Hernia" known commonly as Post Herpetic Abdominal Pseudohernia (PHAP).

The first case report of a motor paresis following Herpes Zoster was published in 1866 by¹¹.

The phenomenon of pseudohernia was first described in 1936 by Loewe in the context of a local anaesthetic injection into the abdominal muscles of a guinea pig.

He postulated that pseudohernia was related to a sensory, rather than motor neuron defect and that the bulge resulted from an interruption in the reflex arc that maintained abdominal wall tension.

The onset of PHAP is rather abrupt and manifests itself in 2-3 weeks time of the appearance of rash and includes an abdominal bulge or protrusion in the region of classically affected dermatomes⁶. The pseudohernia is due to increase in abdominal pressure¹³.

As a rule patients have a good prognosis with most having complete resolution within 18 months¹⁴. Reported that abdominal bulging occurred between 7 to 60 days (mean 24 days) after the onset of cutaneous rash.

Definition, Diagnosis :

Clinically the "PHAP" will be defined as an ipsilateral dermatome- related paretic (lower motor neuron) protrusion of abdominal wall/ musculature in corresponding myotome without any evidence of a muscular or aponeurotic defect or disruption. Relaxation of abdominal wall will cause it to bulge with any increase in intra-abdominal pressure. Diagnosis



Fig 1 — Showing erythematous rash in the affected dermatome is primarily clinical, based on temporal correlation of HZ with the appearance of Abdominal bulge. A physical examination may reveal decreased or absent segmental reflexes. An electroneuromyographic study can be useful¹⁵. Abdominal tomography will show a thinned abdominal wall ruling out the presence of breach in muscles or aponeurosis and absence of a peritoneal sac. Gadolinium DTPA nuclear magnetic resonance imaging can help define extent of inflammation and exclude compression of spinal nerve roots¹⁶. Differential diagnosis with true hernia is essential by means of clinical and radiological examination as it is the one which does not require surgery and tends to disappear spontaneously within a year unlike a true abdominal hernia.

It is important to consider HZ as a cause of unilateral segmental paralysis of the abdominal muscles, which resembles an abdominal wall hernia and is necessary for making a correct diagnosis so that unnecessary investigations and interventions can be avoided¹⁷.

Apart from HZ infection, a pseudohernia may also occur with variety of syndromes involving neuropathy or denervation including Diabetes Mellitus and following a trauma to nerves as after surgical operations, rib fractures etc¹⁸. Complete recovery in PHAP occurs in 6-12 months in 55-75% of cases⁶. There are reports of even higher (79.30%) recovery^{19,20} reporting incidence of PHAP as 0-5%, also emphasised upon recognition of this entity to save costly consultations and evaluations. Pertinently, the authors recorded their patient as the 37th case of PHAP appearing in literature, till date.

The literature seems to be silent about patients needing surgical treatment for "Pseudohernia". Since, as a rule, an abdominal bulge represents the wall laxity

without facial defect and no true hernial sac, there is no risk of incarceration. However, abdominal cramping, pain, bloating, nausea, early satiety and poor cosmesis are frequently reported symptoms. Recommendations include wearing a corset to manage the bulge, weight loss and management of pain. Rarely in a long standing pseudohernia, the pouching effect may be so severe and deep as to entrap some abdominal viscera, presenting as a subacute or acute-on-subacute obstruction requiring operative interference (Fig 2 & 3).

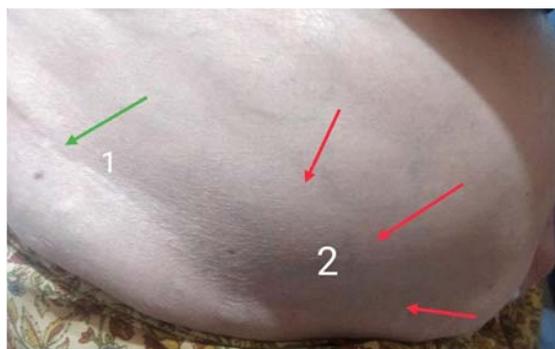
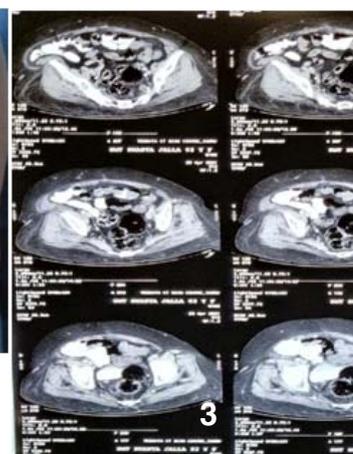


Fig 2 & 3 — Demonstrating pouching effect presenting as subacute or acute on subacute obstruction



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Review Article

A Primer on Pandemic Preparedness for Health Care Facilities Drawn from the SARS-CoV2 Pandemic

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In late 2019, an epidemic of Novel Corona Virus infection later named SARS-CoV2 hit China followed by rapid spread of infections across the World. Notwithstanding Government mandated measures like lockdown, rigorous testing, universal masking and COVID-19 screening camps, it is important for hospitals to be prepared to face the pandemic. A proper triaging facility with appropriate infection control precautionary measures, adequate supply of Personal Protective Equipment (PPE), rational usage of disinfectants and PPE, protection of health care workers and prevention of cross transmission of infection in a health care setting needs to be implemented through appropriate guidance and experts. In this review article, we share our experience and key areas that need to be addressed by any institution during a pandemic situation.

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Key words : COVID-19, Pandemic, Infection Control

In December, 2019, an increasing number of pneumonia cases of unknown aetiology were identified in Wuhan, China¹. By early January it was an epidemic in China and thereafter due to rapid spread of the virus, was declared a pandemic by WHO in March, 2020. Risk mitigation and preparedness in the early phase of an outbreak is of utmost importance during a pandemic. Low- and Middle-income countries (LMICs) are uniquely susceptible to the direct and indirect effects of pandemics due to a combination of unfortunate characteristics: increase in the travel due to globalization²; densely populated urban areas with large migrant populations³, strained health facilities and bed status⁴; low Government expenditure on Public health⁵; greater reliance on the private health care sector to cater to healthcare needs, and a high proportion living below the poverty line that limit awareness of, and access to, health care⁶.

Even though the attention of the world during the SARS-COV2 pandemic has been monopolized by issues of testing and lack of kits⁷, experimental drug

Editor's Comment :

- Health care institutions especially in low and middle income countries are susceptible to direct and indirect effects of a pandemic situation.
- The key principle to combat a pandemic crisis in an institution is to make hospital infection control committee as nodal point with representatives from each department by engaging all the stakeholders of the institution.
- Based on the lessons learnt from the COVID-19 pandemic in 2020, we understand that a coordinated, multi-disciplinary system is helpful to manage the crisis in an institution.

therapies⁸, and the race to develop a vaccine⁹, the issues on the ground for LMICs are far more prosaic and need tailored strategies to build up the health care system. Every nation has adopted draconian measures including complete lockdown, travel restrictions, stay-at-home, and social distancing. Many of these strategies to limit community spread cannot be implemented in a hospital. Instead, every hospital needs a preparedness policy based on their infrastructure, number of patients, speciality units in the hospital, hospital bed capacity, intensive care unit capacity, patient to health care worker ratio and annual budget⁴. In the pandemic phase, despite information overload and uncertain scientific evidence, health care providers need an effective infection prevention policy to work at the frontline. It is the primary role of the Hospital Infection Control (HIC) team to act as the core defence team for health care providers, patients and employees to prevent COVID-19 infection. In this article, we list key areas institutions need to address

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when responding to a pandemic, based on our experience.

Team Building :

The key principle of team formation is to have broad representation from administrative, medical, nursing, and paramedical cadre ensuring diversity of gender, skill sets and experience. Each team should have a Designated Team Leader, Pager Number and Institutional Email Address which should be prominently displayed throughout the institution. Teams should have rolling meetings at a designated time and frequency either in person or virtually, during which relevant protocols are formulated, critically appraised, and updated based on emerging evidence, institutional resources, and feedback from end users regarding loopholes and barriers to implementation.

The nodal point for any pandemic preparedness programme is the Hospital Infection Control Committee (HICC). Its mandate is to monitor local and international infection trends to recognize emerging epidemics, gather all relevant information regarding the mode of transmission, reproduction number (R_0) and clinical presentation, and make a realistic assessment of the preparedness of the country, state, district and institution to counter the threat. Consequent to this assessment, the HICC must immediately set up an Infection Prevention and Control (IPC) Team.

IPC Team : This team, with representatives from the HICC, Infectious Disease, Microbiology/Virology, Nursing, Paramedical, Administrative, Clinical and Triage teams, should be led by a senior administrator who has prior experience with handling outbreaks/epidemics, and has the following key roles.

- Formulating and updating protocols and guidance for infection prevention and control taking into account existing local, national and international guidelines. Where, in the judgement of the IPC, these guidelines are lacking, or do not fully address all aspects of the problem, the IPC may need to incorporate best practices, based on prior experience with similar epidemics in the past.

- Formulating protocols to prevent infection in operation theatres, in-patient, out-patient, diagnostic, therapeutic and laboratory services and working with independent departments to rationalize their protocols in line with Institutional Guidelines

- Coordinating with the PPE team to formulate the institutional PPE use and re-use policy

- Updating protocols regularly based on WHO and national situation reports or directives (eg, the list of high epidemiological risk countries or states)

- Making all protocols available and accessible on the institutional intranet.

- Coordinating with all pandemic teams

- Tabulating daily statistics for reporting to the local health authority

- Organizing contact tracing where required.

- Issuing travel advisories to staff, working with the Staff and Student Health Service to institute quarantine for staff returning from high risk areas, and monitoring them for symptoms

Administrative Team : The administrative team should comprise personnel with leadership roles in medical, nursing, allied health and support services along with a representative from the HICC. This is the apex team in that it is responsible for ratifying all policies and protocols and its leaders must liaise directly with local health or administrative authorities to ensure smooth functioning of the institution, while also communicating with the staff and student body to enjoin their cooperation and allay fears. The team should meet daily to review the following key areas: (a) Case statistics, stratified by gender, age group, co-morbidities, geographical area and presumed mode of infection (b) Updates from international, national or local health or administrative authorities that directly impact patient care and the running of the institution (c) Status of key resources required for preventive and curative management – Manpower and infrastructure (d) Infection control (e) Employee and student safety and wellbeing (f) Protocol amendments required in light of the above.

Triage Team : Primarily comprising members from Emergency Medicine, General Medicine, Paediatrics, Surgery, Obstetrics, Nursing, HICC, Hospital Management, Medical Records, Outpatient and Security Services, this team develops strategies for crowd management while following norms of social distancing, in order to implement symptom screening at all entry points and minimize the risk of cross-infection. Strategies may include triaging by teams at entry points and subsequent fast-tracking along pre-designated pathways, travel history notices and self-declaration forms at the time of appointment booking, etc.

Clinical Team : The Clinical Team ensures that vulnerable populations are represented in developing protocols related to clinical case definition, testing and treatment, which are the key responsibilities of this team. Based on the relative proportion of patients with Influenza Like Illness (ILI)/Severe Acute Respiratory Infection (SARI) and asymptomatic/vulnerable patients from epidemiologically high-risk areas, outpatient and in-patient testing capacity will need to be augmented and duty rosters for HCWs need to be revised.

Laboratory Testing Team : Comprising members from Infectious Disease, Medicine, Virology and the HICC, this team develops protocols for sample collection, transfer, testing and reporting. It also ensures that testing kits used are available in the required quantities are reliable, validated by a nationally accredited laboratory, and have a minimal turnaround time.

PPE (Masks and supplies) team : The main responsibility of the PPE team is formulating a PPE policy which specifies terms for use, disposal, storage, re-use and sterilization. This policy and implementation should involve coordinating with individual departments to ascertain their degree of comfort with the institutional PPE policy, address any fears or misconceptions and selectively modify the policy in cases where such change is justified. Mathematical modelling to estimate requirement of each PPE item given data on current usage (average usage in the previous 3 months) and projected requirement for the worst case scenario if demand increases by 25, 50, 75 or 100%, given the terms of the institutional PPE policy, case load growth trend, and the number of staff and patients in each location, stratified by risk category, is helpful. In-house testing of sterilization techniques for hard-to-procure or expensive PPE like N95 masks and working with CSSD to implement the sterilization policy are also crucial. We can use information technology (IT) tools to track PPE issue to and use by, individual employees and departments, and ensure strict adherence to guidelines on rational use of PPE.

Environmental Cleaning and Waste Management team : Its mandate is training and roster management of house keeping staff in order to implement the environmental cleaning and waste management protocols of common areas, high risk areas and high touch surfaces put forward by the IPC

team, while ensuring availability of adequate supplies to do so.

Logistics Support Team : Transfer of suspect or confirmed patients between triage, treatment and diagnostic areas requires coordination between the HICC, nursing services, hospital and floor managers, security services and the Environmental Disinfection Team. A Central Command Centre (CCC) pager number which can be activated whenever patient transfer is required can help coordinate all these elements.

Staff training team : Modules for each category should cover core knowledge relevant to their work and daily routine, and liberal use of culturally and linguistically appropriate audiovisual aids (eg. videos or live demos to demonstrate PPE donning and doffing) is recommended. Identifying trained volunteers from within the institution who can be provided with a standard set of slides or teaching materials to teach small groups can help achieve training targets within a short span of time. Pre-and post- test exercises and feedback in paper or online format are important to study the impact of training and identify areas for improvement. Subsequent phases of training are required to address changing protocols and an expanding evidence base.

Staff and student health service (SSHS) team : SSHS liaises directly with the HICC to ensure it is updated on policy changes related to testing and quarantine and in turn communicates the list of tested and/or quarantined staff and students on a day-to-day basis to HICC and the Administrative Team. A subgroup within this team is tasked with overseeing and facilitating home quarantine of staff and students by arranging quarantine rooms for those who wish to quarantine away from their immediate family, and a regular supply of food, groceries and other essential services such as waste disposal for staff quarantined with or away from family.

Staff and Student Counselling Service Team : The emotional well-being of staff and students is an often-neglected area which is nevertheless crucial in order to avoid burn-out, attrition and preventable mistakes in high stress situations. Counselling can be offered in person or online via Chaplaincy department, Psychiatry or dedicated counselling services.

Patient Education and Publicity Team : This team prepares culturally appropriate posters, signs and

videos aimed at patients and various groups of staff, in all relevant local languages. The key areas to focus on are interventions that, if universally adopted, can reduce the risk of infection transmission. For the SARS-COV2 pandemic these interventions were hand hygiene, respiratory etiquette, wearing a mask, and social distancing for the general public, and the appropriate use of PPE (donning, doffing, re-use) for staff.

Pandemic Research Team : All pandemics offer exciting opportunities for Clinical, Economic and Social Research. The research team should comprise representatives from the core clinical departments engaged in treating patients, apart from a data management team which should ensure data is collected, captured and analyzed efficiently. The research team should work closely with the institutional research office and Ethics Committee to ensure research proposals receive expedited approval provided they answer important and relevant questions, are robust in their design and are technically and financially feasible. Where institutional funding is insufficient to meet research requirements, it should connect individual researchers with external funding agencies.

Information Technology (IT) Team : The IT team is responsible for developing applications or IT solutions to solve pandemic specific issues. Examples relevant to the SARS COV2 pandemic included a PPE and hand-rub tracking application, a roster management application that takes into account quarantine and staggered work norms, helping the transport department design new routes based on staffing norms, work timings, and places of residence, developing a tele consultation application, and helping individual departments shift their meetings and educational programmes to online platforms. The IT team also updates the Institutional Website with triaging, testing and quarantine information relevant to patients and visitors, and uploads the latest versions of protocols on the intranet while archiving earlier versions.

Protocols :

Protocol implementation is a complex pathway and involves knowledge of the protocol (achieved through staff training), ensuring that all resources necessary to implement the protocol are available at all sites where the protocol needs to be implemented (achieved through coordination between the administration and various institutional teams) and that the institutional

climate encourages individuals to make behavioural changes required for rigorous adherence to the protocol. This last aspect is the most difficult to ensure, but can be aided by audits.

Audits are an integral component of quality improvement programmes and are invaluable in the setting of a pandemic, where the margin for error is miniscule. The institutional Quality Management Cell and the HICC should be actively involved in auditing all aspects of Institutional pandemic preparedness and Audit results should be directly communicated with the respective teams in order to ensure that loopholes are plugged and protocols modified in the light of audit findings. The cycle of auditing then begins again. In a pandemic, auditing key performance indicators needs to continue in addition to pandemic specific audits on hand hygiene, rational use of PPE, triaging, etc. In addition, Department Quality Managers (DQMs) should be encouraged to Audit their individual departments.

MANPOWER MANAGEMENT : Manpower management requires close cooperation between the Hospital administration, Clinical team, and Staff training team. Management should stagger work schedules based on the priority and categorisation of patients to avoid overcrowding in hospitals. It is very important to create a volunteer corps who are willing to help core teams in pandemic related activities such as protocol vetting, running triage clinics, stitching cloth masks for use by staff and students, developing patient and staff education materials, staff training, fundraising, supporting frontline staff with childcare, groceries, care of the elderly, etc. during this crisis.

MATERIALS MANAGEMENT : Materials management involves ensuring that the institution has an adequate supply of drugs, consumables and equipment to provide uninterrupted, high quality service. In order to achieve this goal, the administrative, finance, HICC and clinical teams have to work closely with the pharmacy, purchase and stores departments. An attempt to provide in-house replacements (eg: use of sterilised masks, in-house preparation of handrubs) should be encouraged to meet demands and cut costs. An IT solution track the usage of critical resources (eg masks, hand rubs) will minimize pilferage by patients and staff.

INFRASTRUCTURE MANAGEMENT : If a geographically separate facility is not available for the triage and treatment of suspected or confirmed

patients, it is crucial to identify areas within the hospital for the same, with a view to achieve water-tight separation between pandemic related and routine services via dedicated movement pathways for staff and patients in order to avoid cross-infection. Existing facilities in outpatient departments, operation theatres, emergency departments, wards and ICUs may need to be upgraded to facilitate triaging and treat suspected or confirmed patients (eg constructing donning/doffing rooms and shower cubicles in isolation wards and ICUs, using partitioning to convert ICU and general ward beds into individual cubicles, converting air-conditioning ducts into single duct units, converting operation theatres from positive pressure to negative pressure areas, providing pipelines and RO systems in order to offer dialysis in pandemic wards). Patients and staff working in pandemic services and quarantined staff should be provided food on-site, to reduce risk of cross-infection.

Challenges Faced by Frontline Workers :

The SARS-COV2 pandemic saw, for the first time, the parallel rise of 'infodemics'. This has deleterious consequences on the morale of HCWs, and those working on the frontline in particular. Each category of staff may have its own set of fears. Ambulance drivers may be wary of transporting suspects to the hospital, housekeeping staff may be reluctant to be posted in pandemic wards and doctors engaged in non-high-risk areas or procedures may demand to be provided PPE reserved for high-risk staff or demand that protocols being followed in the developed world be implemented regardless of the financial costs. Peer-to-peer support, training volunteers within each service group or department to act as motivators, and above all, calm, consistent leadership, are the best antidotes.

Conclusion :

This outline of our experience provides an understanding of how a tertiary health care institution can prepare for a pandemic in collaboration with all relevant stakeholders to develop a coordinated, multi-disciplinary system that can successfully manage a pandemic. We encourage other institutions to adapt these policies and protocols based on their individual needs.

