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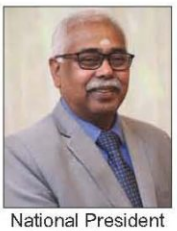
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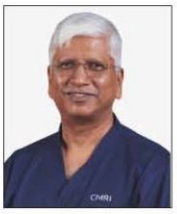
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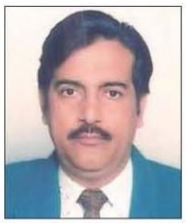
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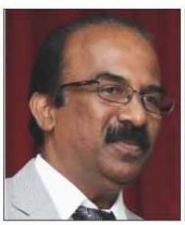
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Contents

(Continued next page)

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Contents

Editorial

Medical Negligence

— **Sanjoy Banerjee**
Hony Editor, JIMA

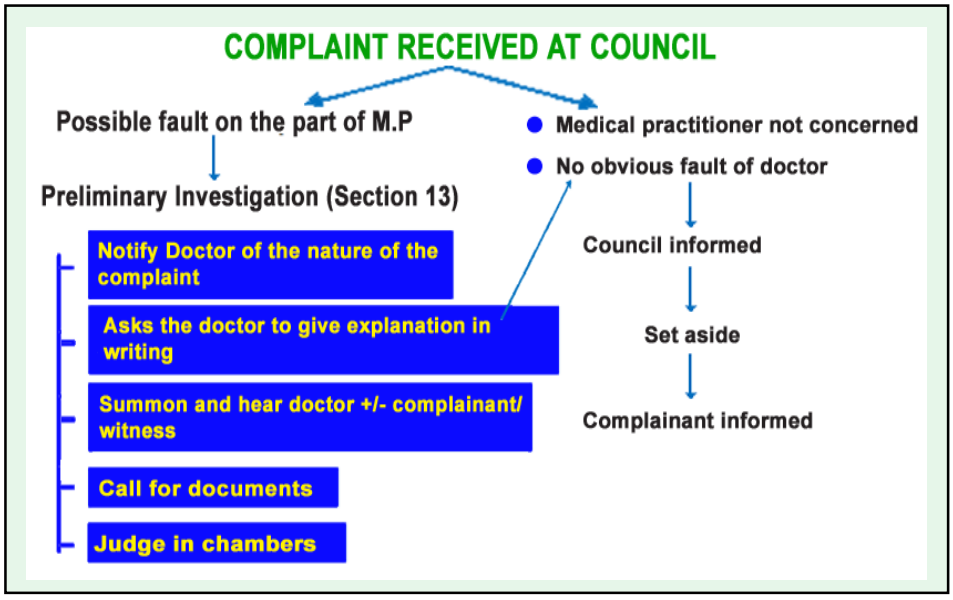
As per the Medical Council Act, **"negligence" includes failure on the part of a registered person to exercise the proper and timely care expected from a registered person**;

The Burden of proof that the doctor is negligent lies with the Patient under usual circumstance

***To succeed in a claim for negligence, a patient must prove, on a balance of probabilities,* the following :**

- **The defendant doctor owed him a duty of care**
- **The defendant doctor breached that duty by failing to exercise the necessary level of care**
- **Harm and injury was caused by that breach and**
- **He suffered damages which was not too remote *(ie, it was foreseeable by the doctor)***

The flow chart of a case of alleged medical negligence at Medical Council



The law has made it mandatory that the prosecution of doctors cannot be made until it is accompanied by the credible opinion of another competent doctor supporting the charge of rashness or negligence. Doctors accused of rashness or negligence may not be arrested simply because charges have been levelled against them.