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Review Article

Role of Biomarkers, Scoring Systems and Platelet Indices in the Diagnosis of Acute Appendicitis — evidence based approach

Balakrishnan Gurushankari¹, Sathasivam Sureshkumar², Debdatta Basu³, Vikram Kate⁴

Acute Appendicitis is one of the most common causes of acute abdomen. A systematic approach beginning with history followed by examination and investigations which include blood parameters and imaging studies, is carried out for the conventional diagnosis of Acute Appendicitis. Conditions like mesenteric adenitis in children, diverticulitis in elderly and Pelvic Inflammatory Diseases (PID) in women can mimic appendicitis. Although radiological investigations such as Ultrasound (USG), Computed Tomography (CT), and Magnetic Resonance Imaging (MRI) of the abdomen have good efficacy in the diagnosis, continuing research is being carried out to devise algorithms using other investigations to avoid radiation exposure and cost. There are several novel biomarkers for appendicitis reported such as Interleukin 6 (IL-6), Serum Amyloid A (SAA), leucocyte gene expression (ribonucleograms), Granulocyte Colony-stimulating Factors (G-CSF), Urine Leucine-rich Alpha-2-glycoprotein (LRG), Calprotectin or S100A8/A9, procalcitonin (PCT) and Pentraxin-3 (PTX-3). Multiple scoring systems including the Alvarado score, appendicitis Inflammatory Response (AIR) score, Adult Appendicitis Score (AAS), Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score and the Pediatric Appendicitis Score (PAS) are also being used. These scoring systems guide the clinician in risk stratification of the patient with acute appendicitis and decide upon the need for admission and surgical intervention. The various platelet indices such as Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and platelet count have been reported to be an indicator of disease severity in Appendicitis.

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Key words : MPV, PDW, Negative appendectomy, Alvarado score.

When it comes to the possibility of considering appendicitis as a differential for acute abdomen – “appendicitis should never be lower than second”

— **Sir Alexander Cope**

The vermiform Appendix, once considered to be a vestigial organ, is thought to play an important role in the maintenance of normal colonic flora and may have a protective function against *Clostridium difficile* infection and prostate cancer¹. Acute Appendicitis is one of the most common cause of acute abdomen and is usually the first major operation carried out by a surgery trainee in emergency. Shah *et al* reported that the prevalence, mortality and Disability Adjusted Life Years (DALY) of Appendicitis in India from the year 1990 to 2016 has decreased by 4.7%, 10.8% and 21.5% respectively². A systematic approach beginning

Editor's Comment :

- A systematic approach is required to diagnose acute appendicitis in order to reduce the negative appendectomy rates, complications and hospital costs.
- Although computed tomography is most sensitive and specific for the diagnosis of acute appendicitis, issues in its wide use are due to high cost and feasibility in basic health facilities.
- Platelet indices as well as biomarkers are most researched for its role in appendicitis and are cost-effective and widely available.
- A combined approach in the use scoring system with appropriate biomarkers and blood parameters can aid in the early diagnosis and treatment of acute appendicitis.

with History followed by examination and investigations which include blood parameters and imaging studies, is carried out for the conventional diagnosis of acute appendicitis (Fig 1). Various physical signs like Rovsing sign, Psoas sign and the obturator sign has been described in the literature which aids the diagnosis of acute appendicitis (Fig 2). Atypical presentations are not uncommon in appendicitis. Diagnostic dilemma arises as other conditions like Mesenteric Adenitis in children, Diverticulitis in Elderly and Pelvic Inflammatory Diseases (PID) in women can mimic appendicitis. Thus, supporting laboratory and radiological investigations are routinely carried out as part of evaluation to arrive at a definitive diagnosis.

The various imaging modalities used for the

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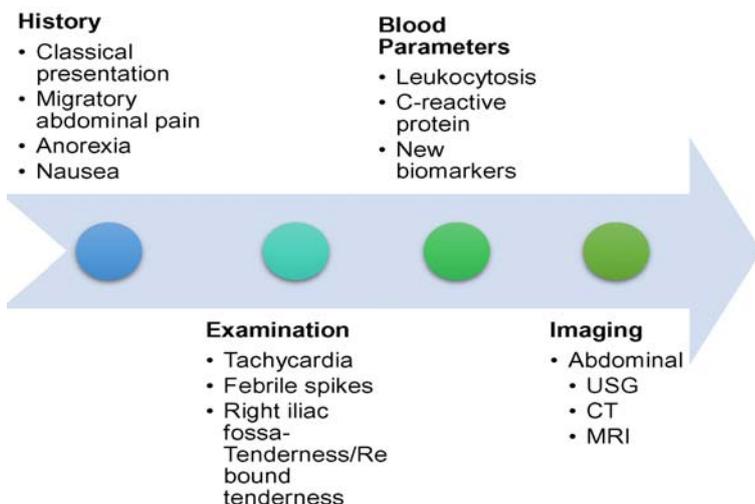


Fig 1 — Systematic approach to the diagnosis of acute appendicitis
USG- Ultrasound; CT- Computed tomography; MRI-Magnetic resonant imaging

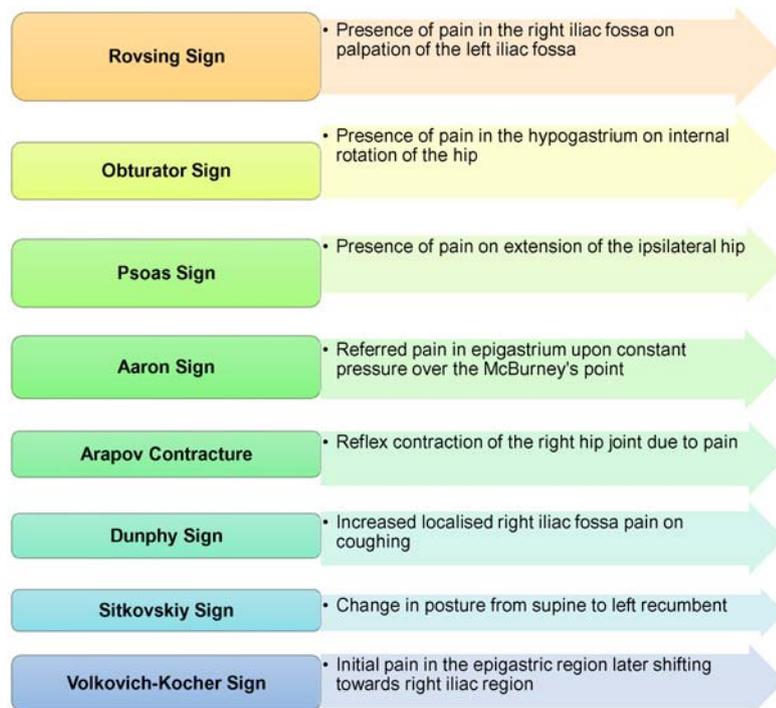


Fig 2 — Physical signs in acute appendicitis

diagnosis are ultrasound (USG), computed tomography (CT), and magnetic resonance imaging (MRI) of the abdomen. USG abdomen is a commonly used investigation for the diagnosis with a sensitivity and specificity of 83.1% and 90.9% respectively³. In USG there is no risk of radiation and is time-efficient, making it a screening investigation of choice and well suitable for paediatric population and pregnant patients. CT scan of the abdomen is the most effective, accurate and the gold-standard imaging modality to diagnose acute

appendicitis with a sensitivity of 89.9% and a specificity 93.6%³. Though MRI has a high sensitivity and specificity of 89.9% and 93.6% respectively for diagnosing acute appendicitis, it has a very limited role in the clinical practice and is reserved for pregnant patients with diagnostic dilemma. The details of various radiological investigation is summarised in Table 1. An elevation of Total Leukocyte Count (TLC) with neutrophilic leucocytosis is seen in 90% of the patients with acute appendicitis. The most commonly used score in the clinical practice is “Alvarado score” which includes components from symptoms, signs and laboratory tests. The use of single blood parameter such as elevated TLC may not be reliable in the diagnosis of acute appendicitis. A combination of markers such as elevated TLC, C- reactive Protein (CRP) and the proportion of polymorphonuclear cells (PMN) are more accurate in the diagnosis of acute appendicitis. However, these are non-specific inflammatory markers and they need to be correlated clinically.

Acute appendicitis despite its common presentation, remains a disease with difficult diagnosis and most surgeons rely on their clinical skills in its diagnosis aided by laboratory parameters and radiological imaging. But still 55% of the patient presents with atypical clinical signs such as right flank pain in case of retrocaecal appendix, isolated periumbilical pain, absence of fever in elderly patients etc. or a negative laboratory parameter. The rate of negative appendectomy has been constant over the due course of time which ranges from 10-34%⁴. It not only affects the mental and physical health of the patients as there is a possibility of them contracting secondary infections, it also

has a huge burden on the health care system. On the other hand, a mis-diagnosis can lead to catastrophe of complications such as gangrene, perforation, intra-abdominal abscess formation, sepsis and adhesions. Therefore, it is important as a clinician to improve the diagnostic accuracy in order to avoid complications arising from unwanted surgery and delayed intervention. Studies have been conducted to validate and compare these scores such as Alvarado score described early in the literature to the most recent

Table 1 — Details of radiological investigations in the diagnosis of acute appendicitis

Radiological investigation	Findings (Main and Additional)	Sensitivity Adults (Children)	Specificity Adults (Children)	Utility
Ultrasound abdomen	Enlarged, immobile, non-compressible appendix Free fluid abdomen, hyperaemia of adjacent bowel loops, mesenteric fat stranding, regional lymphadenopathy	83.1% (91.3%)	90.9% (95.2%)	Routine investigation of choice
Computed tomography of the abdomen	Appendix more than 7 mm in diameter with thick inflamed wall associated with mural enhancement Mesenteric fat stranding Air specs and periappendiceal fluid - perforated appendix	89.9% (96.2%)	93.6% (94.6%)	Reliable and accurate Used in the presence of diagnostic dilemma
Magnetic resonance imaging of the abdomen	Enlarged appendix of size more than 7 mm with thickness of more than 2 mm Presence of surrounding inflammation	89.9% (97.4%)	93.6% (97.1%)	Reserved for pregnant patient

ones like Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score.

Although adequate evidence is available on the efficacy of radiological imaging such as CT and MRI, continuing research is being carried out to devise algorithms to avoid radiation exposure and cost expenditure. The various scoring systems, diagnostic tests and algorithms are predominantly devised towards the target population which includes children, pregnant patients and elderly where atypical presentations are common and performing these diagnostic tests might not be feasible in all possible situations. The focus of this review is on the role of various biomarkers, scoring systems and platelet indices in the diagnosis of acute appendicitis.

Biomarkers and Scoring Systems :

Acute appendicitis being a clinical diagnosis, a diagnostic dilemma arises in atypical presentations. No single parameter has high accuracy in the diagnosis of acute appendicitis thus, a combination of them is recommended. They predominantly help in ruling out the disease rather than diagnosing it. Therefore, there is need for devising scoring systems which includes all reliable parameters for an accurate diagnosis. This section will be dealing with the routine biomarkers used in clinical practice and the novel biomarkers which are under research. It will also be describing the various scoring systems used in the diagnosis of appendicitis.

Biomarkers for Acute Appendicitis :

TLC done on day-to-day basis for acute abdomen has a low sensitivity and specificity as it is a non-

specific marker for appendicitis. It is generally elevated in all inflammatory conditions including appendicitis. However, a TLC count of $> 10^9/L$ has a better sensitivity and can be complementary with a reliable history pointing towards appendicitis. An acute phase reactant used in the diagnosis of acute appendicitis is CRP which peaks at 24-48 hours of onset of inflammation⁵. Although it is non-specific and a poor predictor in an uncomplicated appendicitis, it is a strong predictor of complicated appendicitis. The granulocyte count and polymorphonuclear cell (PMN) ratio is another blood parameter commonly used in acute appendicitis. A count of $>11 \times 10^9$ cells/L has a better likelihood ratio and is clinically significant when the value is $>13 \times 10^9$ cells/L. The

presence of immature PMN, or band forms, also known as left shift of $>700/\text{microliter}$ has a higher sensitivity and specificity in comparison to elevated TLC in the diagnosis of acute appendicitis. This has been well demonstrated in paediatric patients. A combination of biomarkers increases the likelihood of a definitive diagnosis of appendicitis. Studies have reported that a combination of these markers such as TLC and PMN, TLC and CRP etc, when within normal limits rules out the possibility of appendicitis. More research is required in this field to devise a multi-marker approach for the diagnosis of acute appendicitis.

Novel Biomarkers :

There are several novel biomarkers for appendicitis reported such as interleukin 6 (IL-6), Serum Amyloid A (SAA), leucocyte gene expression (riboleukograms), Granulocyte colony-stimulating factors (G-CSF), urine leucine-rich alpha-2-glycoprotein (LRG), calprotectin or S100A8/A9, procalcitonin (PCT) and pentraxin-3 (PTX-3). Most of these biomarkers are not routinely used in clinical practice as these are non-specific markers for appendicitis⁵.

Interleukin 6 (IL-6) and Serum Amyloid A (SAA)

The activation of the immediate inflammatory response is predominantly mediated by a cytokine IL-6 which has been reported to be raised in the initial phase of appendicitis. It has a sensitivity of 73% and specificity of 72%. It is reported to have a better accuracy of 80% in comparison to TLC and CRP but is has not been put into clinical practice⁶. Serum Amyloid A (SAA) is a non-specific marker of

inflammation and is reported to have a dynamic response to inflammatory diseases in contrast to WBC and CRP. It has a sensitivity and specificity of 86% and 83% respectively⁵. This could aid in the early diagnosis of appendicitis but further studies are required.

Leukocyte gene expression (Riboleukograms) and Granulocyte colony-stimulating factor (G-CSF)

The sensitivity and specificity of riboleukogram is 89% and 66% respectively and is reported to be a highly sensitive marker for appendicitis⁵. But implementing this marker in clinical practice is difficult owing to its cost and technical difficulties. The sensitivity and specificity of G-CSF is 91% and 51% with an accuracy of 76%⁵. It has been reported that this marker aids not only in the diagnosis of acute appendicitis but also helps in predicting the severity of the diseases. This factor stimulates the bone marrow thereby leads to the production and release of neutrophils into the peripheral circulation and is a marker of inflammation.

Urine Leucine-rich alpha-2-glycoprotein (LRG) and Procalcitonin (PCT)

These are primarily the markers of infection. LRG is a novel marker with a variable accuracy of 99% with mass-spectrometry and 80% with the conventionally used LRG-ELISA. The sensitivity and specificity of 5-Hydroxy Indoleacetic Acid (HIAA) is reported to be 72% and 86% respectively. Studies have reported the presence of LRG much earlier than the release of neutrophils. But it has been reported to be raised in other bacterial infections as well such as pyelonephritis which makes it non-specific. The normal plasma levels of procalcitonin (PCT) is 0.1 to 0.5 ng/ml and is a prohormone of calcitonin which rises in response to bacterial and fungal infection. It also has an ability to predict the severity of the infection, which is detected based on its levels. A meta-analysis on procalcitonin as a marker for appendicitis in children reported a sensitivity of 62% and a specificity of 86%. The authors also reported a much higher sensitivity and specificity of PCT in cases of complicated appendicitis ie, 89% and 90% respectively indicating it has a better accuracy in the diagnosis of complicated appendicitis⁷.

Calprotectin (S100A8/A9) and Pentraxin-3 (PTX-3)

Calprotectin is a calcium-binding protein which has been reported to be a gastrointestinal tract specific inflammatory marker with a sensitivity of 93-96% and a specificity of 16-54% according to various studies⁵. Although it has been reported to have high sensitivity, it is not a preferred biomarker due to its low specificity. Pentraxin 3 (PTX3) is one of the members of the

superfamily of pentraxin which includes CRP and Serum Amyloid P. It is an acute phase reactant protein which was described in the year 1990, known to rise in response to inflammation. The normal value of PTX3 is reported to be < 2ng/ml. It is also known to have a role in humoral immunity and interact with components of complement pathways. PTX3 has a sensitivity of 95% and a specificity of 100% and when combined with IL-6 yields a better result⁸. The overall accuracy of PTX3 was reported to be 97.2% and IL-6 was 90.4%. Thus, it has been suggested that a combination of these two markers if added to Alvarado score may improve its diagnostic accuracy. The various biomarkers with their sensitivity and specificity has been summarised in Table 2.

Although the data is available on the utility of these markers in various research studies, none has been used in the day-to-day practice for the diagnosis of acute appendicitis. The major reason behind this is the cost of these markers, need for the specific laboratory set-up and testing kits. Many of these markers have limited data in the form of randomised controlled trails and meta-analysis. As CT is routinely available in most of the centre the utility of these markers are overlooked. These markers once established in clinical practice can reduce the amount of CT scans performed and reduce the risk of radiation and the hospital cost. Future studies should focus on the role of these novel biomarkers for the diagnosis of appendicitis in routine clinical practice.

Scoring Systems and Acute Appendicitis :

Clinical scoring system also known as screening tool, prediction algorithm, clinical decision rule, risk score etc. are algorithms designed to diagnose, predict risks and outcomes, and aid in the management of any condition. These scores improve the clinical efficiency and reduces the medico-social burden in terms of unnecessary admissions, imaging, and intervention. A good scoring system should reduce the uncertainty in the diagnosis, guide through the

Table 2 — The sensitivity and specificity of biomarkers for acute appendicitis

Biomarker	Sensitivity	Specificity
Total leukocyte count >11,000 cells/mm ³	79%	55%
C-reactive protein	76%	50%
Granulocyte count/ Polymorphonuclear ratio	29-89% 32-93%	48-94% 46-90%
Interleukin 6 (IL-6)	73%	72%
Serum Amyloid A (SAA)	86%	83%
Riboleukograms	80%	66%
Calprotectin	93-96%	16-54%
Pentraxin-3 (PTX 3)	75-95%	100%
Procalcitonin (PCT)	36%	88%
Urinary 5-HIAA	72%	86%

management and give an idea on the outcomes⁹. It should be user friendly, patient-centred and individualized. The main drawback of these scoring systems are their complexity, which limits its use in basic centres like primary health care center where the junior trainees are employed.

Acute appendicitis is one such surgical condition with multiple scoring systems including the Alvarado score, appendicitis inflammatory response (AIR) score, Adult Appendicitis Score (AAS), Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) score and the Pediatric Appendicitis Score (PAS). The various parameters used in these scoring systems are described in Fig.3. These scoring systems guide the clinician in risk stratification of the patient, decide upon the need for admission and surgical intervention. They also guide in predicting the prognosis or outcome of patients and reduce the medical burden. Although the utility, validity and accuracy of these scoring systems have been studied by researchers, the choice of scoring system used is left to surgeon's discretion.