Preventing Medical Litigation :

1. **You are a professional person so you must have professionalism. Your way of talking, your dressing and behaviour everything matters.** Some key areas you should maintain sincerely: a. **Dress like a doctor b. Speak like a doctor. and c. Behave like a doctor.**
2. The registered medical practitioner **must not guarantee cure of his patient irrespective of clinical condition of the patient.** He should **not exaggerate or minimize** the clinical condition of the patient.
3. **He should keep his professional knowledge including technical advances up-to-date** by participating in CME, Conferences, seminars, workshops and regular studying recent edition of standard text books, reputed journals etc. **There is no end of studying for a medical professional.**
4. **The capacity of a professional colleague and his efficiency and knowledge should not be publicly criticised. Follow PROFESSIONAL ETIQUETTE**
5. The same rule is applicable for **senior doctors while on round with junior doctors including interns, house physicians, post graduate trainees**. **If the visiting notices that certain mistake has been done by any junior doctor, he should never openly criticize the junior doctor before the patient or patient party.**
6. It is not wise to accept patient **beyond your speciality and qualification and degree of competence**.
7. He should apply due care/ reasonable care and skill during the treatment of the patient.
8. He should take **written informed consent in all steps of treatment** irrespective of any risk involved and apply the **rule of full disclosure** either to patient or the next of the kin of the patient with due consideration of therapeutic privilege.
9. **Always inform your patients regarding all foreseeable, known and expected risks** involved in the process of diagnosis and treatment.
10. Blanket consent has no role in medical practice. It is not legally valid.
11. Implied consent should not go beyond physical examination involving inspection, palpation, percussion and auscultation. For genital (including pubic and Suprapubic region), rectal and breast examination always take written consent.
12. Any consent should be taken before a disinterested third party (better take two independent witnesses).
13. **It is advisable that consent should be taken from both husband and wife if either of them is going to have a treatment which may cause sterility or impotence.**
14. **Laboratory investigations should be advised whenever necessary to come to a sound diagnosis or to confirm a clinical diagnosis**. Never miss to advice X-ray examination (or CT and MRI whenever indicated) when you are suspecting bony injury or foreign body in wound.
15. **Condition of the patient and the treatment are to be regularly recorded in detail as mentioned in the section of medical record**. **Medical record of the patient must be complete but relevant and should be in chronological order. Tampering must not be done in any ways.**
16. **Preserve medical records as per the guidelines** laid down by the MCI, Ministry of Health and Family Welfare, Govt of India or as per the provisions of your State Health Ministry
17. **Patient's condition is to be assessed regularly, in different hours of the day and night by the doctors of different tires associated with the treatment of the patient** including Unit-in-charge, interns, housestaffs, post graduate trainee, SR, RMO etc so that even a early complication can be detected by the resident doctors and consultant can be informed accordingly.
18. Unit in charge should be well aware of the functions of the trainees working under his supervision, involving treatment of the patient.
19. He should consult a professional colleague whenever necessary
20. The condition of the instruments or equipments must be checked regularly
21. **Always check yourself and also ask the nurse to check cautiously before injecting a particular drug.** Particular attention to be paid on the **label of a medicine** while giving it to a patient for internal use.
22. **Never mix two or more different types of injectable drugs in a single syringe before giving injection to the patient**. It may produce chemical reaction which is not known and cause

adverse reaction and even anaphylaxis in a patient. Instruct the nurses about the same.

23. Whenever necessary, **the patient should be immunised** against a disease.
24. **Injury due to assault and poisoning** cases should be specially dealt with. Always take a second opinion.
25. **No method should be tried beyond the skill of the doctor concerned in which he is not confident.**
26. **Always treat patient maintaining accepted standard treatment protocols**
27. Experimental treatment should be generally avoided. But if it is necessary then it should be done only with the written informed consent of the patient or the guardian of the patient.
28. During any emergency, the patient should not be left unattended except when there is more emergency of another patient. **Never leave a pregnant woman unattended during active stage of labor.**
29. Sensitivity test should be performed before injecting a drug which is known to cause allergic reaction or anaphylaxis. **Please remember a previous negative history of sensitivity to a drug or negative result of skin sensitivity testing never rules out the possibility of future adverse fatal anaphylactic or anaphylactoid reaction in an individual.**
30. **Prescription is better to be given in printed format.** If not possible then write the prescription in clear, legible handwriting in capital letters. Follow the guidelines laid down by MCI in relation to prescription.
31. The prescription must contain clear instructions to the patient in relation to **medicine, diet, life style modification, follow-ups** etc. Always mention to inform you or to come to you whenever necessary.
32. **Never assess the condition of the patient by hearing over telephone**, ask him to visit you if possible or otherwise you can make a home visit to see the patient.
33. Never tell any prescription to the patient or any family member of a patient over telephone as there is a high chance of misunderstanding the name of the medicine or its dosage.
34. **Anaesthesia should be administered by a qualified and experienced doctor.**
35. **Necessary pre-anaesthetic check-up** should be done in cases of elective surgery.
36. Anaesthetist should not leave the patient before the patient's full recovery from anaesthesia.
37. **In case of death of the patient under anaesthesia or on the operation table,** an inquest should be recommended by informing the police.
38. Surgical procedures should be carried out in those **hospitals or Nursing homes where there is adequate infrastructure and qualified man power including proper anaesthetic support** and moreover those institutions should be capable of managing post operative complications.
39. **During the course of surgery if any complication arises** or **the surgeon is forced to change the agreed course** which he did not plan before starting the operation, and for which informed consent has not obtained, but it is necessary for the benefit of the patient, in such case the **surgeon himself should communicate with the relatives of the patient** to take their consent and in no case he should delegate this duty to any junior doctor/ nurse/ anaesthetist.
40. Before the surgery **informed consent should be taken separately for anaesthesia**, in a separate form.
41. Informed consent is essential for blood transfusion.
42. **Informed consent should be taken directly by the doctor under whom the patient was admitted/ the chief surgeon going to operate on the patient and the chief anaesthetist who is going to give anaesthesia,** and never by other team members involved in the treatment of the patient or any members involved in surgery or anaesthesia.
43. **Informed consent must be obtained before a particular procedure**, not during the time of admission in hospital.
44. Due care must be exercised **while choosing an assistant** during an operation or otherwise.
45. **Post-operative care should be optimum involving liability of the surgeons and anaesthetists.**
46. **If the doctor is unable to attend the patient due to any cause for the time being**, then the patient should be informed of the same, well in advance with the advice to arrange for a competent substitute.
47. **Whenever necessary, the patient should be referred to another higher centre with availability of better facilities if your facility is inadequate to manage the case**. But never refer to another centre which is also incapable of managing the same. Also the **hospital should provide adequate support and facilities during the process of transfer.**

Acceptable conclusion is —

- The practitioner must bring to his task a reasonable degree of skill and knowledge, and must exercise a reasonable degree of care.
- A medical practitioner would be liable only where his conduct fell below that of the standards of a reasonably competent practitioner in his field

Landmark judgements in medical Negligence :

Case Laws Related to Legal Maxim In India

There are several case laws in India where the principle of res ipsa loquitur has been applied in cases of medical negligence. Here are some examples:

1. Dr. Laxman Balkrishna Joshi v. Dr. Trimbak Bapu Godbole (1969)[i] :

In this landmark case, the Supreme Court of India held that the principle of res ipsa loquitur could be applied in medical negligence cases when the facts and circumstances of the case suggested that negligence had occurred, and when the burden of proving negligence was on the defendant.

2. Spring Meadows Hospital and Anr. v. Harjol Ahluwalia (1998) [ii] :

In this case, the National Consumer Disputes Redressal Commission (NCDRC) applied the principle of res ipsa loquitur to a case where surgical patient suffered from an injury to their urethra during surgery. The NCDRC held that the injury was of a type that would not ordinarily occur in the absence of negligence, and that the burden of proof was on the hospital to prove that they were not negligent.

3. Poonam Verma v. Ashwin Patel and Ors. (1996)[iii] :

In this case, the Supreme Court of India applied the principle of res ipsa loquitur to a case where a surgical patient suffered from a facial nerve injury during surgery. The court held that the injury was of a type that would not ordinarily occur in the absence of negligence, and that the burden of proof was on the defendant to prove that they were not negligent.

4. Jacob Mathew v. State of Punjab (2005) [iv] :

In this case, the Supreme Court held that res ipsa loquitur could be applied in medical negligence cases where the injury was of a type that would not ordinarily occur in the absence of negligence, and where the facts surrounding the injury suggested that the healthcare professional was responsible.