The Alvarado score was described in the year 1986 and is one of the commonly used scores in clinical practice. The various parameters in Alvarado score is described in Fig 3. The tenderness in the right iliac fossa and elevated counts are given two points each and rest all are given one point each. A score of less than 4 rules out appendicitis but a higher score may not be very specific for the diagnosis of acute appendicitis with a sensitivity of 93.5% and a specificity of 80.6%. Employing Alvarado score in emergency situations reduces prolonged hospitalisation and radiation exposure. It is also the most simple scoring system and can be used at the level of primary care physician. The disadvantage of Alvarado score is that it cannot really differentiate between complicated and uncomplicated appendicitis in elderly and retro-positive patients. It also has low accuracy in pregnant patients especially in first trimester as confounding symptoms such as nausea and vomiting and elevated leucocytes counts are commonly

seen in these patients. In the year 2008 two other scores were reported, the AIR and RIPASA score, both of which have been reported to have better sensitivity and specificity in comparison to Alvarado score. The AIR score is more objective and also incorporates the CRP as one of the parameter, which was studied for a long time as an independent factor for acute appendicitis. The AIR score is the most efficient and most pragmatic score with a sensitivity of 92% and specificity of 63%. The use of AIR score in a study showed lesser number of imaging, admission and negative laparotomy in low-risk patients. The RIPASA score has been reported to have better sensitivity and specificity, and is exclusively designed for the Asian population with various parameters including age, gender, and duration of symptoms. However, a study evaluating its use in Western population reported a sensitivity, specificity and diagnostic accuracy of 85.39%, 69.86% and 80% respectively at the cut-off point of 7.5. At this cut-off point it also has a specificity of 96% in pregnant population but larger studies are

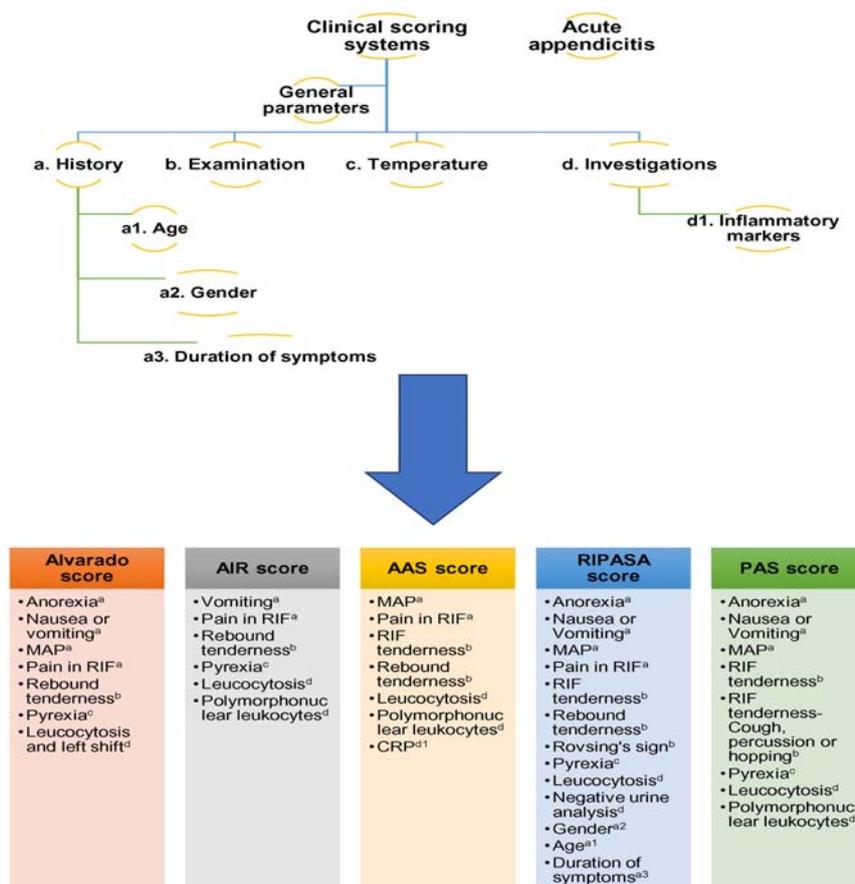


Fig 3 — Various parameters used in different scoring systems
 MAP- Migratory Abdominal Pain; RIF- Right Iliac Fossa; CRP- C-Reactive Protein
 AIR- Appendicitis Inflammatory Response Score; AAS- Adult Appendicitis Score; RIPASA- Raja Isteri Pengiran Anak Saleha Appendicitis Score; PAS- Pediatric Appendicitis Score

recommended for its validation. A reliable stratification is provided by the Adult Appendicitis Score (AAS), which stratifies patients as high, intermediate and low risk. A study on AAS score, reported 93% specificity in high risk patients for the diagnosis of acute appendicitis and its receiver operating curve (ROC) was significantly larger when compared to Alvarado score and AIR score¹⁰. In the recent World Society of Emergency Surgery (WSES) guidelines, the authors recommend an individualised approach for the diagnosis of acute appendicitis based on age, gender, clinical symptoms and signs. The authors also recommend the use of these scores for ruling out appendicitis rather than only diagnosis and also decide upon the need for imaging in patients with intermediate-risk.

The challenge in making the diagnosis in pediatric population is that a reliable history might not be possible in all circumstances, thus a scoring system should be more dependent on clinical signs. The PAS score is one such scoring system exclusively designed for pediatric population which includes the specific signs such as pain in right lower quadrant on coughing, hopping or percussion. Although several studies have validated its use in pediatric population it is also reported to over diagnose appendicitis in 35% of the patients. In preschool age group atypical presentations are common and is reported to have rapid progression and increase complication rates. A study on preschool age group population reported AIR score to have better efficiency in discriminating acute appendicitis in comparison to PAS score and Alvarado score. A recent score, the Pediatric Appendicitis Laboratory Score (PALabS), includes clinical signs, leucocyte counts, neutrophil counts, CRP and calprotectin, has sensitivity of 99.2% at a score of less than or equal to 6. The authors of WSES guidelines recommend a combined approach in children rather using only the clinical scoring systems.

These scoring systems when employed hasten the decision making process and guide if radiological imaging are necessary in the diagnosis and whether the patient needs an urgent surgical intervention. It also aids in reducing the number of negative laparotomies thereby reducing the morbidity and hospital cost. It is important to understand that a single scoring system may not be always accurate and each has its own advantages and disadvantages. Implementing them at lower trainee level in a busy emergency set-up is a challenge which needs to be addressed. Making the scores simpler with the least possible components might increase its wide-spread use. As a clinician it is important to individualize the

diagnostic approach and the use of the scores based on presentation, patient-population and the resources available.

Platelet Indices :

The clinical history, laboratory parameters and radiological imaging may not always yield a reliable result in patients with acute appendicitis in the day-to-day practice. Although the recent focus of research is towards biomarkers, the limitation is the cost and its difficulty in the implementation in the emergent settings. Thus, a need for markers which are cheap, easily available, and non-invasive. These markers should not only diagnose appendicitis reliably, but also should be able to differentiate between complicated and uncomplicated appendicitis. The platelet indices is one such marker which may fulfil these criteria and is now being studied.

Why platelets? Apart from their commonly known functions such as Hemostasis and Thrombosis, platelets play a vital role in the inflammatory response of the body to an invading infection. The activation of platelets lead to a cascade of inflammatory reactions leading to the release of various cytokines, chemokines which alter the cellular level functions. The various platelet indices include mean platelet volume (MPV), Platelet Distribution Width (PDW) and platelet count are the biomarkers of platelet activation. These parameters have been reported to be an indicator of disease severity not only in appendicitis but also in other inflammatory disorders and infectious diseases such as inflammatory bowel disease, rheumatoid arthritis, etc.

Platelet indices — A diagnostic and prognostic marker :

The Mean Platelet Volume (MPV) is a measure of thrombocyte volume and normally ranges from 7.2 to 11.2 femtoliter (fL)¹¹. The platelets have different morphological structure based on their stages of maturity which correlates with their functions. This leads to a heterogeneity in the volume of platelets when compared at the different stages of a disease. The activation of platelets due to inflammation or infection leads to the change in their shape from biconcave to spherical with pseudopod formation and thus, increasing the MPV. The inflammatory cytokines such as thrombopoietin, interleukin 6 and interleukin 3 regulate the megakaryocyte pathway ie, increase their production and thus, play a major role in producing larger number of large platelets. In cases of bone marrow suppression, where production of megakaryocyte is affected, the existing platelets in circulation enlarge in size leading to the increase in

the MPV in response to inflammation. MPV can decrease or increase in response to inflammation thus can act as a negative and positive acute phase reactant. The release of megakaryocyte from the bone marrow in response to high-grade inflammation increases the MPV (increased production and release) whereas, at times the platelets can be sequestered in the vessels where active inflammatory process is present and thereby reducing the MPV (consumption of platelets). Studies link MPV to acute as well as chronic inflammation, where it decreases with acute inflammation and increases in chronic inflammatory conditions. It is associated with sepsis, ankylosing spondylitis, myocardial infarction, unstable angina, pancreatitis, rheumatoid arthritis and Mediterranean fever^{12,13}. It can also be used for evaluation of treatment response in chronic inflammatory conditions such as ankylosing spondylitis and rheumatoid arthritis where the MPV is low during the disease process (due to their consumption in inflammatory areas) and increases in response to the therapy. Sepsis leads to increased cytokine release, bone marrow suppression and endothelial damage leading to an imbalance between the immune and haemostatic pathways. Thus, an elevated MPV indicates poor prognosis in these patients. Platelet Distribution Width (PDW) is an indicator of morphological heterogeneity of platelet size and ranges from 8.3 to 56.6%. It is a distribution curve which indicates the variability in volume in association with its size. The values increase with anisocytosis of platelets. The MPV and PDW in normal physiological conditions change in the same direction but reports from literature are conflicting and suggest that both have different mechanisms. Plateletcrit (PCT) is the measure of volume of platelet in the blood which ranges from 0.22-0.24% and is calculated using the formula $\text{platelet count} \times \text{MPV} / 10,000$. The other platelet indices which are not commonly used in routine practice are the Platelet Larger Cell Ratio (P-LCR), Mean Platelet Component (MPC), Mean Platelet Mass (MPM), Platelet Component Distribution Width (PCDW), and Immature Platelet Fraction (IPF).

P-LCR is the percentage of circulating large platelet i.e., >12 fL in the blood which ranges from 15-35%. It is a marker of platelet activity¹⁴. MPC is the refractive index of platelets which is a marker of platelet activation. The other platelet activation parameters are PCDW and MPM. IPF is the percentage of circulating immature platelets in the blood in comparison to the total platelet population. The various platelet indices and their characteristics have been summarised in Table 3.

Platelet Indices and Acute Appendicitis :

The role of platelet indices in the diagnosis of acute

appendicitis is being studied similar to that of acute cholecystitis and mesenteric ischemia. Most of these data are from retrospective reports and the results of the studies were not uniform and conflicting in some aspects. The predominant parameter used was MPV in the diagnosis of acute appendicitis, and PDW in few studies. Varying results have been documented where most studies reported a decrease in MPV and an increase in PDW, with few reporting an increase in MPV. Few studies also reported no change in MPV in patients with acute appendicitis. Apart from the regular comparison of values of these platelet indices in patients with appendicitis with that of controls, studies have been carried out to find the significant cut-off of these markers for an accurate diagnosis. The sensitivity, specificity and accuracy of MPV with a cut of <7.6 fL was reported as 83.73%, 75% and 83.56% respectively. Boshnak et al reported that an increased TLC (neutrophils) with an increased PDW can be used in the diagnosis of acute appendicitis with a diagnostic accuracy of 77% and 69.5% respectively¹⁵. The authors however suggested that MPV and RDW (Red cell distribution width) levels may not be useful in the diagnosis of acute appendicitis. On the contrary, a systematic review and meta-analysis reported in the year 2017, included 88 studies with a total of 1416 patients of acute appendicitis and 685 controls¹⁶. The authors reported a significant low level of MPV in appendicitis patients in contrast to the controls. Similarly, in a recent systematic review and meta-analysis, the authors concluded that appendicitis patients have decreased MPV but the utility of other platelet indices such as PDW, platelet count needs further research to establish its role in acute appendicitis. Both the meta-analysis reported a high heterogeneity between the inflammatory markers and acute appendicitis, the later reported, sample size, patient age, appendicitis type, sample collection time and study quality to be the factors associated with inconsistent results among various studies. The authors emphasised on the need for further studies on prospective basis with large sample size and considering the association of these factors.

In a summary, although there are several advances in clinical practice in diagnosing appendicitis such as CT, MRI and diagnostic laparoscopy, there are several limitations in the routine use of these investigations particularly in paediatric and pregnant patients and also in rural areas especially in developing countries owing to its cost and feasibility. It is also very difficult to implement them in routine clinical practice as they are time-consuming and there is a need for professionals for their interpretation. Hence, there is a

Table 3 — Platelet indices and their characteristics

Platelet indices	Definition	Units	Normal Value	Uses in clinical practice
Mean platelet volume (MPV)	Measure of the average size of platelets in circulation	Femtolitre (fL)	9.4-12.3 fL	High- ITP, myeloproliferative diseases, Bernard-Soulier syndrome Low- Aplastic anemia, inflammatory bowel disease
Platelet distribution width (PDW)	Measure of platelet anisocytosis	Percentage (%)	8.3-56.6%	High- Acute cholecystitis, ST elevation myocardial infarction Low- Non-malignant tumors
Plateletcrit (PCT)	Product of MPV and platelet count; Volume of circulating platelets	Percentage (%)	0.22-0.24%	High- Acute cholecystitis, Crohn's disease Low-ITP
Platelet large cell ratio (P-LCR)	Percentage of circulating large platelets measuring over 12 fL	Percentage (%)	15-35%	High- ITP Low- Myeloid insufficiency
Mean platelet component (MPC)	Measure of mean refractive index of the platelets- intrathrombocytic protein concentration	Gram per decilitre (g/dL)	21.5-30.5 g/dL	Myelodysplastic syndrome
Mean platelet mass (MPM)	Calculated from the histogram of platelet dry mass	Picogram (pg)	-	Platelet activation marker
Platelet component distribution width (PCDW)	Measure of platelet shape variability	Gram per decilitre (g/dL)	-	Platelet activation marker
Immature platelet fraction (IPF)	Percentage of immature platelets	Percentage (%)	1.1-6.1%	Low- Thrombopoiesis

need for simple, cost-effective, commonly used parameter which can be interpreted without the need of expertise. Considering the lack of evidence from prospective studies, there is a need for a large population-based cohort study or a well-structured and planned randomised control trial to establish the role of inflammatory markers in the diagnosis of acute appendicitis. It is also important to note that a single parameter may not be accurate for the diagnosis, a combination of commonly available markers proven to have a role in acute appendicitis can be used in order to increase the accuracy. The overall aim is to improve the diagnosis of acute appendicitis and reduce the negative appendectomy rate even in primary health care facility and low-volume centres.

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Review Article

COVID Management and Prophylaxis among Rural, Hilly and Tribal Population of India

Surya Kant¹

The Covid-19 pandemic has been around us for more than a year now, with millions of confirmed cases and related deaths around the World.

Recently, during second wave in India we observed a large number of infected cases with high mortality and scarcity of health infrastructure and manpower. The worst hit states were Rajasthan, Maharashtra, Uttar Pradesh, Karnataka, Andhra Pradesh and Kerala.

The uncertainty and hopelessness of the disease is more exaggerated in remote rural, hilly and tribal areas of our country because of scarcity and inefficiency of health care facilities.

A streamlined treatment and prophylaxis protocol is the need of the hour. Uttar Pradesh was the first State in India that issued a Government order for Ivermectin prophylaxis to household contacts, health care workers and to treat mild to moderate cases of Covid-19 with combination of Ivermectin and Doxycycline.

This author was one of the external experts who was behind the formulation of this Government order. He further observed the miraculous effect of combination of ivermectin and doxycycline which became the backbone of the treatment protocol designed by him for the people living in remote areas of the country. Author's concept is just the simplified version, mainly based on Indian Council for Medical Research (ICMR) protocol and the Government order issued by Uttar Pradesh which is more applicable and feasible and accessible in such resource poor localities of our country.

Author's strategy for such areas is simply based on COVID symptoms and pulse oximetry measurement to diagnose, categorise and treat the mild and moderate cases of COVID. This innovative strategy can be very helpful for rapid and prompt treatment of Covid-19 in remote areas considering the scarcity of COVID testing, health infrastructure and difficult connectivity and transport facilities in these areas.

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Key words : Covid Treatment, Rural, Hilly, Tribal, Remote Areas.

The coronavirus disease 2019 (Covid-19) is a global pandemic that was first detected in China in December, 2019.¹ The pandemic affected around 200 countries² with number of cases reported globally now exceeding 180 million till now³. The virus is rapidly changing and new variants being discovered. The second wave of this deadly disease emerged with new mutant variant with higher virulence and higher mortality⁴. Newer strains are not only more transmissible but also affect the younger population. Presentation with unusual symptoms, higher rate of infections among younger people and an exponential rise in daily cases leading to delayed RTPCR test reports, have been seen in the second wave of COVID.

India was among the badly hit countries by the second wave, with more than 3 crore confirmed cases and around 4 lakh total deaths.⁵ The two main

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Editor's Comment :

- Health Infrastructure, healthcare facilities, and healthcare workers are very poorly available in rural, hilly, tribal remote areas of India hence presumptive covid diagnosis based on symptoms only and monitoring of Oxygen saturation by Pulse Oximeter is a key diagnostic approach in these remote areas, Covid 19 treatment strategy based primarily on ICMR Protocol and Ivermectin-Doxycycline regimen can be the best strategy for Covid-19 treatment in the remote areas.

challenges faced by India in fighting the pandemic are the population size and poor healthcare infrastructure.

Furthermore, there is vast diversity in the availability of healthcare facilities between rural and urban India. There are approximately 7 lakhs villages across India and around 70% of Indian population lives in rural areas with scheduled tribes contributing to 11.3% of the total population of rural areas and 2.8% of urban areas.⁶ There is only a single health care centre at every 40 kms and that too mostly with no oxygen beds and with untrained staff and doctors. There is scarcity of

qualified medical professionals in this region with a shortfall of 11.6% of medical officers at the primary health care level and 81.2% of medical specialists at community health centres as reported in 2016.⁷ The doctor-patient ratio of 1:1445 is way less than the ratio suggested by the World Health Organisation (WHO) in this regard (1:1000)⁸. Furthermore, this ratio is even lesser in villages and tribal areas. Transportation facilities are poor, making access to medical facilities even more difficult. Providing health care to people in rural areas is thus the biggest task faced by the country which worsens with pandemics such as Covid-19. The relocation of the urban crowd to small towns and villages post-lockdown led to a surge in rate of COVID infection in rural India.

Challenges for Covid Management in Rural, Hilly and Tribal areas :

It has been reported in May 2021 that rural districts accounted for almost 50 percent of all new cases in the country and therefore to win the battle against COVID adequate management strategies should be adopted for both prevention and treatment of the disease.

Challenges faced in COVID management of these patients were,

- Scarcity of health care facilities
- Scarcity of healthcare workers including doctors, nurses, paramedical staff (ANM, ASHA worker etc)
- Lack of ambulance services
- Lack of transport and connectivity
- Lack of standards of home isolation, small houses and no attached bathroom facility
- Non availability of medicines
- Lack of COVID health awareness
- Improper information and management system by untrained nonqualified fellows (quacks)

If a fellow residing in these areas complains of symptoms consistent with Covid-19 infection where diagnostic tests like Rapid Antigen Test and RT PCR are not easily accessible, samples are sent to closest town and the reports are always delayed by 4-5 days.

These problems are a hurdle in providing optimum health care facilities to the residents of these areas. Though Government is trying to make test accessible to all, practical scenarios indicate that there is a long way to go.

To overcome this, the author has

come up with a pulse oximeter-based treatment strategy to initiate the basic treatment of Covid-19. Before going into the details of the treatment there are few points regarding the appropriate diagnosis of Covid-19 infection that should be kept in mind. Those patients who have signs, symptoms and /or radiological findings suggestive of COVID with negative RTPCR report are assumed as presumptive COVID.

Author has modified this definition for early detection and prompt management of COVID.