Related Provisions For Medical Negligence In India

- **Section 304A of the Indian Penal Code :** This section deals with causing death by negligence. If a medical professional causes the death of a patient due to negligence, they can be punished with imprisonment for up to two years or a fine, or both.
- **Section 337 of the Indian Penal Code :** This section deals with causing hurt by an act endangering life or personal safety. If a medical professional endangers the life or safety of a patient due to negligence, they can be punished with imprisonment for up to six months or a fine, or both.
- **Section 338 of the Indian Penal Code :** This section deals with causing grievous hurt by an act endangering life or personal safety. If a medical professional causes grievous hurt to a patient due to negligence, they can be punished with imprisonment for up to two years or a fine, or both.
- **The Consumer Protection Act, 1986 :** Under this act, patients have the right to file complaints against medical professionals and seek compensation for medical negligence[2].

Latest Updates :

Bharatiya Nyaya Sanhita

Punishment for the doctors for criminal negligence: Currently, medical negligence resulting in deaths is punishable under Section 304A of the Indian Penal Code (IPC) with imprisonment of up to two years, a fine, or both. Previously, in the BharatiyaNyaya (Second) Sanhita (BNS) 2023, Clause 106, the punishment was up to five years. However, the amended (BNS) 2023, clause 106 (section-1) has reverted to the original IPC terms ie, punishment of two years and fine.

The new Consumer Protection Act came into effect in June, 2019.

Section 2(42) of the act defines 'services' however the section clearly does not include 'healthcare' within its ambit. The word has been not specifically included but not even excluded because of the words of the section which clears that the services are not restricted and limited to the meaning as given but may also include definitions which may have the same meaning and effect. By this, the legislature has created an ambiguity as to the "healthcare" services, whether included under the Act or not.

However, the Supreme Court while laying down the law upon the relevancy of Consumer Protection Act, 2019 on services rendered by the doctors held that the doctor who has drawn salary from the hospital but rendered his services for free shall not fall under the Consumer Protection Act[3].

Further Readings

1 "Textbook of Forensic Medicine and... by Anil Aggrawal." https://www.amazon.in/Textbook-Forensic-Medicine-Toxicology-Aggrawal/dp/8177394193.
2 "Medical Negligence Laws In India - Legal Service India." https://www.legalserviceindia.com/legal/article-10686-medical-negligence-laws-in-india.html.
3 "The Consumer Protection Act, 2019: A critical analysis from a medical ...." 27 Nov. 2023, https://ijme.in/articles/comment-the-consumer-protection-act-2019-a-critical-analysis-from-a-medical-practitioners-perspective/?galley=html.

Original Article

Use of Remdesivir as an Investigational Therapy in Moderately Severe COVID-19 Cases

Anjan Jyoti Talukdar[1], Raj Pratim Das[2], Basanta Hazarika[3], Priyam Saikia[4], Sangitanjan Dutta[5], Achyut Chandra Baishya[6]

Background : The lack of an effective and safe pharmacologic agent to combat COVID-19 pandemic has led researchers to evaluate several molecules indicated for use in other diseases either as anti-viral or immune-modulating agents.

Materials and Methods : This observational study was conducted in patients with moderately severe COVID-19 disease that were treated with steroids and anti-thrombotic agents with or without Remdesivir. All patients received Remdesivir for 5 days (200 mg IV on Day 1 followed by 100 mg IV daily for 4 days). The primary outcome was the time to recovery or survival benefit, if any. Total 478 patients were studied (226 received Remdesivir and 252 received only steroid and heparin). Analysis revealed marginal survival benefit in patients treated with Remdesivir (p Value <0.108). It was also seen that starting Remdesivir early in the course of the disease offers greater benefits. However, the duration of hospitalization was not favorably affected by use of Remdesivir. Use of Remdesivir also resulted in early viral clearance. No serious adverse events were noted.

Conclusions : Remdesivir along with steroid and heparin improved survival in moderate COVID-19 infections and led to early viral clearance.