Protocol for pre-sumptive COVID (without waiting for test reports) (Fig 1) :

The author recommends early treatment with a combination of Ivermectin and Doxycycline along with symptomatic and supportive therapy in patients with mild disease who have oxygen saturation above 94 % and early institution of a short course of steroid in patients who have oxygen saturation between 90- 94%.

These patients actually belong to the MODERATE category of COVID infection who are recommended hospitalization according to ICMR protocol (Fig 2) and any delay in instituting treatment in these patients can lead to increase in severity of the disease from MODERATE to SEVERE category which leads to a higher mortality in these patients. This strategy highlights the use of Ivermectin as a frontline drug in the treatment of Covid-19 infection.

Role of Ivermectin in COVID Prophylaxis and Moderate Infection :

There have been more than 100 trials Worldwide for the use of Ivermectin in the treatment of COVID infection. Ivermectin not only has role in treatment but is also useful as a preventive therapy.

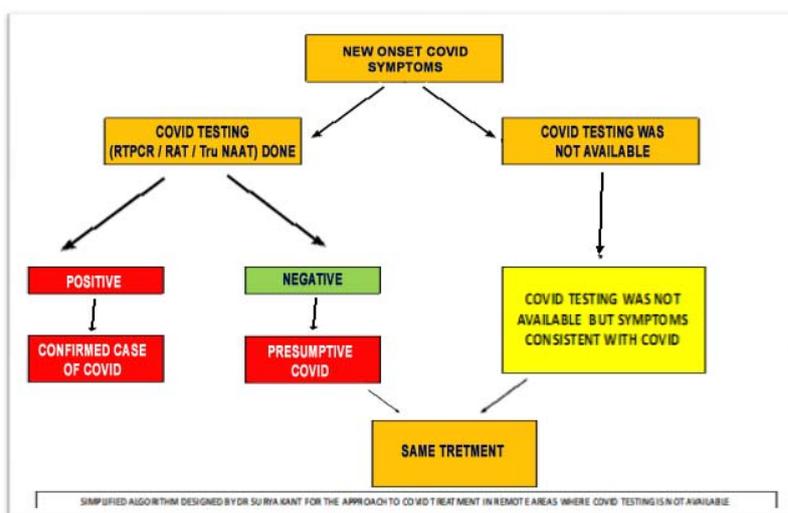


Fig 1 — Simplified algorithm designed by Dr Surya Kant for the approach to COVID treatment in remote areas where COVID testing is not available

An observational study, conducted in a tertiary hospital in Dhaka that enrolled 118 health care workers showed that Ivermectin has a role in Covid-19 prevention as well. Another study done at AIIMS, Bhubaneswar also reemphasized that Ivermectin prophylaxis reduces the risk of contracting COVID infection.

The author was a part of a group of experts, all having enormous clinical experience who gathered and explored the role of Ivermectin, an old molecule in Covid-19 management. After critical panel discussion, they all came to an inference that Ivermectin can be a prospective molecule for prophylaxis and treatment of people infected with Coronavirus because of its Anti-viral activity and good safety profile and tolerability.

Following this White paper on Ivermectin as a potential therapy for Covid-19 came in July 2020 which later also became a part of global literature on coronavirus diseases available on the official World Health Organization webpage.

Later, Government order for prophylaxis of healthcare workers and household contacts along with the order for treatment with Ivermectin and doxycycline was released on 6/8/2020 by the UP Government. Ivermectin in combination with doxycycline has shown to have a synergistic effect in inhibition of spike protein of ACE 2 receptors and therefore the combination used in this protocol is a good choice in prevention and management of COVID infection.

Treatment Strategy based on Symptoms and Oxygen Saturation for Rural, Hilly and Tribal Areas :

A simplified protocol has been suggested here, for patients to whom RTPCR/RAPID ANTIGEN TESTING is not readily available (Fig 3). This simplified protocol can be beneficial for the doctors working at CHCs/PHs for early detection, better management and monitoring of such patients.

- If the oxygen saturation (SpO2) is >94 %: The patient should be isolated and given ivermectin and doxycycline. Symptomatic and supportive treatment should also be provided.^{9,10}

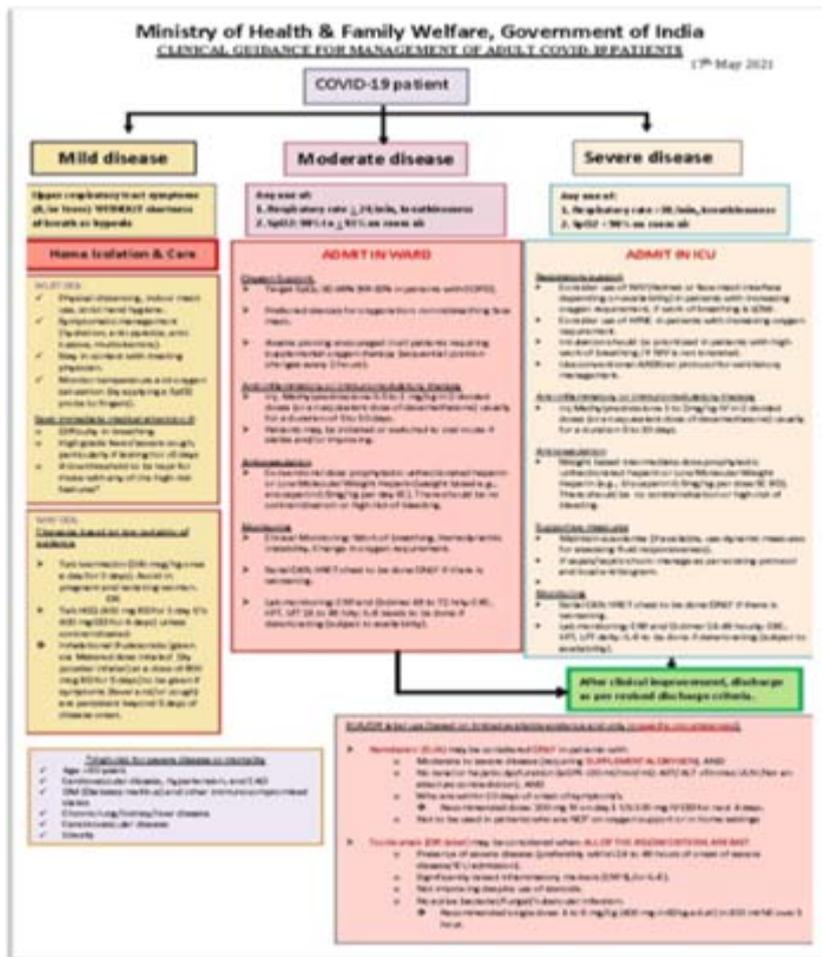


Fig 2 — ICMR/AIIMS COVID 19 Treatment Protocol

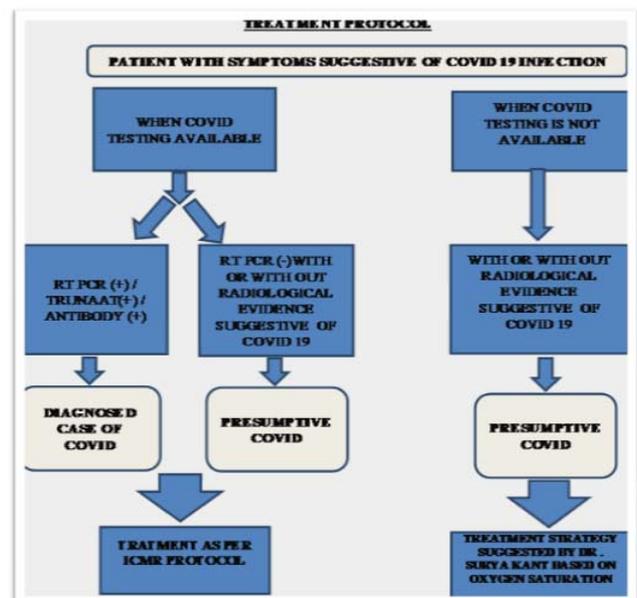


Fig 3 — Treatment Algorithm Based on Clinical Experience

• If the SpO₂ is between 94 to 90 %: The patient should be placed in prone position and steroid can be added to the above treatment regimen after consulting the physician.

• If the SpO₂ is <90%: The patient needs oxygen support/hospitalization

For patients living in villages where COVID testing as well as other diagnostic modalities are readily available, the initial management can still be based on SpO₂ level of the patient (Fig 4). Following stepwise treatment protocol has been suggested:

If the patient is Covid positive or has presumptive Covid (Symptoms/ Chest X-Ray/HRCT Thorax Suggestive of Covid but Covid Test Negative) and the SpO₂ is:

Above 94%

- Isolation
- Ivermectin (12 mg)- two hours after dinner for 5 days
- Doxycycline (100 mg) twice daily after meals for 5 days
- Paracetamol (500 MG), when body temperature is >99°F

Between 94 to 90%

- Isolation prone position
- Ivermectin (12 mg) - two hours after dinner daily for 5 days
- Doxycycline (100 mg) twice after meals for 5 days
- Prednisolone (20mg) one daily after breakfast for 5 days
- Paracetamol (500 mg), when body temperature is >99°F.

The patient should be carefully monitored and hospitalization will be required if SpO₂ falls below 90% or patient develops unconscious-ness, bluish discoloration of lips, tongue, nails, breathlessness or the body temperature does not fall below 104°F.

Currently Available Medications for Treatment of Covid-19:

With no effective antiviral drugs in sight, the repurposing of many currently available drugs has been considered the mainstay of treatment.

Ivermectin was formerly approved as an antiparasitic agent but it has been shown to also exhibit antiviral

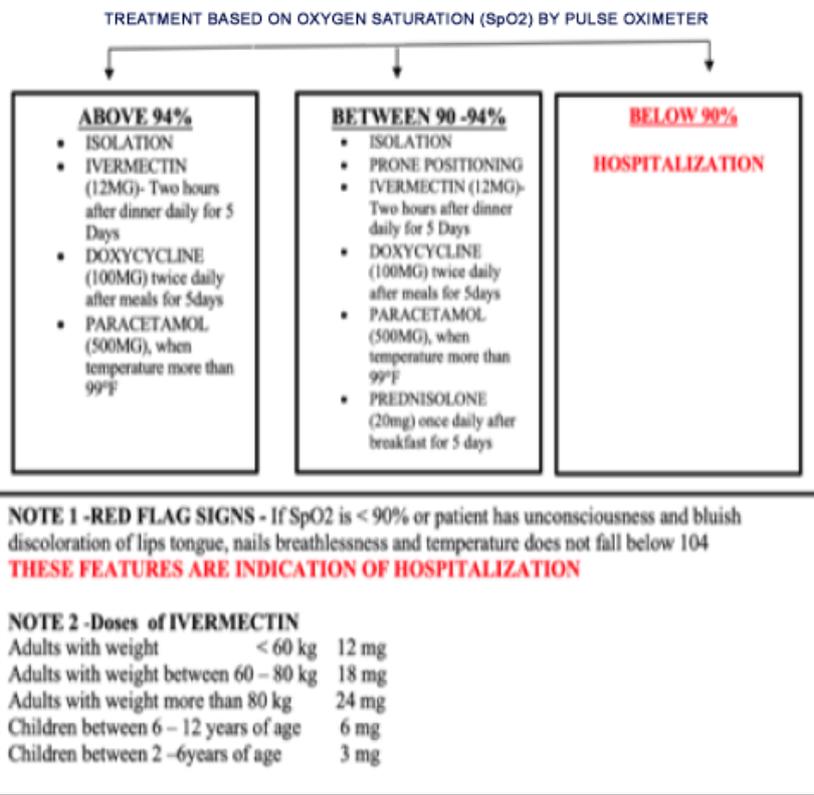


Fig 4 — Treatment Strategy Suggested By Dr . Surya Kant (Based Mainly On ICMR Protocol) For Covid 19 Patients in Rural Population Where Covid Testing is Unavailable

activity against a wide range of viruses. Ivermectin is an excellent composition that has the potential to treat various classes of diseases because it has antimicrobial, anticancer and antiviral properties. Therefore, Ivermectin is investigated and studied to be used in the treatment and prophylaxis of Covid-19 as well because of its multidimensional mechanism of action including inhibition of viral replication, blockade of the entry of the virus into the host cell, action as an ionophore molecule, and prevention of microvascular thrombosis.¹¹

Uttar Pradesh was the first State in India to use Ivermectin. Government order of UP Government for the use of Ivermectin in treatment and prevention of Covid-19 was released on 6/08/2020 and since then it has been adopted in treatment and prevention of the disease in various States of India — West Bengal, Maharashtra, Karnataka, Kerala, Assam and Goa. Goa Government recommended a new Covid-19 treatment protocol which endorses prescription of five tablets of the Ivermectin to all residents >18 years of age in order to prevent the steep and sometimes fatal viral fever, which accompanies a Covid-19 infection.

The recommended dose of Ivermectin in adults with

body weight <60 kg is 12 mg/day, weight between 60 to >80 kg is 18 mg/day and for those with weight >80 Kg, it is 24 mg/day. Children in between 6 to 12 years of age can be 6 mg/day.

Doxycycline : Doxycycline is a broad-spectrum antibiotic class which is used in treatment of various bacterial infections like community acquired pneumonia, acne, chlamydia infections, Lyme disease, cholera, typhus and syphilis. It has an established safety profile with a potential efficacy against viral pathogens leading to dengue fever and chikungunya therefore, it may regulate pathways important in initial infection, replication, and systemic response to SARS-CoV-2. Ivermectin-Doxycycline vs Hydroxychloroquine-Azithromycin in mild to moderate cases [Bangladesh Study] showed that Ivermectin – Doxycycline to have a faster rate of recovery.¹²

Steroids: Covid-19 is a multisystem inflammatory disease and not just a disease confined to the lungs. Covid-19 triggers an hyperinflammatory response in the form of cytokine storm which is often lethal and is the main reason for increasing mortality in these patients. These deleterious effects can be prevented or mitigated by Anti-inflammatory effects of corticosteroids. The Randomised Evaluation of Covid-19 Therapy (RECOVERY) trial in patients admitted to hospitals with Covid-19, that the mortality from Covid-19 was lower among patients who received Dexamethasone than among those who were given the standard of care¹³.

Isolation in Rural Setup for COVID Patients :

It is important to isolate the patient to reduce the risk of infection spread. If dedicated COVID Care Centres are available in rural areas, the patient should be kept there under the observation. If not, following method of home isolation should be followed:

- People having only one room should use that room as isolation room and rest of the members should sleep outside in the portico area outside the house.
- The patient using the common washroom should sanitize it with commercially available sanitizer (if available) or 1% Hypochlorite solution (if available) or simply soap water can be sprayed for sanitization.
- Other family members should use bathroom after 3hours as virus remains in air for 3 hours. This will reduce the chance of other members getting infected.
- All members of the house including the patient, should use mask at the time of using washroom and should sanitize before and after using washroom.

For the monitoring of patients, we can use the services of ASHA workers. ASHA workers should be

sensitized about the symptoms and basic management of the COVID disease when it is in mild form and to identify the Red Flag Signs (Box). They should visit the patient twice in a day and monitor their oxygen saturation level and inform the doctors at nearby CHCs/PHCs. They should also take with them glucometer and monitor random blood glucose levels of diabetic patients. ASHA workers should also inform about any Red Flag Signs to doctors immediately, thus speeding up the transfer of such patients to hospital facility.

RED FLAG SIGNS

1. PERSISTENT FEVER
2. BREATHLESSNESS
3. DECREASING OXYGEN SATURATION
4. INCREASED BREATHLESSNESS
5. UNCONSCIOUSNESS
6. BLUISH DISCOLOURATION OF LIPS, TONGUE OR NAILS

Role of ASHA workers :

Since community participation is an irreplaceable strategy for strengthening of health system in a densely populated country like India, a new cadre of community health volunteers [Accredited Social Health Activists (ASHA)] was created across all villages in India with a goal of increasing community engagement with the health system. ASHA worker is primarily a woman resident of the village preferably in the age group of 25 to 45 years and her services are of prime importance for managing the diseased and suspected cases of COVID. In order to properly avail their services ASHA workers should be sensitized about the symptoms and basic management of the COVID disease specially when it is in its mild form so that the disease can be nipped in the bud (Fig 5). She should be fully aware of her responsibilities which are as follows -

- ASHA worker is responsible to take pulse oximeter and glucometer door to door with her to screen for suspected COVID patients.
- Send a photograph of patient's oxygen saturation and random blood sugar to the doctors available at the PHC/CHC so that they can advise appropriate treatment and take an informed call for starting steroids in a patient.
- She should provide a detailed information about the Red Flag Signs of COVID infection.
- She should provide her contact number to the family and tell them to report if they notice any red flag signs in their family members.

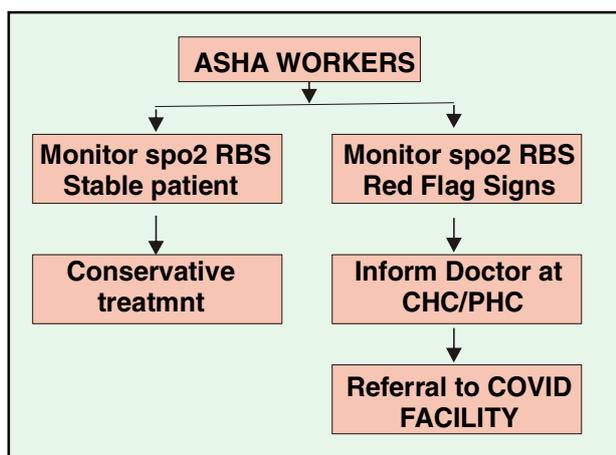


Fig 5 — Role of ASHA Workers in Management of COVID patients (Endnotes)

- If Red Flag Signs are noted in any member of the village she should immediately inform the doctors at the PHC/CHC.
- She is responsible for the arrangement of safe transport of the sick patient to the nearest PHC/CHC.
- If none of the Red Flag Signs are noted in a COVID patient then he should either be isolated at isolation centres established in the village or be in home isolation.
- ASHA workers also have the responsibility to inform the Gram Pradhan of the respective village about the number and health status of COVID patients in his village so that accordingly he can help to arrange for any emergency services such as ambulance for the patients.

PROTOCOL FOR COVID-19 PROPHYLAXIS IN VIEW OF UPCOMING THIRD WAVE

In a densely populated country such as India, with a population of around 1,39 billion people, just treatment doesn't suffice. Prophylaxis is needed to arrest the spread of COVID cases.

Ivermectin is not only a potent antiviral agent but also an effective drug for prophylaxis of Covid-19 infection. It possesses potent antiviral properties and also helps in eliminating parasitic diseases — by mass administration that too with negligible side effects and cost.

A systematic review and meta-analysis of 24 RCTs (n = 3328) showed that ivermectin treatment reduces inflammatory markers, achieves viral clearance more quickly and improves survival compared with standard of care. This was especially so in mild/moderate patients, with stronger viral clearance at higher doses and longer durations of treatment. There was a 70%

improvement in survival in the subgroup of mild/moderate participants¹⁴.

Another meta-analysis based on 18 randomized controlled treatment trials of ivermectin in Covid-19 has found large, statistically significant reductions in mortality, time to clinical recovery, and time to viral clearance¹⁵.

Efficacy of ivermectin in Covid-19 is supported by evidence from clinical trials in animal models and humans. It has been seen that Ivermectin prevents transmission and development of Covid-19 disease in those exposed to infected patients. It hastens recovery and prevents deterioration in patients with mild to moderate disease treated early after symptoms. Ivermectin leads to temporally associated reductions in case fatality rates in regions after ivermectin distribution campaigns¹⁵.