[*J Indian Med Assoc* 2024; **122(2):** 15-20]

Key words **: COVID-19, Remdesivir, Investigational Therapy.**

Since the identification of the COVID-19 virus (SARS-CoV-2) in China in December, 2019 till date, the pandemic caused by this highly infectious virus has taken the whole world by surprise[1]. Even the best of the health care facilities of the world appeared insufficient to tackle the menace caused by this organism. The lack of an effective pharmacologic agent has added to the mortality. Several molecules used as antivirals and immuno-modulating agents in various other diseases have been utilized to treat COVID-19 with variable benefits[2]. Remdesivir, which inhibits viral RNA dependent RNA polymerase, showed some benefits in treating patients with SARS-CoV and MERS-CoV and therefore was an obvious candidate trials in COVID-19[3]. Animals treated with Remdesivir did not show signs of respiratory disease, had reduced pulmonary infiltrates on radiographs and virus titers in bronchoalveolar lavages were significantly reduced as early as 12 hours after the first treatment was administered[4].

Editor's Comment :

- Remdesivir is seen to benefit patients with moderate severe COVID-19 infection.
- The benefit was noted in the form of decreased hospitalisation days, reduced need for supplimental oxygen and ICU care.

This study was conducted to evaluate the clinical efficacy and safety of Remdesivir in patients with moderately severe COVID-19 infection in Gauhati Medical College and Hospital.

Materials and Methods

Study Design :

The patients admitted in Dedicated Covid Hospital of Gauhati Medical College and Hospital (GMCH) from May to August,2020 were enrolled into the study. The patients fulfilling criteria of moderate COVID-19 disease as per ICMR/MoHFW, Government of India,defined as SPO2<95% in room air, respiratory rate >24 or respiratory distress were enrolled.

Remdesivir was available for use in GMCH from July, 2020. Therefore, the patients who were admitted

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in July and August received Remdesivir in addition to steroid and anti-thrombotics and this group constituted the study arm.The group of patients admitted in May and June, 2020, were treated with steroids and anti-thrombotics and they constituted the comparator arm.

All patients continued to receive the standard supportive care as per Government of Assam guidelines that comprised of Azithromycin 500 mg OD for 5 days, Zinc 50 mg OD, Vitamin C 500 mg OD, Vitamin D 60K IU Once Weekly and Famotidine 20 mg BD[5].

Steroid was given in the form of Dexamethasone 6 mg once daily (Intravenous or per oral) for a period of 10 days. Low molecular weight Heparin in a dose of 1mg/kg once daily subcutaneous (Or 5000 U Unfractionated Heparin subcutaneously once daily in case of patients with Chronic Kidney Disease) was given for a period of 10 days.

Remdesivir was administered intravenously as a 200-mg loading dose on day 1, followed by a 100-mg dose given daily on day 2-5.

Remdesivir was not administered to patients who had altered liver function (AST or ALT >5 times the upper limit of normal or patients with decompensated cirrhosis) and significant renal insufficiency (eGFR<30 ml/min) at the time of enrollment.

The study protocol was approved by the Institutional Ethical Committee of GMCH and use of Remdesivir was approved as an Investigational Agent for use in COVID-19 after obtaining informed consent from patient or from the patient's legally authorized representative.

Monitoring :

Patients were assessed daily during their hospitalization, from day of enrollment till the day of discharge or death. The patient's clinical status was recorded each day. Laboratory investigations including CBC, DLC, NLR (Neutrophil:Lymphocyte Ratio), Creatinine, LFT was done at baseline and repeated on Day 5 and Day 14 or Day of discharge. RTPCR for COVID-19 was repeated every 3rd day till tested negative or death. All adverse events were recorded.

Statistical Analysis :

The primary outcome measure was survival benefit, if any, attributable to the use of Remdesivir added to steroids and anti-thrombotics in moderately COVID-19 infection.

Other outcome measures included :

(1) Reduction in duration of hospitalization by either discharge or shifting to a non-covid set-up for patients who tested negative for COVID-19 but requiring hospitalization for other medical conditions

(2) Viral clearance was defined as the time taken for RTPCR test to turn negative

Sub-group analyses comparing the effects of age groups (18-40 years, 40-60 years and >60 years), gender, presence of co-morbidities and duration of symptoms before initiation of therapy on the outcome measures was also carried out to look for statistically significant associations.

Results

Patient recruitment :

A total of 478 patients admitted in Gauhati Medical College Covid Hospital, were enrolled in the study.All patients were diagnosed with RTPCR for COVID-19.

A total of 226 patients, who received Remdesivir along with Steroid and Heparin were hereafter referred to as Group A. All patients in Group A completed 5 days of Remdesivir therapy.

Another Group of 252 patients who were treated with Steroid and Heparin were enrolled as comparator and this group is hereafter referred to as Group B.

Both the Groups (A & B) continued to receive standard supportive care protocol followed in Gauhati Medical College, that consists of Azithromycin 500 mg OD for 5 days, Zinc 50 mg OD, Vitamin C 500 mg OD, Vitamin D 60K IU Once Weekly and Famotidine 20 mg BD.

Both the groups, were closely monitored during the entire period of hospitalization for clinical improvements / deterioration (Tables 1&2).

Baseline characteristics :

The mean age of patients in Group A was 54.27 years and 49.80 years in Group B.

Group A had 15.90% patients below 40 years of age and 35.40% patients above 60 years of age. Group B had 27.40% patients below 40 years of age and 29.80% patients above 60 years of age. Males constituted 74.80% of patients in Group A and 65.50% of patients in Group B.

Both the groups had patients with co-morbid illness, commonest being Diabetes Mellitus, Hypertension, Chronic Kidney Disease and Coronary Artery Disease, with similar distribution in both the groups.

A total of 181 patients (37.9%) out of 476 enrolled had one or more co-existing medical illness. Out of these Group A had 18.4% and Group B had 19.5% patients with co-morbidities. The most common conditions were T2DM (26.6%-35.9%), CKD (17.4%-24.2%), Hypertension (21.95-23.9%), CAD (7.6%-7.8%) besides others (15.2%-19.5%). Others included Bronchial Asthma, Systemic lupus Erythematosus, Rheumatoid arthritis, Congenital Heart Disease, Seizure Disorder, Allergic Rhinitis etc.

Most patients had either one (27.0%) or two or more

Table 1 — *Baseline Demographic and Clinical Characteristics of Participants in both the Groups*

Parameters	Group A n= 226	Group B n= 252	P value
Clinical characteristics [absolute no (percentage) or Mean ± Standard Deviation]			
Age (years)	54.27±15.33	49.80±17.48	0.003
<40	36 (15.9)	69 (27.4)	0.0036
40-60	110 (48.7)	108 (42.9)	0.2370
>60	80 (35.4)	75 (29.8)	0.2238
Gender :			
Male	169 (74.8)	165 (65.5)	0.0269
Female	57 (25.2)	87 (34.5)	
Duration of symptom (Days)	3.55±1.90	2.98±0.99	0.004
Co morbidity [absolute no (percentage)]			
CAD	7 (7.60)	10 (7.80)	0.9555
DM	33 (35.9)	34 (26.6)	0.1832
HTN	22 (23.9)	28 (21.9)	0.8472
CKD	16 (17.4)	31 (24.2)	0.2928
Others	14 (15.2)	25 (19.5)	0.5173
Laboratory Investigations (Mean ± Standard Deviation)			
Hb	11.7±2.55	12.9±2.13	0.131
TC	12.04±7.49	10.0±4.07	0.014
Neutro	75.75±10.48	70.68±11.45	0.001
Lympho	18.74 ±11.20	23.05±10.05	0.003
NLR	5.94±4.73	3.97±2.78	<0.0001
Platelet	210.82±82.81	201.88±76.46	0.436
RBS	179.60±111.86	124.08±50.10	0.005
Creatinine	1.38±2.26	1.54±1.96	0.595
Billirubin	1.57±4.25	2.30±6.67	0.402
AST	85.53±201.10	65.89±43.91	0.421
ALT	90.14±184.63	60.18±61.55	0.218
Albumin	4.26±6.87	3.73±0.91	0.598
Alkaline Phosphatase	111.11±45.325	128.04±59.539	0.447
SpO_2 (Mean ± Standard Deviation)	95.09±5.05	95.98±1.94	0.01
O_2 requirement (L/min)	6.23±2.60	4.67±2.36	<0.0001

(52.1%) of the prespecified coexisting conditions at enrollment, most commonly hypertension (49.6%), obesity (37.0%), and type 2 diabetes mellitus (29.7%).