Uttar Pradesh was the first state that released a Government order, with the author as one of the experts involved in formulation, for Ivermectin prophylaxis in household contacts and health care workers way back in August 2020, followed by Karnataka, Kerala, Rajasthan and West Bengal.

Vaccination along with mass prophylaxis with ivermectin are the only means of safe guarding the population from the tide of the upcoming waves of COVID.

Strategy for mass prophylaxis to general population (based on extrapolation from a study done in Bangladesh for weekly prophylaxis with Ivermectin)

Dose of Ivermectin recommended for mass prophylaxis by the author is as follows

- **2-6 years of age: Ivermectin 3 mg once weekly**
- **6-12 years of age: Ivermectin 6 mg once weekly**
- **More than 12 years of age: Ivermectin 12 mg once weekly**

DISCUSSION

The medical practitioners in rural areas are the first contact person where patients present with symptoms suggestive of Covid-19 infection. However, the knowledge about the disease is rapidly changing and with growing number of cases, the healthcare providers in these areas are not often adequately trained and equipped to deal with these infections¹⁶. Thus, there is a need of handy guideline that would aid the diagnosis and management of Covid-19 infection at the level of first contact of the patients in rural India.

In this simplified treatment protocol that has been proposed, SpO₂ measurements using pulse oximeter,

which is readily available and does not require specialized training, is the only requirement. Before the confirmatory diagnosis is made using the Rapid Antigen Test or a RT-PCR, treatment can be initiated using this protocol that includes Ivermectin. While repurposed antimicrobials such as, hydroxychloroquine, lopinavir/ritonavir, remdesivir and interferon-beta have shown no significant survival benefit, ivermectin has shown benefits in mild/moderate disease and subsequent survival¹⁴. Use of this protocol before getting a confirmatory result would prevent aggravation of the disease for the lack of proper management and also help decreasing the healthcare cost to certain degree.

Involvement of the local Non-governmental Organizations like ASHA workers is also vital to boost up the human resource dearth that the country is facing. Educating people to recognize the symptoms and seek support and treatment whenever necessary is equally important. It should be noted that rural India often lives in houses that does not have more than 1 room, the washroom used is also common. In such situation, isolation and social distancing are distant reality. Measures to overcome these issues should also be brainstormed; opening more isolation centres for the infected may help to deal with this issue.

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Case Report

Percutaneous Transluminal Coronary Angioplasty in a COVID-19 Positive Patient with Dextrocardia : A Case Report

Sagarjyoti Roy¹, Abhijit Girish Borse¹, Arunava Mitra², Tirthankar Roy¹, Palash Kumar Mondal³, Kanak Kumar Mitra⁴

Percutaneous Transluminal Coronary Angioplasty (PTCA) is technically challenging in Dextrocardia patients due to inverted orientation of the coronary arteries. We report a case of acute Anterior Wall Myocardial Infarction (AWMI) in a 54 years old male patient with Dextrocardia with COVID-19 positive status, managed successfully with coronary angioplasty & stenting of Left Anterior Descending Artery (LAD) via right femoral route.

[J Indian Med Assoc 2021; 119(9): 70-1]

Key words : Dextrocardia, Percutaneous Transluminal Coronary Angioplasty, Anterior Wall Myocardial Infarction, COVID-19.

Dextrocardia defined as anomalous position of the apex of heart to the right side¹ of the thorax with right sided base to apex cardiac axis. This is a very rare anomaly, accounting for 1 in 10000 live births¹, commonly associated with Situs Inversus Totalis. Usually having no other cardiac anomaly (excepting 3%)² and leads normal life. The incidence of Coronary Artery Disease (CAD) is same as that of general population in these patients. But Percutaneous Coronary Intervention (PCI) in such patients becomes challenging due to the inverted orientation of the coronary arteries. We report a case of mirror image Dextrocardia who presented with acute anterior wall myocardial infarction with COVID-19 positive status, underwent successful angioplasty & stenting of Left Anterior Descending Artery via right femoral approach using conventional hardware.

CASE REPORT

A 54 years non diabetic, non-hypertensive and chronic smoker male patient presented to our emergency with severe retrosternal and right sided chest pain of 10 hours duration. On admission, pulse was 90 bpm and BP was 110/70 mm Hg. Physical examination revealed right sided apex and first & second heart sound were better audible in the right side of chest. The ECG finding were inverted P&R-waves in leads I and aVL and prominent S-wave, with non-progression of R wave in the left precordial leads along with ST elevation in V1 and V2, suggestive of Dextrocardia & possible Acute Coronary Syndrome (ACS). Repeat ECG done with lead reversal;

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Editor's Comment :

- Dextrocardia with situs inversus totalis is a rare, relatively benign congenital anomaly.
- Acute Coronary Syndrome Including acute myocardial infarction can occur in these patients as in normal population. But it poses a diagnostic dilemma in the interpretation of ECG, as well as challenge in doing Percutaneous Coronary Intervention, due to mirror image disposition of coronary arteries. However, proper physical examination, and C-Xray & echocardiography will help the diagnosis.
- Good interventional knowledge and skill can overcome this interventional challenge.

unmask ST elevation in V1, V2, V3R and V4R. Troponin T test was positive. Echocardiography shows hypokinesia of anterior wall of left ventricle with moderate LV systolic dysfunction (LVEF-40%). The typical ECG changes, C-Xray, Echocardiography & positive Troponin T test confirm the diagnosis of Acute Anterior Wall Myocardial Infarction with mirror image Dextrocardia with Situs Inversus Totalis (Figs 1A & 1B).

Due to unknown Covid status, as per institutional protocol we adopted pharmaco-invasive strategy. Thrombolysis was done with Tenecteplase and initial standard conservative management was given. Next day patient was detected to be Covid-19 RTPCR positive & shifted to COVID CCU ward in a stable hemodynamic state with SpO2 98% and was conservatively managed as per Covid protocol along with optimal medical management of STEMI. On the 11th day Covid RTPCR was negative. Then the patient was transferred back to Cardiology Ward due to several episodes of rest angina and Coronary Angiography & Revascularisation was planned. Coronary Angiography done through traditional right femoral approach. The Left Main Coronary Artery (LMCA) arising from anatomically right sided left coronary sinus was engaged with 6F Judkins Left (JL) diagnostic catheter, using clockwise rotation. The Right Coronary Artery (RCA) arising from anatomically left sided right coronary sinus was engaged with great difficulty with 6F



Fig 1 — (A) ECG showing inverted P&R -waves in leads I and aVL, upright P-wave with prominent R-wave in aVR and prominent S-wave with non-progression of R wave in the left precordial leads along with ST elevation in V1 and V2. With reversed lead position unmasking ST elevation in V3R & V4R suggestive of dextrocardia with anterior wall myocardial infarction. (B) CXRAY showing heart in the right hemithorax.

Judkins Right (JR) diagnostic catheter giving counter clockwise rotation. Images were acquired in RAO & LAO mirror image angiographic angles. Angiography showed 95% critical ostio proximal lesion in LAD & 60% to 65% intermediate lesion in mid RCA. Angioplasty with stenting of LAD lesion (culprit artery) was decided. The LMCA was engaged with 6F JL guide catheter. The lesion was crossed with a Run-through Floppy PTCA wire. The lesion was pre-dilated with 2 X 10 mm balloon. Then a 3.5 x 24 mm Everolimus eluting Platinum Chromium stent (PROMUS ELEMENT) was deployed across the LAD lesion. The stent was post dilated with 4 x 10 mm non-compliant balloon with achievement of TIMI-III flow. Patient was haemodynamically stable during and after the procedure with relief of chest pain. The post procedure hospital stay of the patient was uneventful and the patient was discharged after 3 days and planned for FFR/ischemia guided PTCA of the residual intermediate lesion of RCA (Figs 2 & 3).

DISCUSSION

Dextrocardia with situs inversus is a very rare condition occurring in 1 in 10,000 population. The first cardiac catheterisation on a Dextrocardia patient was done in 1973³ and the first angioplasty was done in year 1987⁴. PTCA in such patients is very difficult and technically challenging due to inverted orientation of coronary arteries, difficulty in engagement of sinuses with standard catheters & difficulty in image acquisition in standard views. Initially multipurpose catheters were used but later on successful PTCA were performed using standard coronary catheters. To overcome these difficulties, technique of reverse torque for engagement of the catheters & image acquisition in the mirror image angles are being adopted. Goel *et al* have suggested double-inversion technique⁵, which involves right/left image reversal, to obtain normal angiographic images in patients with dextrocardia, thereby leading to easier

interpretation of images in such patients.

We did the successful PCl using standard diagnostic and guide catheters and adopting mirror image views via conventional right femoral approach. There are very few reports of successful PCI in dextrocardia patients in both Indian & world literature. Probably our case was done first in a post Covid status patient.

CONCLUSION

STEMI in situs inversus Dextrocardia poses diagnostic



Fig 2 — Coronary angiography in Right Anterior Oblique Caudal view showing osteo- proximal lesion in LAD



Fig 3 — Left Anterior Oblique Cranial view showing the final result post angioplasty and TIMI-III flow in LAD

challenges in initial ECG interpretation, as well as technical challenges for performing PCI due to abnormal anatomy. This can be overcome by reverse torque technique of catheter engagement and adopting any special image acquisition protocol.

Limitation of Study : Post Covid status of the patient deferred the scope of early intervention as per prevailing protocol.

Conflict of Interest Statement : All authors unanimously declare no conflict of interest.

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Case Report

Laparoscopic Cholecystectomy and Choledocholithotomy and T-tube Drainage In Mirizzi's Syndrome Type I in a Case of Situs Inversus Totalis

Biswarup Bose¹, Subhadip Sarkar², Banyeswer Pal²

A male patient aged 41 years had a history of epigastric pain few times with occasional vomiting for few months. There was no history of Jaundice. On Ultrasonography (USG) abdomen imaging, the left sided Gall Bladder with stones and dilated Common Bile Duct (CBD) was diagnosed. USG confirmed Situs Inversus. Chest X-ray showed Dextrocardia to establish Situs Inversus Totalis (SIT). Subsequent MRCP confirmed Gall Bladder (GB) Stones with a single CBD calculus at its lower end in approximately 10mm dilated CBD in a SIT patient. Pre-operative Liver Function Tests and coagulation profile were within normal range. There was no comorbidities.

Mirror image ports of regular Laparoscopic Cholecystectomy were made with few modifications. In French position the Surgeon standing in between the legs of the patient makes better hand eye coordination. Interchanging the fundal traction instrument and the needle holder between the left mid-clavicular and left anterior axillary line port helps ergonomically better for endo suturing while closing the Choledochotomy.

In our case, apart from Gall Bladder calculi and Common Bile Duct (CBD) calculus, patient had Mirizzi's Syndrome Type I. The patient went home after uneventful recovery. No publication was found on reviewing literature in PubMed & Medline search about Laparoscopic Cholecystectomy with Choledocholithotomy with Mirizzi's Syndrome Type I in a case of SIT.

[J Indian Med Assoc 2021; 119(9): 72-4]

Key words : Situs Inversus Totalis, Mirizzi's Syndrome Type I, Common Bile Duct Calculous, Laparoscopic Choledocholithotomy and Cholecystectomy.

The first reported Situs Inversus Totalis (Dextroversion) was in 1600 by Fabricius¹. First described Left sided Gall Bladder was in 1886 by Hochstetter². Left sided Gall Bladder is a very rare entity. SIT is found in 1 : 10,000 - 1:20,000 of the population³ whereas Sinistro position of Gall Bladder is more rare. In Situs Inversus, the left sided Gall Bladder can be diagnosed preoperatively. In Sinistro position of Gall Bladder, it is usually discovered during the Surgery for Gall Bladder. The patient GB and CBD stones with SIT has been successfully operated Laparoscopically in four cases published earlier of which one underwent Choledochoduodenostomy⁴⁻⁷. Our case had Mirizzi's syndrome type I with GB and CBD calculus in SIT. Laparoscopic Cholecystectomy has been accepted as the Gold Standard care universally. So the primary approach towards the case was Laparoscopic.

CASE REPORT

A male patient of 41 years attended the hospital with complains of pain epigastric region for few months with occasional vomiting. There was no history of Jaundice. Ultrasonography of abdomen revealed Cholecysto-

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Editor's Comment :

- Situs inversus totalis patients with Gall stone disease with or without CBD calculus and associated other anomalies can be operated successfully by MAS in experienced hands with some modification in port positions.

lithiasis with 8.2mm dilated CBD in a case of SIT. Liver function test and coagulation profile was within normal range. Chest X-ray revealed Right Sided Heart (Fig 1). The patient was not having any other Comorbidities. MRCP confirmed SIT with contracted Gall Bladder with calculi and a 7mm calculus in a 10mm dilated CBD (Fig 1). The Patient was sent twice to two different Gastroenterologist for ERCP CBD clearance prior to Laparoscopic Cholecystectomy. Both times the attempts failed with comments of Inability to cannulate the CBD due to congenital anomaly. It was decided to perform Laparoscopic Choledocholithotomy followed by Laparoscopic Cholecystectomy.

Written consent for possible conversion of the procedure from Laparoscopic procedure to open was taken after informing the congenital anomaly. The patient under general anaesthesia with endotracheal intubation, was supine with 20 degree Anti-Trendelenberg position with approximately 20 degree right tilt. In French position, the Surgeon stood in between the patient's leg with the monitor at patient's head end. Four mirror image of Standard ports were made on left side with exception of

the left mid-clavicular port, which was made 10mm. The Epigastric port was made a bit at lower level with 12mm Optiview disposable Trocar (Fig 6). The Gall Bladder was having features of Chronic Cholecystitis with Mirizzi's Syndrome Type I. It was decided to perform a reconstituting partial Cholecystectomy. Following posterior dissection, an extra-corporeal number one vicryl was placed through the epigastric port to have a traction at the neck of the Gall Bladder. Cystic artery was dissected and isolated and doubly clipped and transected. Choledochotomy was performed with an endo-knife. Intra Operative Cholangiogram (IOC) done through Choledochotomy due to conglomeration of calculi in Mirizzi's Syndrome Type I (Fig 5). A4F1.5cc capacity Fogarty catheter was introduced through the epigastric port to introduce in Choledochotomy (Fig 3) downwards in duodenum. The bulb was inflated with 1cc water and pulled until a resistance was felt where it was deflated. The catheter was withdrawn for approximately a centimetre and was re-inflated to avoid damage to the Sphincter of Oddi. The inflated Fogarty catheter was gradually withdrawn through the Choledochotomy. This manoeuvre extracted the solitary calculous (Fig 4) from the lower CBD, which was retrieved. Similarly, Fogarty excluded any possibility of stone upstream. The CBD was thoroughly irrigated with normal Saline. A repeat IOC done to confirm CBD clearance (Fig 5). A T-Tube was placed and the CBD closed with 000 vicryl continuous endosuture.

The Gall Bladder was opened at the lower end of the body to clear all the calculi followed by application of



Fig 1 — Dextrocardia
Chest X-ray



Fig 2 — MRCP showing lower
CBD calculus



Fig 3 — Fogarty catheter through Choledochotomy

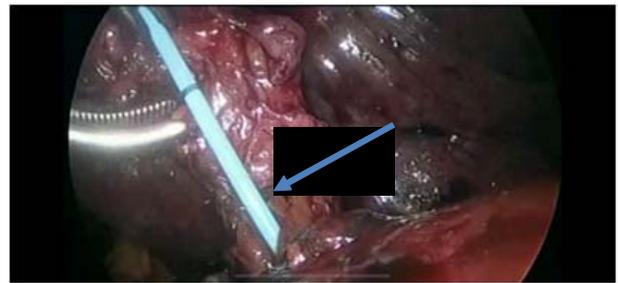


Fig 4 — CBD calculus extracted (arrow)

extracorporeal Roeder's knot with 1 vicryl at the infundibulum. A tube drain kept in the sub hepatic space. The T-Tube was brought out from the left mid clavicular port and the abdominal drain through left anterior axillary port. Postoperative recovery was uneventful. Drain removed after 72hrs. A T-Tube Cholangiography (Fig 7) was performed on the 10th postoperative day. It showed complete clearance of the CBD. On request of the patient and his relatives (due to apprehension of necessary ERCP, which twice failed, for retained stones), postoperative MRCP (Fig 8) was performed which also confirmed CBD clearance, following which the T-Tube was removed. The patient was discharged after uneventful recovery.

DISCUSSION

The first successful left sided Laparoscopic Cholecystectomy was reported in the year 1991⁸. Left sided Gall Bladder are of two different variant (A) In Situ Inversus (B) Sinistro position (mal-position) of Gall Bladder. Sinistro position of Gall Bladder can be subdivided into two on the basis of embryological hypothesis² (a) Gall Bladder migrates to the left lobe of the liver but the cystic duct remains in its normal position crossing the CBD in front. (b) Here Gall Bladder starts developing on both sides. The left one continues developing while the right sided Gall Bladder atrophies. In such case cystic duct either joins common hepatic or left hepatic from the left side. The symptoms in Sinistro position of Gall Bladder develops on the right side as it is believed that there is no transposition of the visceral nerves. Even imaging investigations are misleading. In Sinistro position, the Left sided Gall Bladder is diagnosed commonly during surgery⁹. In SIT, symptoms develop on the left side. Imaging investigations can confirm left sided Gall Bladder.

To perform Laparoscopic choledocholithotomy to extract the stone in SIT, few modifications were made. The epigastric 12mm Optiview disposable Trocar port was made a bit lower than the usual position. This helped to manipulate the Fogarty Catheter easier to introduce in the CBD along with a Maryland without gas leak to extract the stone. Moreover, the 10 to 5 reducer was not required while endo suturing. The guide wire of the Fogarty catheter was previously removed for easy maneuver. The left mid-clavicular port was also a 10mm at a lower level than the usual port position on the right side. This port eased the

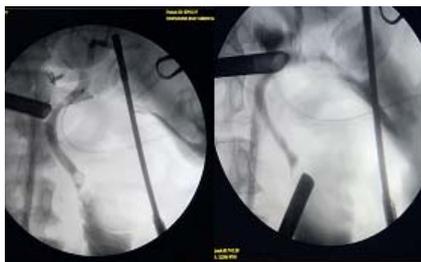


Fig 5 — Pre & Post IOC showing calculous and clearance

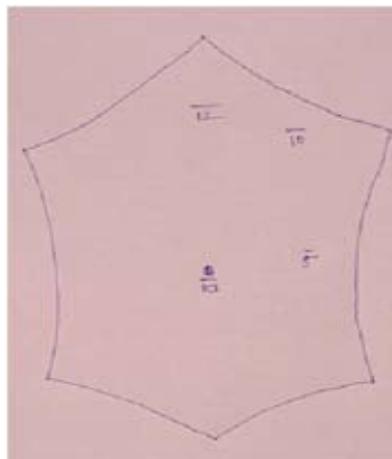


Fig 6 — Port positions

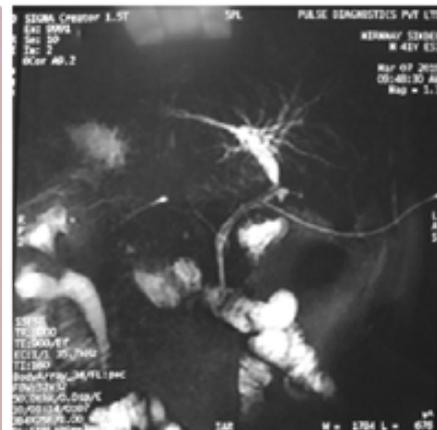


Fig 8 — Postop MRCP with T-tube in situ shows clear CBD



Fig 7 — T-tube Cholangiography & showing clear CBD

The needle holder introduced through the left anterior axillary port helped for better ergonomic control of suturing being right handed person. The Surgeon stood in between the patient's legs of the patient (French Position).

ERCP twice failed not due to the difficulty in extracting the CBD calculous but due to inability to cannulate an anomalous duct. That is why a T-Tube was kept for any accidentally slipped calculous in CBD needs to be removed later through the T-Tube tract.

CONCLUSION

Few modifications in the position of the Patient, Surgeon position, placement of Monitor, selection of Trocar and adjustment of the Port positions, Laparoscopic Choledocholithotomy as well as Left Sided Laparoscopic Cholecystectomy can be done safely with a better ergonomic control. Pre & Post stone extraction IOC can confirm the clearance on table. Roedor's knot at distal Gall Bladder could have been replaced by endo-suture closure

Conflict of Interest : There was no conflict of Interest.

Acknowledgement : We are grateful to Prof Siladri Sengupta of our Department, for transferring the patient under us for Laparoscopic approach.

Consent : Written consent from the patient was taken after informing him about his rare Congenital anomaly. The consent also included that Laparoscopic approach shall be adopted which may be converted to open if

application of the clip with 10mm clip applicator in cystic artery and was also used later for maintaining the fundal traction while suturing the Choledochotomy

necessary. Consent for necessary video recording & publication of the case was also taken.

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Case Discussion in Urology

Case Based Discussion on Benign Prostatic Hyperplasia (BPH)

Sandeep Gupta¹

Benign Prostatic Hyperplasia (BPH) has been historically used to define a disease characterized by symptoms of urinary dysfunction as a consequence of an obstacle to micturition caused by an enlarged prostate. Recently, BPH has been referred to a histologic diagnosis characterized by the proliferation of smooth muscle and epithelial cells within the transition zone of prostate. LUTS (lower urinary tract symptoms) are considered as a clinical manifestation with multifactorial pathophysiology including prostatic and non-prostatic etiology. The proper diagnostic assessment of men with LUTS represents a major issue in the everyday clinical practice. The workup should aim at evaluating severity of symptoms and their impact on quality of life so that severity of disease, response to therapy and risk of disease progression could be assessed. IPSS (international prostate symptom score) is currently considered the international standard tool to investigate LUTS severity. Based on the IPSS, the treatment of BPH can differ for each patient. Here, we present some case-based discussion of BPH at each stage of disease and how the treatment of each case differs from each other case.

[J Indian Med Assoc 2021; 119(9): 75-7]

Key words : BPH, LUTS, IPSS.

Benign Prostatic Hyperplasia (BPH) is a pathologic process characterized by an increased number of epithelial and stromal cells in the periurethral area of prostate. Normal prostate consists of 70% glandular and 30% stromal component. Prostate volume of approximately 20 ml may be regarded as normal.

Androgens not only are required for normal cell proliferation and differentiation in the prostate but also actively inhibit cell death. Etiological factors include high levels of prostatic dihydrotestosterone (DHT) & androgen receptors (AR), increased levels FGF-1, FGF-2, FGF-7, VEGF, IGF, first-degree male relative of surgically treated BPH with autosomal dominant inheritance.

BPH result in anatomic Bladder Outlet Obstruction (BOO), through two distinct mechanisms: first, an increase in prostate volume, termed the static component. Second, an increase in stromal smooth muscle tone, termed the dynamic component. Notably, two factors complicate the natural history and clinical presentation of BPH, BOO and LUTS; first, prostate volume does not linearly correlate with the severity of BOO or LUTS. Second, progressive BPH and BOO can lead to primary bladder dysfunction, which in turn

Editor's Comment :

- Clinical examination of patient, assessment of symptom severity and risk of disease progression and associated comorbidities are utmost essential before determining the definitive treatment of BPH.

can exacerbate the severity of LUTS independently of BOO.

Approximately 50% of all men >50 years, with BPH will eventually develop Lower Urinary Tract Symptoms (LUTS). Nocturia is most common symptom followed by frequency and urgency. The International Prostate Symptom Score (IPSS) is recommended as the symptom scoring instrument to be used for the assessment of symptom severity in men presenting with LUTS.

Case 1 :

A 60-year-old male presented with increased frequency, narrow stream of urine and sensation of incomplete evacuation of urine for 2 years.

History of Poor urinary stream (2), Straining during micturition (2), Intermittency (1), Incomplete urinary bladder emptying (2), Frequency (4), Urgency (2), Nocturia (4); IPSS 17/35. There was no history of hematuria, urethral discharge, constipation, low back pain or limb weakness.

Surgical history and family history were not significant. External genitalia – normal, Hernial sites – no cough impulse. DRE- peri-anal skin – normal,

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anal tone – normal, prostate-grade II, firm, smooth, non-nodular, non-tender, median sulcus palpable, rectal mucosa freely mobile.

On further investigation ultrasound examination showed no evidence of bilateral hydronephrosis, urinary bladder wall thickened, prostate – 42 cc without median lobe enlargement, PVR- 94ml. No evidence of UTI and hematuria on urinalysis. Serum urea / creatinine was 22/0.8 and S. PSA- 2.4 ng/ml. Uroflowmetry showed – Voiding volume 260ml, Q max – 13 ml/sec.

As the patient presented with moderate IPSS, PVR <300 ml and no absolute indication for surgical intervention; the patient was planned for medical therapy for BPH.

Alpha adrenergic blockers- the rationale for its use is based on the BPH mediated BOO, which is due by α_1 adrenergic receptor associated with prostatic smooth muscle causing dynamic obstruction. ADRs includes postural hypotension, 1st dose hypotension, dizziness, fatigue, headache, asthenia, nausea. Tamsulosin (0.4 mg OD HS) is currently the most widely employed α_1 blocker (higher affinity for α_{1a} and α_{1d}) for BPH as it has minimum effect on BP, no dose titration needed; common side effect is retrograde ejaculation. Slow release alfuzosin allows for once daily dosing regimen (10 mg once a day); because of lack of adverse effects and blood pressure changes, it has been described as uroselective drug.

Androgen manipulation- the rationale for androgen suppression is based on that the embryonic development of prostate is dependent on DHT. 5ARIs (alpha reductase inhibitors) may be used to prevent progression of LUTS secondary to BPH and to reduce the risk of urinary retention. Dutasteride is a dual inhibitor of 5 α reductase type 1 and 2, so greater impact on suppressing serum DHT. Other agents are antiandrogens, GnRH analogues, progestational agents have limited role in BPH. Combination therapy with α adrenergic blocker and 5 α reductase inhibitor is usually preferred.

Phosphodiesterase inhibitors (PDEIs)- they act by smooth muscle relaxation in prostate, bladder neck or erectile tissue, increase oxygenation of bladder and prostate, has antiproliferative effect, decrease urgency. They improve urinary symptom score (level 1 evidence); especially for men with LUTS and significant ED. Sildenafil, Vardenafil, Tadalafil are some of the agents

used. Headache, dyspepsia, flushing are some commonly observed side effects. Combination therapy with α blocker may lead to symptomatic hypotension and should be avoided

Case 2 :

67-year-male presented with acute urine retention which was relieved by per urethral catheterization. History of Poor urinary stream (5), Straining during micturition (4), Intermittency (2), Incomplete urinary bladder emptying (5), Frequency (5), Urgency (3), Nocturia (4); IPSS 28/35. Patient was a known case of diabetes for 20 years on inj insulin. He also had history of myocardial infarction 5 months back and on antiplatelet agents since then. There was history of bilateral inguinal hernia surgery 2 year back.

External genitalia – normal, Hernial sites – scars of previous surgery at bilateral inguinal region, no cough impulse. DRE- peri-anal skin – normal, anal tone – normal, prostate-grade 3, firm, smooth, non-nodular, non-tender, median sulcus not palpable, rectal mucosa freely mobile.

On further investigation ultrasound examination showed bilateral kidney mild raised cortical echogenicity without any hydronephrosis, urinary bladder wall thickened, prostate – 92 cc with median lobe projection 1 cm, PVR- 163ml. No evidence of UTI and hematuria on urinalysis. Serum urea / creatinine was 38/1.3 and S. PSA- 3.9 ng/ml. Uroflowmetry showed – Voiding volume 160ml, Q max – 8 ml/sec.

Patient was diagnosed having BPH and started on medical therapy. Trial without catheter (TWOC) was given after 1 week and 4 weeks of α blocker therapy but patient could not void on both trial and hence put on PUC.

Considering the failed medical therapy and failed TWOC, the patient was planned for surgical intervention. Surgical options available for this patient were monopolar TURP (transurethral resection of prostate), bipolar TURP, LASER enucleation of prostate; of which we preferred for Thulium laser enucleation of prostate (THULEP) as procedure of choice, taking in account with continuation of antiplatelet agent.

Case 3:

A 59-year-male presented with bilateral pedal oedema, facial swelling for 3 weeks h/o overflow incontinence, increased frequency, nocturia, sensation

of incomplete evacuation of urine for 1 year.

History of Poor urinary stream (5), Straining during micturition (4), Intermittency (3), Incomplete urinary bladder emptying (5), Frequency (5), Urgency (4), Nocturia (5); IPSS 31/35.

Patient was a known case of hypertension on medications. Bilateral pedal oedema present. On abdominal examination bladder was palpable up-to the level of umbilicus, no other organomegaly. DRE- perianal skin – normal, anal tone – normal, prostate-grade 3, smooth, firm, non-nodular, non-tender, median sulcus not palpable, rectal mucosa freely mobile.

On further investigation ultrasound examination showed bilateral hydronephrosis, urinary bladder wall thickened, prostate – 64 cc with median lobe projection 1 cm, PVR- 358 ml. Urinalysis showed plenty pus cells. Serum urea / creatinine was 67/2.3 and S. PSA- 7.9 ng/ml.

Patient was diagnosed having obstructive nephropathy. Patient was admitted and PUC was done. Post obstructive diuresis and decompression hematuria were looked for. Serial electrolyte monitoring and urine output measurement done. Patient had hyponatremia which was corrected as per protocol. S. PSA repeated after 3 weeks when UTI was ruled out on urinalysis, which was 1.89ng/ml. Repeat serum urea / creatinine was 45/1.8. As there was definitive indication

of surgery in this patient, this patient was planned for monopolar TURP.

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Special Correspondence

[We are publishing this Special Correspondence to commemorate World Suicide day on 10th September]

World Suicide Prevention Day, September 10 : Creating Hope Through Action

Ranjan Bhattacharyya¹

Every year on 10th September, World Suicide Prevention day is being observed. The theme of 2021 is 'Creating hope through action' will persist till 2023. Since suicide is preventable not inevitable, the awareness building will instill hope which has become more relevant during this pandemic times. In every 40 seconds, someone in this world terminating the life which had been the notion of campaign as '40 seconds of action'. The findings of research reiterate the need for conversation, 'let's talk' which infact reduces the risk of suicide and provide relief. It's the high time to break the barrier and reduce stigma. The global campaign of preventing suicide by World Health Organization (WHO) emphasizes the need for organizing activities and events throughout the year especially on World Suicide Prevention Day which has been restricted mostly in virtual platform this year.

[J Indian Med Assoc 2021; 119(9): 78-80]

Key words : World Suicide Prevention Day, Awareness building, Psychological autopsy, Biopsychosocial model, Targeted interventions.

In every year, 10th September is being observed as World Suicide Prevention Day (WSPD) by organizing various media and mass awareness programs, campaigns, seminars, CMEs at local, regional, state, national and international levels by Government, Institutional and professional bodies. The International association of Suicide Prevention (IASP) in association with World Health Organization (WHO) is arranging these activities since 2003. Around 44,000 death per year and 129 deaths per day has been reported due to suicide in United States (US). Males are 3.5 times more commonly complete suicide, one in every seven young adults are having suicidal ideation and it has been the tenth leading cause of the death in US¹.

Every death is regrettable and suicide is doubly so as the suicide survivors are left with a state of bitter bewilderment. They have to carry forward the stigma, shock, shame, self criticism and long term guilt over years. Suicide condemnation just adds to the existing stigma which acts as a barrier for seeking help. The people who commit suicide are not losers, wicked or cowards. The medical model of suicide has to be understood by common people. Suicide is a cry for help to society, which is preventable and once committed successfully no longer remains treatable. It's a medical emergency and early intervention has proven successful impact on suicide prevention strategies. The Beck's cognitive triad of negative view about self (worthlessness), environment

(helplessness) and future (hopelessness) needs to be restructured by providing adequate individual and family support and providing structure cognitive behavioural therapy and necessary pharmacological interventions by professionals. Silence is often fatal and the individual having suicidal wish will not be in a state to brought themselves to medical care system if the pain and sufferings become unbearable and intolerable as per the Martin Seligman's 'Learned Helplessness' model².

Suicide has remained the largest and preventable cause of premature and untimely death. These awareness programs, helplines, working together at individual, community and collective levels will help immensely to vulnerable population. The Government of India (GOI) has made a step forward to decriminalize by abolishing Indian Penal Code (IPC) section 309 after getting approval from 18 states and 4 Union territories. As per this law whoever would made an attempt to commit suicide or does any act to do so shall be punished for imprisonment of one year with fine³.

In every 3 seconds an individual is attempting and in every 40 seconds an individual is becoming successful of committing suicide. So, in every 41st second an individual's name is being removed from this world. Around 1 million people are committing suicide globally of which 2740 suicides per day. Globally 78% suicides completed suicides occur in Low And Middle Income Countries. (LAMIC). Suicide attempts are 30 times more than the completed suicides. The most of the statistics of completed suicides are derived from the National Crime Record Bureau (NCRB). These statistics are believed to be far away from the actual figures as most of the cases

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remain unreported due to stigma and legal hazards⁴.

As high as one third of the suicides committed are due to use of pesticides worldwide, the indiscriminate selling and use should be restricted. Around 75% of suicides committed in between 1996-2006 in China, Malaysia and Srilanka and Caribbean countries were due to pesticide ingestion. The same trend is on rise in central and South America. The viewpoint in favour of voluntary euthanasia is building up and the awareness generation, decriminalization, destigmatization will probably change the roadmap in the future⁵.

Goals for Suicide Prevention : For strategic planning, few goals need to be formulated which are (i) raising awareness that it is preventable, (ii) educating people through mass and media awareness programs, (iii) spreading the awareness that help lines are available and (iv) reducing stigma and decriminalization of suicide. It is a deep rooted belief prevailing in the mindset of section of a common people that those who commit suicide are 'weak', 'selfish' or 'cowards'. The acronym 'ACT' to describe 'Ask, Care and Treat' is applicable as the first approach to combat stigma⁶.

Psychological autopsy : Suicide has been the second leading cause of death globally in the age group 15-29 years. Among the various causes of fatal accidents occurring daily, suicide is representing 15% of all of these accidents. The major risk factor behind the suicide is the history of previous suicide attempt. The other contributing factors are harmful substance use, financial and job loss, strong family history, underlying major psychiatric and physical illness, genetic and biological factors, economic loss, loss of job, relationship break up and death of close members in family etc. The appropriate interventions at multisectorial level is utmost important which include strengthening of infrastructure and mental health policies, providing better healthcare access and giving more importance on Suicide Prevention in National Mental Health Program (NMHP). The healthcare workers must be trained at grassroot level and should be actively utilized. By legislation, the restriction of access of means of suicide (selling pesticides, acids, firearms and certain drugs) can be provided. The emphasis should be given to reduce the harmful substance abuse by implementing NDPS and other acts. The electronic and print media have remained very active these days. The coverage of suicide stories shouldn't be printed in front page of the newspaper and it shouldn't be made sensational. The intricate details of means of suicide and simplistic superficial explanation shouldn't be given⁷.

Targeted approaches : As suicide is only preventable, the physician should learn that that whoever is going to attempt suicide, will give a verbal or behavioral

cue and warning signs. Most of the times, family members and friends ignore these signs and cues which eventually leads to a catastrophe. The suicide behaviours are largely a reflection of profound happiness and dissatisfaction to one's life. The approaches to suicide attempters include to provide compassionate care, giving them respect and autonomy listening their problems and sufferings empathetically. The mental health professionals are utmost required to provide 'psychological first aid', diagnose and treat the underlying mental disorder if any⁸.

The psychological autopsy is a process to find out the underlying cause of suicide. The most common causes which have emerged as the underlying psychiatric cause are Major depressive disorder, Bipolar disorder especially in depressive and mixed phase of the illness, schizophrenia, use and dependence on psychoactive substances and personality disorders especially Borderline Personality disorder^{9,10}. The various biopsychosocial risk factors of suicide have been summarized in Table 1.

The suicide amongst youth needs special mention. They are more vulnerable to emotional trauma and their contribution to society is very important with respect to human resource values. This can be correlated with their highly charged up amygdale which is the centre of emotion. Most of the times, the impulses come momentarily and the attempts are impulsive. The two important primary underlying factors are failure in examination and break up in relationships. Giving their important or precious possessions, writing suicide notes, making specific plans are certain indicators of imminent suicide attempt. The survival skills and crisis management can be summarized by the acronym 'ACCEPTS' (Activity, Contributing, Comparison, Emotions, Pushing away, Thoughts and Sensations)¹¹.

The suicide is being escalated in three phases. The first phase is known as 'Ramp up period'. This begins with triggering of an event when the idea of suicide first arises. It then proceeds to the second phase which is called 'Peak period'. During this phase the desire to commit suicide reaches its peak and this period needs to be aborted by all means to prevent a suicide. The final phase is known as 'Ramp down' or fall phase when the impulse to commit suicide gradually returns to the baseline. The resilience is the most important predictor for coping during this phase. It is the ability of an individual to bounce back to the previous normal level of daily work following a trauma or adverse situation. The stress level is on rise in our daily life due to extreme busy schedule which has been augmented during this pandemic period. The majority of people can handle the stress but they are facing 'burnt outs' in their personal and professional

Table 1 — Biopsychosocial risk factors of suicide

Bio-psychosocial Risk Factors	Environmental Risk Factors	Social factors
Common mental disorders like major depressive disorders, anxiety disorders; severe mental disorders like schizophrenia, bipolar affective disorder, substance use disorders, personality disorders etc.	Loss of job, facing economic loss, school drop out.	Lack of social support, social position, homelessness, sense of isolation.
Beck's cognitive triad of 'Helplessness, hopelessness and worthlessness.	Relationship issues and break ups.	Stigma (self and perceived).
Making impulsive or aggressive attempts.	Easy access to lethal means like access to firearms and poisons.	Barriers to access mental health services.
Any history of trauma or abuse.		Socio-political-cultural factors.
Major physical illnesses (chronic or terminal) like Chronic Kidney Diseases (CKD), Malignancy etc.		Role of media and 'copycat suicides'
Previous suicide attempt (single most important predictor).		
Family history of suicide (signifies genetic load and biological underpinning)		

life. Still they are capable of managing these adversities. The positive and negative life experiences needed to be taken care of to revert back from potentially challenging traumatic experiences to a favourable and constructive ones.¹² The themes of 'World Suicide Prevention Day' since its inception from the year 2003 have been summarized in Table 2¹².

We need to work together to extend a helping hand so that valuable life can be saved. Suicide is a selfless act done for selfless reasons as the person thinks world would be better off and best way to make them feel that we need, care and think for them.

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Conflicts of interest : Nil

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Table 2 — Themes of World Suicide Prevention Day (2003-2021)

Year	Theme
2021	Creating hope through action.
2020	Working Together to Prevent Suicide.
2019	Working Together to Prevent Suicide.
2018	Working Together to Prevent Suicide.
2017	Take a Minute, Change a Life.
2016	Connect, Communicate, Care.
2015	Preventing Suicide: Reaching Out and Saving Lives.
2014	Light a candle near a Window.
2013	Stigma : A Major Barrier to Suicide Prevention.
2012	Suicide Prevention across the Globe: Strengthening Protective Factors and Instilling Hope.
2011	Preventing Suicide in Multicultural Societies.
2010	Families, Community Systems and Suicide.
2009	Suicide prevention in different cultures.
2008	Think globally, plan nationally, act locally.
2007	Suicide prevention across life span.
2006	With understanding new hope.
2005	Prevention of suicide is everybody's business.
2004	Saving lives, restoring hope.
2003	Suicide can be prevented

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Image in Medicine

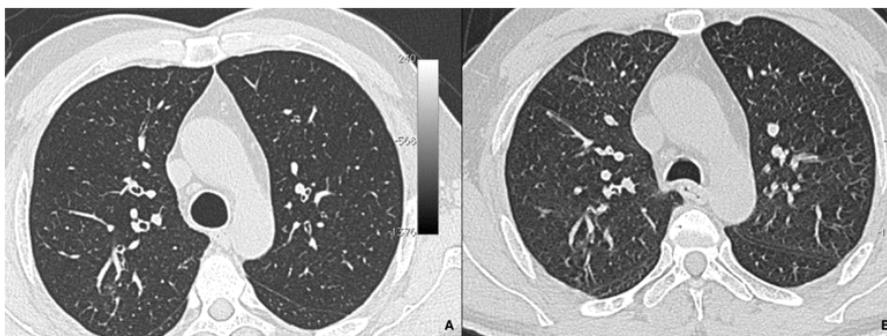
Bhoomi Angirish¹, Bhavin Jankharia²

Quiz 1

CT scan images of the chest in inspiration and expiration.

Questions :

- (1) How to identify expiratory images?
- (2) What is the purpose of an expiratory scan?
- (3) What are the common indications of an expiratory scan?



Answers :

(1) The trachea is usually taken as a reference to assess the technique. The trachea appears round / elliptical in shape on inspiration (a) and crescent shape with bowing of its posterior membranaceous wall on expiration (b). Diffuse increase in lung attenuation is also seen in expiration.

(2) Expiratory scans are performed to highlight the areas of air trapping since during expiration, rest of the normal lung parenchyma will show increase in attenuation.

(3) Expiratory scan should be performed in all airways disease and interstitial lung disease. It is also useful in assessment of tracheobronchomalacia.

Quiz 2

X-ray forearm (AP and lateral view) of a 6 year old girl who presented with history of fall on an outstretched hand.

Questions :

- (1) Name the fracture?
- (2) What are the mechanism of this fracture?
- (3) How to differentiate greenstick fracture from torus fractures?



Answers :

(1) Incomplete fracture with cortical breach of only one side of the bone in mid-diaphysis of radius and ulna is seen associated with mild angulation -suggestive of greenstick fractures.

(2) Greenstick fractures occur when the force applied to a bone results in bending of the bone such that the structural integrity of the convex surface is overcome resulting in fracture of the convex surface. The bending force applied does not break the bone completely and the concave surface of the bent bone remains intact. These are usually seen in young children, less than 10 years of age.

(3) Greenstick fracture is different from torus fracture which results in buckling of the cortex on the concave side of the bend and an intact convex surface.

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Student's Corner

Become a Sherlock Holmes in ECG

M Chenniappan¹

Series 7:

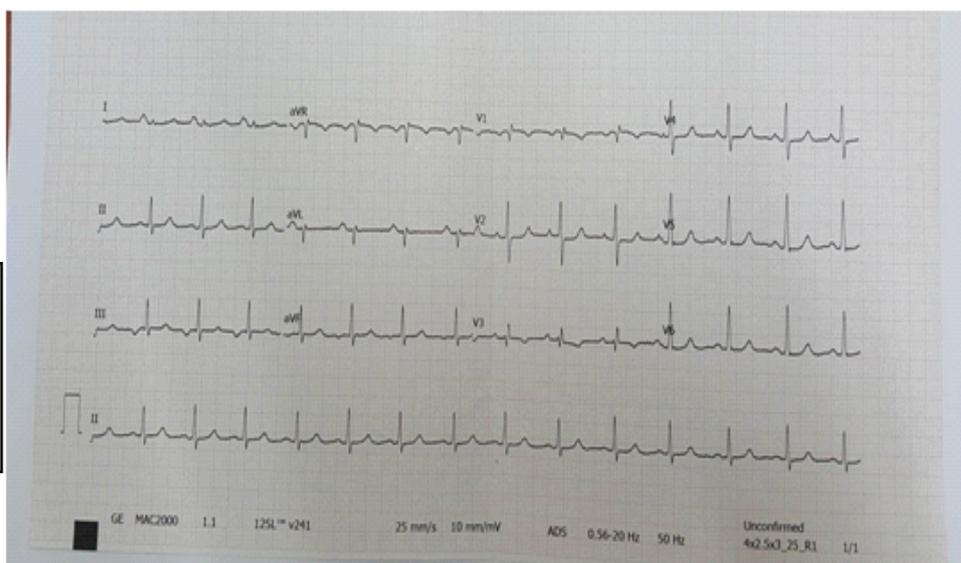
“ECG can be Poorman’s ECHO”

This is the ECG of 29-year-old female presenting with breathlessness.

Questions :

- (1) What are all ECG findings?
- (2) Why is this clue?
- (3) What are practical implications?

Answers :



ECG Findings :

The ‘P’ wave is inverted in L III and aVF due to left axis deviation of P wave and not due to Junctional Rhythm or Low Atrial Rhythm because P wave in L II is upright. If you look at the ‘P’ wave in L I and aVL it is bifid and wide and with predominant negative component in V1 one should suspect left atrial enlargement.

CLUE :

ECG as Poorman’s ECHO: In addition, left atrial enlargement described above, patient qR in V1. The R wave in with Right Axis deviation in limb leads is suggestive of Right Ventricular Enlargement (RVE). So, with the presence of Left Atrial Enlargement (LAE) and RVE in 29-year-old female are suggestive of severe Mitral

Stenosis (MS) with Pulmonary Hypertension. The qR pattern in V1 is suggestive of severe Right Atrial Enlargement (RAE) because in severe RAE, the V1 will face RA and show qR pattern. In the presence of pulmonary hypertension (PHT), severe RAE is suggestive of significant tricuspid regurgitation (TR). So, if carefully seen, ECG has given almost all findings shown in ECHO – that why it is “Poor man’s Echo”.

PRACTICAL IMPLICATIONS :

The ECG itself has indicated severe MS, Severe PHT, Severe TR and it definitely needs either non-surgical (Balloon Mitral Valvotomy) or Surgical intervention. (MVR)

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Book Review

McMaster Text book of Internal Medicine South Asian Edition by expert authors, Publisher - Medycyna Praktyczna, Kraków, Poland, Pages - 1552 (2022 South Asian Edition: 1728), Price of current edition : 35 USD (2022 South Asian Edition: not yet set),

The *McMaster Textbook of Internal Medicine* has been developed at McMaster University in Hamilton, Canada, the birthplace of problem-based learning (PBL) and evidence-based medicine (EBM) and one of the leading medical schools in the world, in collaboration with the Polish Institute for Evidence Based Medicine in Kraków, Poland.

Covering the essential fields of internal medicine, the textbook is aimed at answering the needs of medical professionals as well as residents and students who seek access to updated, verified medical knowledge useful in everyday practice, in both ambulatory and in-patient settings. It is not intended for subspecialists in the area of their specialty. The reasons for the development of the *McMaster Textbook of Internal Medicine* included an increasing need for on-demand and on-site access to reliable information, growing cost of many resources, and our belief in the ability to meet the needs of medical professionals accurately. In short, the goal is a textbook that is practical, accessible, current, and affordable.

What makes the *McMaster Textbook of Internal Medicine South Asian Edition* unique is the combination of expert authors from South East Asian countries, along with its practicality, and accessibility. Also, the Textbook ensures a pragmatic approach employing the GRADE system, which supports physicians in making evidence-based decisions about management and allows for an explicit differentiation between strong and weak recommendations.

The team behind the *McMaster Textbook of Internal Medicine South Asian Edition* includes over 500 experienced contributors from North America, Europe as well as India Bangladesh Pakistan and Nepal. By combining the expertise of authors from around the world, the *McMaster Textbook of Internal Medicine* South Asian edition boasts a uniquely broad and versatile approach that enhances the practical value of the book.

The authors of this book have extensive hands-on experience in treating patients around the world. Being remarkably successful in translating this knowledge into practical instructions for other medical professionals, many of them have participated in the development of clinical practice guidelines and consensus statements, which shape the modern medical practice. Many of the authors have been also involved in pioneering research and designed groundbreaking clinical trials that guide today's clinical practice.

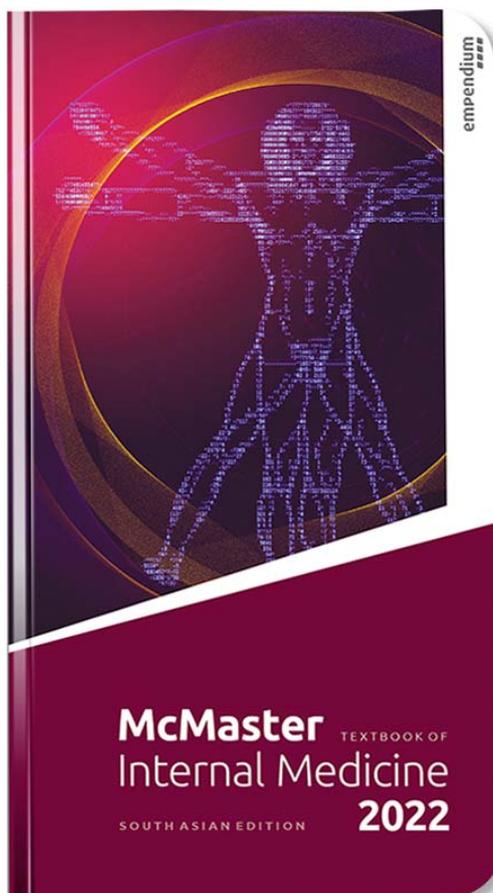
As a fully electronic resource, the *McMaster Textbook of Internal Medicine* takes advantage of the digital format to supplement the text with additional materials, such as lectures, talks, reviews, and links to external articles.

What distinguishes the *McMaster Textbook of Internal Medicine* from other textbooks used around the globe is that editions for different regions are developed in close cooperation with local experts and opinion leaders in order to take into account differences in health care systems, epidemiology of diseases, availability of diagnostic and therapeutic methods, etc.

What makes the *McMaster Textbook of Internal Medicine* South Asian edition exceptional:

- Developed according to the principles of evidence based medicine (EBM).
- Available in multiple formats: print, web based, and as an app for mobile devices.
- It highlights regional variations in disease presentations ,management strategies and outcomes in separate box charts below the chapters.
- Gives insight into some tropical infectious diseases, their emerging resistance patterns and management.
- Addition of some new chapters of regional importance like poisoning and envenomation.
- Updated on an ongoing basis.
- Affordable.

The launch in South Asia (both printed and electronic versions) is scheduled for early 2022.



Letters to the Editor

[The Editor is not responsible for the views expressed by the correspondents]

Effect of Deranged Thyroid Profile on Glycated Hemoglobin : Pre and Post Treatment

JIMA, Vol 119, May 2021

SIR — The authors have done a wonderful study regarding the “Effect of Deranged Thyroid Profile on Glycated Haemoglobin : Pre and Post Treatment”. It has been rightly pointed out that thyroid disorders can have a significant effect on blood glucose levels and, if left untreated, can affect glycemic control. Hyperthyroidism has long been recognised to promote hyperglycaemia. There also exists a relationship between insulin resistance and oxidative stress. The interrelationship between thyroid dysfunction and insulin resistance has also been established by some studies that have shown normalisation of long-term indicators of glycemic controls (HbA1c) among non-diabetic thyroid disorder patients following thyroxine replacement therapy. Thus, normalisation of HbA1c values in such patients by only treating their thyroid dysfunction can clearly decrease the diabetic burden to a great extent.

In this regard the editor has correctly commented that, one should be cautious in interpretation of HbA1c values in patients suffering from thyroid dysfunction as they may be falsely elevated in untreated hypothyroid patients (who have found to have normal fasting and post prandial blood glucose levels), which was found to be normalised on levothyroxine replacement therapy.

On the other hand, patients with hyperthyroidism do not show such correlation between glycated haemoglobin levels and thyroid hormone levels both pre and post treatment.

So tests like serum fructosamine assay and glyclated albumin have been proposed to overcome this fallacy.

This study has brought to light the need to such larger scale studies to understand the pathophysiology behind the false elevation of HbA1c in overt hypothyroidism.

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Best Practices In D-Dimer Testing; In COVID-19 and Beyond : Expert Group Recommendations

SIR — The early part of year 2020 witnessed the evolution of D-dimer as one of the most vital laboratory parameters in the management of COVID-19; the clinicians and laboratorians ensured an intense usage in the testing and clinical utilization of D-dimer. A parameter, often less utilized and even lesser understood, stood in the driving seat of predictive value pertaining to risk and prognosis around COVID-19 associated coagulopathy. Whilst always considered as a VTE exclusion parameter, and sometimes used in sepsis, it

was evidenced to be of immense use in evaluating and managing a disease which was over a year old and already caused a damage of decades. Never had, in the history of hemostasis parameters, a test become so common that it evolved as a over the counter (OTC) test parameter. These developments also presented a major challenge as to how to appropriately interpret and use the values of this incredible parameter, particularly with the growing utilization of the parameter, within and beyond COVID-19. D-dimer, now, and often, is being ordered as a walk-in test parameter, follow up test parameter, "test package" parameter and even a establish / rule out test parameter of COVID-19 as such, we wonder if the depth of knowledge around it can support the adequate and appropriate utilization of this wonder parameter. Here is an attempt to revisit and put together the recommendations on the best practices around D-dimer testing, particularly in the post COVID era, not only to counter the challenges in D-Dimer testing but also to ensure that D-dimer joins the league of Prothrombin time (PT), activated partial thromboplastin time (aPTT) and fibrinogen as the basic minimum tests done at any hemostasis laboratory.

D-dimer is a fibrin split product derived from the plasmin-mediated degradation of cross-linked fibrin formed due to thrombin. D-dimer can hence be considered a biomarker of clot/thrombus formation and intravascular coagulation (DIC).

Blood sample for D-dimer should be collected in 3.2% Trisodium Citrate Anticoagulant (9:1) followed by Heparin and EDTA (CLSI and WHO). *Serum samples are unsuitable since it obtained from clotted blood in tubes containing clot activators which could increase products of thrombin (fibrin breakdown).*

The routine reporting units of D-dimer are ng/mL, μ g/L, μ g/mL, or mg/L. *Theoretically they can further be expressed in DDU and FEU. Among the measure units that can be adopted, "mg/L" (or "ng/mL") is probably the unit that best approximates the International System (IS). (For sake of example, a value of 500 ng/mL is same as 0.5 μ g/mL which is same as 500 μ g/L and same as 0.5 mg/L.). Although, FEU is roughly double of DDU, the practice of conversion from DDU to FEU and vice versa is not recommended.*

D-dimer values are not transferable/comparable between methods and equipments.

There is no WHO / International Reference standard (IS) for D-dimer. The reference range/cut-off value for D-dimer is ideally established by the performing laboratory, or, if a cut-off value published in the literature is used, the value has to be verified and accepted by the users (*those ordering the test*).

Higher values may be observed in liver disease, inflammation, infections (including ARDS), malignancy, trauma, pregnancy, recent surgery as well as advanced age. These high levels in D-dimer could be physiological

like in pregnancy or due to the pathophysiology of the condition itself but D-dimer is not routinely used in these conditions either for diagnosis or in the assessment of its progress except when suspecting venous thromboembolism (*wherein a higher cut-off will be required before ruling out VTE*) or intravascular coagulation (*for calculating DIC score*).

Significant lower D dimer values may be observed if the sample is taken either too early after thrombus formation or if testing is delayed beyond the recommended time duration.

Pre-analytical variables affect D-dimer values. Proper sampling techniques, transportation and centrifugation procedures as per recommendations need to be followed as per recommendations and guidelines.

D-dimer values typically increase in parallel with aging, Adjusting the D-dimer cut-off values to the age of outpatients >50 years increases specificity while hardly affecting sensitivity.

It has been observed that heterophilic antibodies may occasionally develop after infection by rubella, measles, adenovirus, enterovirus, and varicella-zoster viruses. These may be associated with raised D dimer levels.

An isolated elevation of D-dimer should always be interpreted with caution (assessment of clinical probability).

D-dimer in COVID-19 :

- The upper reference range / cut-off, mentioned in most of the reports, is valid for Venous Thromboembolism.
- The scientific knowledge and clinical evidence around coagulopathy in COVID-19 is still evolving and hence the use of D-dimer as a vital component of evaluation and management should be best correlated with available data.
- There are fair chances of interference with known entities (such as heterophilic antibodies and substances in patient sample) as well as unknown entities (this disease being very new in terms of available data)
- The D-dimer test value needs to be interpreted in context of the clinical profile of the patient, other coagulation and inflammation parameters (although they may not always correlate) as well as previous values/future values on the same platform.
- Comparing D-dimer values across different labs or analysers should be discouraged since it is highly likely that the values (number) will not match.
- Sometime, D-dimer can be the only laboratory parameter elevated in the early stages of disease and it may be so even ahead of any clinical signs and symptoms. Similarly, D-dimer may remain elevated in the terminal stages of illness and even in the convalescence phase when all other parameters might be within normal limits.
- D-dimer should NOT be used as a sole criterion to

start therapeutic thromboprophylaxis or perform radiological examination to evaluate evolving thromboembolism. Similarly, anticoagulant therapy should NOT be intensified based only on the biomarkers like D-dimer.

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Nitin Dayal³,
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Rajesh Phatale⁵,
Renu Saxena⁶,
Sukesh Chandran Nair⁷**

IMA AWARDS NOTIFICATION - 2021

The State/Local Branches Presidents/Secretaries are advised to forward the nominations of the deserving candidates to IMA Headquarters, New Delhi latest by **30th November 2021** as per details given below:

FOR YOUNG DOCTORS (Male/Female)

1. IMA Dharendra Nath Dutta Award in Cardiology:

Type of Award: Article/Paper

Eligibility: Open to all IMA Members not more than 35yrs of age
Topic:

2. IMA Dr C T Thakar Award:

Type of Award: Community Service by young doctors

Eligibility: Open to all IMA Members not more than 35yrs of age
Topic:

3. IMA Dr C S Thakar Award:

Type of Award: Article/Paper (3000 Words)

Eligibility: Open to all IMA members not more than 35yrs of age
Topic:

SAFE MOTERHOOD PROJECT

1. IMA Dr C L Jhaveri Safe Motherhood Activity Award for State/Terr. Branches:

Type of Award: Distinguished Record of service in Family Planning.

Eligibility: Open to all IMA Members with 5 years' Standing
Topic:

2. IMA Dr C L Jhaveri Safe Motherhood Activity Award for Individual Members.

Type of Award: Distinguished record of Service in Family Planning Work.

Eligibility: Open to all IMA members with 5 years' standing.
Topic:

3. IMA Dr Kanak Goel Award: (Only Female Doctors)

Type of Award: Recognition for commendable work in Safe Motherhood Activity.

Eligibility: All Women Doctor Members of IMA.
Topic:

AWARDS GIVEN FOR RESEARCH (Male/Female)

1. IMA Dr D S Munagekar Award:

Type of Award: Best Published Research Work done on Covid-19 during last two years.

Eligibility: Open to all IMA Members not more than 50 yrs of age

2. IMA Dr K Sharan Cardiology Excellence Award:

Type of Award: Recognition of Medical men having specialization in the field of Cardiology or Cardiac Surgery or allied fields who have displayed excellence in academic work, service and research in the above fields.

Eligibility: Open to all members of IMA with not less than 20 years' continuous membership.

Topic:

3. IMA Dr Deepak Banerjee Award for best published paper in JIMA

Type of Award: Recognition of Paper Published in JIMA.

Eligibility: Author of papers published in JIMA.

4. IMA Dr Ramachandra N Moorthy Award in Psychiatry:

Type of Award: Recognition of outstanding achievement/ Research work /Community Service/Published Paper.

Eligibility: All Members of IMA/ individual Branch/Institution.

ORATION (Male/Female)

1. IMA Diamond Jubilee IDPL Oration Award: -

Type of Award: Oration (Subject of Oration to be selected by the Orator)

Eligibility: Open to IMA Members with at least 20 years' Standing

Topic:

2. IMA Dr Jagdishwari Mishra Oration Award (Surgery & Medicine in relation to Obstetrics and Gynaecology)

Type of Award: Oration (Subject of Oration to be selected by the Orator.)

Eligibility: Open to all IMA Life Members.

Topic:

3. IMA Dr B R Ramasubramanian Oration Award

Type of Award: Oration on Covid-19.

Eligibility: Open to all IMA Life Members.

Topic:

4. IMA Prof. Shridhar Sharma Oration Award

Type of Award: Oration

Eligibility: Open to all IMA Life Members.

Topic:

OUTSTANDING & DISTINGUISHED SERVICES AWARD (Male/Female)

1. IMA Dr A P Shukla Memorial Distinguished Services Award:

Type of Award: Recognition of outstanding and distinguished services to IMA (Selection by the IMA Awards Committee)

Eligibility: Open to IMA Members with at least 20 years' Standing

Topic:

2. IMA Dr AKN Sinha National Award (Alkem):

Type of Award: Recognition of outstanding and distinguished services to medical profession.

Eligibility: Open to all members of IMA with minimum 20 years' Standing.

Topic:

3. IMA Dr Jyoti Prashad Ganguli Memorial Award:

Type of Award: Award to be given to the Local Branch or Individual Members of IMA having Distinguished Record of selfless community service amongst the less fortunate in rural areas

Eligibility: Open to all members of IMA with not less than 20 years' continuous membership.

4. IMA Dr P C Bhatla Award:

Type of Award: Recognition of outstanding and distinguished services to medical profession.

Eligibility: Open to all members of IMA with minimum 20 years' Standing

5. IMA Dr M G Garg All Time Achievement Award:

Type of Award: Recognition of outstanding and distinguished services to medical profession.

Eligibility: Open to all members of IMA with minimum 20 years' Standing

6. IMA Dr V Parameshvara Award for Lifetime Achievement in Medicine and Commitment to the Art of medicine:

Type of Award: Recognition of outstanding and distinguished services to medical profession.

Eligibility: Open to all members of IMA with minimum 20 years' Standing.

PRESIDENT APPRECIATION AWARD

1. IMA National President's Appreciation Award for Best adjudged President of State/Terr. Branch.
2. IMA National President's Appreciation Award for Best adjudged Hony.State Secretary of State/Terr. Branch.
3. IMA National President's Appreciation Award for Best adjudged President of a Local Branch.
4. IMA National President's Appreciation Award for Best adjudged Hony. Secretary of a Local Branch.
5. IMA Membership Drive Trophy.(By IMA Hqrs)
6. IMA National President's Appreciation Award for Life Long Services to IMA.
7. IMA Community Service Award to be given to a local Branch assessed as the Best Branch for organising Community Services during the year 2020-2021.
8. IMA Community Service Award for Individuals.
9. IMA Doctor's Day Celebration Award.
10. IMA Best CME / Scientific Programme Award.
11. IMA National President's Appreciation Award.
12. IMA Special Award to Eminent Medical Men for Distinguished Achievement of the highest order.
13. IMA National President's Special Membership Award to be given to an individual member enrolling maximum number of Life Members during the Association Year. (By IMA Hqrs)
14. IMA National President's Life Membership Enrollment Award to be given to a State/Terr. Branch enrolling maximum number of Life Members during the Association Year. (By IMA Hqrs)
15. IMA National President's Life Membership Enrollment Award to be given to a Local Branch enrolling maximum number of Life Members during the Association Year. (By IMA Hqrs)
16. IMA National President's Appreciation Award for Maximum Units of Blood Collected Trophy Of Dr.S.S.Sukumar of a Local Branch
17. IMA National President's Appreciation Award for Best Project of IMA
18. IMA National President's Appreciation Award for Best Wing of IMA
19. IMA National President's Appreciation Award for Best Scheme of IMA
20. IMA National President's Appreciation Award for Best National Office Bearer (Male/Female)
21. IMA National President's Appreciation Award for Best State Office Bearer (other than President/Secretary).
22. IMA National President's Appreciation Award for Best Life Member (Male/Female)
23. IMA National President's Appreciation Award for Best Young Doctor (Male/Female)
24. IMA National President's Appreciation Award for Best Medical Student (Male/Female)
25. IMA National President's Appreciation Award for Best Medical Interned (Male/Female)
26. IMA National President's Appreciation Award for Best Medical Resident (Male/Female)
27. IMA National President's Appreciation Award for Women for Best Social activity.
28. IMA National President's Appreciation Award for Women for Best Education activity.

MEMBERSHIP DEVELOPMENT AWARD

1. Best IMA Local Branch Rotating Trophy of Gujarat State Branch (For Major Branch > 500 members).
2. Best IMA Local Branch Rotating Trophy of Dr. N.S. Chandra Bose (For Medium Branch 101 – 500members).
3. Best IMA Local Branch Rotating Trophy of Dr. (Mrs.) NavamaniBose (For Small Branch 1 –100members)

ORGANISATIONAL AWARDS

1. IMA Special Award ForOrganising All India Medical Conference
2. IMA Special Award ForOrganising Annual National Conference of IMA CGP
3. IMA Special Award ForOrganising Annual National Conference, IMA AMS
4. IMA Special Award ForOrganisingCentral Working Committee Meeting
5. IMA Special Award ForOrganising Hospital Board of India Meeting.

PUBLICATION AWARD

1. IMA News Bulletin Award

ASSESSMENT CRITERIA FOR STATE /LOCAL BRANCHES AWARDS

1. The performance of the State Branch/Local Branch Presidents and Secretaries will be assessed based on the activities carried out during the year under their leadership.
2. The President/Hony. Secretaries, State and Local Branches intending to compete for the above Award for the year 2020-2021 are requested to send in their reports as per the enclosed Performa so as to reach the undersigned latest by 30th November, 2021 positively. Nominations received after that shall not be taken into consideration.
3. The Local Branches should route their entries through their respective State/Terr. Branches.
4. The Awards will be presented to the winning Local Branch/State Branch Presidents and Secretaries at the All India Medical Conference NATCON-2021.
5. Awardees need to essentially register for the IMA Annual National Conference, NATCON-2021

IMA AMSAWARDS

- 1. IMA Medical Education and Research Award II**
Type of Award: Article/Paper (Topic from IMA Hqrs.)
Eligibility: Open to all IMA/IMAAMS members.
- 2. IMA Dr. R.K. Menda Memorial Oration Award:**
Type of Award: Oration (Bio-Data/Topic of Oration & Recent Research Publications recommended by 2 Fellows of IMA AMS to be submitted.
Eligibility: All Members of IMA/ IMAAMS.
- 3. IMA AMS Dr. Satya Pal Aggarwal Memorial Annual Award:**
Type of Award: Article/Paper (Topic from IMA Hqrs.)
Eligibility: All Members of IMA/IMAAMS.
- 4. IMA AMS Award for Best Paper Presented at the Annual National Conference of IMA AMS (3 Prizes).**
Type of Award: Recognition of Papers presented at the Annual National Conference (Selected by a committee of five judges constituted at Annual National Conference).
Eligibility: All Members of IMA/IMAAMS.
No. of Awards:(3) First, Second & Third

IMA CGP AWARDS

- 1. IMA CGP Silver Jubilee Oration Award:**
Type of Award: Oration (Subject to be selected by Orator).
Eligibility: Open to all IMA/IMACGP Members.
- 2. IMA Medical Education and Research Award I**
Type of Award: Article/Paper (Topic from IMA Headquarters).
Eligibility: Open to all IMA/IMACGP Members.
- 3. IMA Dr. C.L. Sahni Award:**
Type of Award: Oration (Subject to be selected by Orator)
Eligibility: Open to all IMA/IMACGP Members.
- 4. IMA Dr. M.G. Bhide Memorial Award:**
Type of Award: Article/Paper (Topic from IMA Headquarters)
Eligibility: Open to Members having membership of IMA for at least 10 years and Life Membership of the IMACGP for at least 5 years
- 5. IMA CGP Annual Award:**
Type of Award: Article/Paper (Topic from IMA Headquarters).
Eligibility: Members of IMA CGP who are life members for 5 years or more.
- 6. IMA Dr.C.L.Jagga Award for best Faculty of IMA CGP**
Type of Award: Recognition of Activity of the Sub-Faculties (detailed reports of activities of Sub Faculty to be submitted to IMA HQRS.)
Eligibility: Open to all Sub Faculties/State Faculty of IMA CGP.
- 7. IMA Dr. I. Venkata Rao Oration Award:**
Type of Award: Oration (Subject of Oration should be selected by the Orator
Eligibility: Open to all Life Members of IMA/IMACGP (15 years Continuous membership)

IMA HOSPITAL BOARD OF INDIA AWARDS

IMA Hospital Board of India Awards are being launched from 2021 to honor HBI subchapters & Hospitals in the country and will be presented during the Awards Ceremony at the annual NATCON. The deadline for entries will on 31st October every year.

IMA HBI Awards will have following categories. Each category presents a unique to showcase outstanding services, programs and projects of hospitals and health service providers. Local & State HBI subchapters can showcase their work in the interests of healthcare establishments.

- 1. State HBI Subchapter Award**
This award is open to HBI STATE SUBCHAPTERS
- 2. Local HBI Subchapter Award:**
This award is open to HBI LOCAL SUBCHAPTERS
- 3. HBI Best Hospital Awards:** The HBI Best Hospital Awards have three sub-categories & are open to IMA HBI Affiliated Hospitals only. Sub-Categories of HBI Best Hospital Awards

a. HBI Best SCHO	(0-50 beds)
b. HBI Best HCO(51-100 beds)	
c. HBI Best Multibed Hospital	(101 + beds)
- 4. Best Hospital Safety Award:**
This award is open to HBI Affiliated Hospitals

ELIGIBILITY AND ENTRY RULES

All entries must be for HBI Affiliated Hospitals only.

The achievements, services, programs, projects or events which have been completed over past 12 months with quantifiable achievements, results and/or outcomes during this timeframe should be presented with entry form.

In addition, projects that were completed before past 12 months can be submitted if the program, project had evidence of recent results or achievements recently. Only hospitals can submit entries. Each Hospital is allowed a maximum of one entry.

**For further details and the application form, please log on to :
www.ima-india.org
[https:// onlinejima.com](https://onlinejima.com)**

**Dr Jayesh M Lele,
Hony. Secretary General, IMA**

Conferment of IMA Teachers' Day Awards, 5th September, 2021, at IMA Headquarters, New Delhi



Teacher of Decade Award (Posthumous)

1 Padmashri Dr K K Aggarwal

Delhi

IMA Professor Emeritus

1 Prof Dr Vedprakash Mishra

Maharashtra

2 Prof Dr Abhijat Sheth

Gujarat

Honorary Professors - IMA Hq

1 Dr Bhavinder Kumar Arora

Haryana

2 Dr M Chenniappan

Tamil Nadu

3 Dr Agamchandradavan Vora

Maharashtra

4 Dr Chinmay J Shah

Gujarat

5 Dr Indudharan A

Kerala

6 Dr V Amuthan

Tamil Nadu

7 Dr Nirmal Fredrick T

Tamil Nadu

8 Dr T K K Naidu

Telangana

9 Dr Om Tantia

West Bengal

10 Dr M V Vijay Sekhar

AP

11 Dr Kamala Kantapanigrahy

Orissa

12 Dr Sankar Kumar Das

Assam

13 Dr K Prakasam

Tamil Nadu

14 Dr Rajat Kumar Ray

Orissa

15 Dr Alok Chandra Agrawal

Chhattisgarh

16 Dr Jiledar Rawat

UP

17 Dr Jugal Kishor Sharma

Delhi

18 Dr Kumar Ratnesh

Bihar

19 Dr Ketan K Mehta

Maharashtra

20 Dr Sachin Bhimashankarjamma

Maharashtra

Honorary Professors – IMA CGP

1 Dr Abbas Ali S

UP

2 Dr Amar Kant Israni

Delhi

3 Dr Surya Kant

UP

4 Dr Sachin Ashok Patharkar

Maharashtra

5 Dr Pradip Kumar Das

West Bengal

6 Dr P A Sivakumar

Tamil Nadu

7 Dr Manoj Kumar Bansal

MP

8 Dr Kunal Sahai

UP

9 Dr Naresh Chawla

Delhi

10 Dr Pragnesh Chinubhai Joshi

Gujarat

Honorary Professors – IMA AMS

1 Dr Sainath Karnappaandola

Karnataka

2 Dr Ashok Rai

UP

3 Dr S Easwaramoorthy

Tamil Nadu

4 Dr Shivkumar S Utture

Maharashtra

5 Dr P N Suresh Kumar

Kerala

6 Dr Ashok Arora

Haryana

7 Dr M S Ashraf

Tamil Nadu

8 Dr Dilip Kumar Acharya

MP

9 Dr Anju Gambhir

Delhi

10 Dr Shiva Kant Misra

UP

National Veteran Academic Excellence Awards

1 Dr S Arulhraj

Tamil Nadu

2 Dr Vinay Aggarwal

Delhi

3 Dr Jitendra B Patel

Gujarat

4 Dr K Vijayakumar

Tami Nadu

5 Dr A Marthanda Pillai

Kerala

6 Dr S S Agarwal

Rajasthan

7 Dr Ravindra Sitaram Wankhedkar

Maharashtra

8 Dr Santanu Sen

West Bengal

9 Dr Rajan Sharma

Haryana

National Young Academic Excellence Award

1 Dr Satyajit Borha

Assam

2 Dr Parulvadgama

Gujarat

3 Dr Divya Saxena

Haryana

4 Dr Erika Patel

Tamilnadu

5 Dr Garima Aggarwal

Karnataka

National Academic Excellence Award

1 Dr Shashank R Joshi

Maharashtra

2 Dr A Murgunathan

Tamilnadu

3 Dr Anilkumar J Nayak

Gujarat

4 Dr Rajeev Sood

Delhi

5 Dr Chintamani

Delhi

6 Dr Akil Contractor

Maharashtra

7 Dr Rajeev Gupta

MP

8 Dr R C Sreekumar

Kerala

9 Dr Gulam Malik

J & K

10 Dr Jyotirmoy Pal

West Bengal

National Best Teacher Award

1 Dr Sahajanand Pd Singh

Bihar

2 Dr S R Veeramani

Tamilnadu

3 Dr Ravi Dosi

MP

4 Dr Prabhakara GN

Karnataka

5 Dr Gargi Patel

Gujarat

6 Dr B L Bhandari

Rajasthan

7 Dr S K Kaushik

Rajasthan

8 Dr Arvind Pancholia

MP

9 Dr Amarendra Kumar Sinha

Bihar

10 Dr Pratibha Singh

Bihar

11 Dr Rajiv Garg

Delhi

IMA Academic Services Award

1 Mr Biswajeet Paul

Delhi

2 Mrs Neeru Bhasin

Delhi



IMA NATCON- 2021

(96th National Annual Conference of Indian Medical Association
82nd Annual Meeting of Central Council of IMA)

Organised by : IMA Bihar State Branch

Date: 27th & 28th December 2021 at Patna (Bihar)

Venue : Babu Sabhagar / S. K. Memorial Hall, Gandhi Maidan, Patna

CONFERENCE SECRETARIAT : Dr. Sahajanand Prasad Singh, Organising Secretary, NATCON-2021
IMA Building, Dr. A. K. N. Sinha Path, South East of Gandhi Maidan, Patna – 800 004 (Bihar),
Email: imanatcon2021@gmail.com, Website : www.imabihar.org, Mob: 9334118698, Ph: 7677253032



REGISTRATION FORM

Name : _____

Membership No : _____

Branch : _____ State : _____ Present Post in IMA : _____

Communication Address : _____

City : _____ State : _____ Pin Code : _____

Mob : _____ Email : _____

Please Tick Category :

Office Bearer of IMA HQ	C.W.C. / C.C. Member	IMA Member	Non Member	Medical / P.G. Member	Junior Resident
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Accompanying Person (s) Name (1) : _____

(2) : _____

Self Registration Charge - Rs. _____

Accompanying Person Charge (1) - Rs. _____

Accompanying Person Charge (2) - Rs. _____

TOTAL - Rs.

Total Rupees (in words) _____

Payment Details : Cheque/D.D. No. _____ dated _____ Bank & Branch _____

NEFT / UTR No. _____ dated _____ Bank _____

All payments to be made in the account of
"IMA NATCON 2021" payable at Patna by Cash/ at par Cheque/ Demand Draft / NEFT.
 A/c Name : **IMA NATCON 2021**, A/c No. - **0357101032465** | IFSC : **CNRB0000357**
 Bank & Branch : **Canara Bank, Kadamkaun, Patna**

Note : For Online Transfer it is mandatory to send Transaction ID/Number or Snap of receipt

REGISTRATION CHARGES (TAX INCLUDED)

Delegate Registration Fees Category	Till 30 th Oct., 2021	Till 30 th Nov., 2021	After 30 th Nov., 2021 or Spot Registration
IMA Members / Non Members	Rs. 5310/-	Rs. 6490/-	Rs. 7670/-
Medical Student / P.G./ Junior Resident (with ID Card)	Rs. 2950/-	Rs. 4130/-	Rs. 5310/-
Accompanying Person (Only participation in sessions and Meals) No Delegate Kit	Rs. 4130/-	Rs. 5310/-	Rs. 6490/-

- Note :**
- Please send separate Cheques/ Demand Draft / NEFT for Registration & Accommodation.
 - Please send Registration Form & Accommodation Form together at Conference Secretariat.
 - Registration Charges is not refundable.



Registration Coordinators :
 Dr. Sahajanand Pd. Singh - Mob - 9334118698
 Dr. Brajnandan Kumar - Mob - 9334787188
 Dr. Sunil Kumar - Mob - 9334116619
 Dr. Dinesh Kumar, - Mob - 7488601084

IMA Delegation met Hon'ble Union Minister of Environment, Forest & Climate Change Shri Bhupender Yadav Ji and Hon'ble Minister of State Shri Ashwani Choubey Ji on 6th September 2021.



Glimpses of IMA Teachers' Day Awards, 5th September, 2021, at IMA Hqs



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Organised by :
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CONFERENCE SECRETARIAT :
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