The mean SPO_2 on oxygen supplementation on the first day of hospitalization was 95.09 % in Group A whereas it was 95.98% in patients enrolled in Group B. The mean O_2 requirement was 6.23 L/min in group A compared to 4.67 L/min in patients of Group B.The mean duration of symptom onset prior to initiation of therapy was 3.55 days in Group A (q2-q3 = 2-6). compared to 2.98 days in Group B (q 2-q3 = 2-4).

Patients enrolled in Group A had a mean Neutrophil to Lymphocyte Ratio (NLR) of 5.94 compared to 3.97 in Group B (p Value ≤0.0001). The mean Random Blood Sugar (RBS) levels was 179.60 mg/dlin Group A whereas it was in 124.08 mg/dl in Group B (p Value ≤0.005).The other laboratory parameters namely Total Leucocyte count, Platelet Count, Creatinine and Liver Function Tests did not reveal any significant differences.

Table 2 — *Presence of Co-morbidities in the study population*

Co-morbidity (overall)	Frequency	Percent
No	258	53.97
Yes	220	46.03
Total	478	100
Co-morbidity (Group wise)	Frequency	Percent
Group A (Co-mrobidity-absent)	134	59.29
Group A (Co-mobidity-present)	92	40.71
Group B (Co-mrobidity-absent)	124	49.20
Group B (Co-mrobidity-present)	128	50.79

Evaluation of Outcome Measures :

The overall mortality in our study was 21.5% (103). 41 patients died in Group A (18%) and 62 died in Group B (24.6%). Although not statistically significant, the survival was marginally better in patients receiving three drugs (Remdesivir+ Steroid+Heparin) compared to those receiving only Steroid and Heparin (p value-0.108) (Table 3).

Time of initiation of Remdesivir and survival (Table 4).

A statistically significant difference in survival status based on the Remdesivir starting day after symptom onset is observed. For those who were alive the mean day of starting Remdesivir after onset of symptoms is 6.4 days compared to those who died when Remdesivir was used at 8.2 days, p=0.003 (Table 3 and Fig 2). Also a 5.9% increased risk of death (HR 1.059, P=0.043) was observed for delay in use of Remdesivir after onset of symptoms (Table 3.2).

Age and Outcome :

Of the 41 patients that died in Group A, 13 patients were more than 60 years of age (31.7%) and 28 patients (68.29%) were less than 60 years of age. In Group B, out of 62 deaths, 13 patients were aged more than 60 years (20.96%) and 49 patients were aged less than

Table 3 — *Showing deaths and survivors in both the groups*

Group A (n=226) Mortality		Group B (n=252) Mortality		Overall Mortality (n-478)		Chi square test, P value
41	18%	62	24.6%	103	21.5%	2.573
Alive (Group A)		Alive (Group B)		Alive (Overall)		
185	82%	190	75.4%	375	78.5%	0.108

Table 4 — *Interval of initiation of Remdesivir in survivor and non-survivors*

Remdesivir used	n	Mean	Standard Deviation	95% confidence interval for mean Lower bound	Upper bound	Minimum	Maximum	p value
Day of starting Remdesivir after symptom onset :								
ALIVE	185	6.4066	2.39434	5.9079	6.9052	1	14	
DEAD	41	8.2113	5.01402	7.0245	9.3981	1	22	0.003
TOTAL	226	7.1975	3.8655	6.5978	7.7973	1	22	

60 years of age (79%). No significant difference in outcome was noted.

Gender and Outcome :

Gender distribution was not significant in Group A comparing Outcome (p value 0.957), whereas males had more mortality in Group B (p value<0.0001).

Co-morbid conditions and Outcome :

With respect to presence of associated Co-morbid conditions, it was found that those with Co-morbid conditions had increased mortality (HR 1.64, 95% CI, p value <0.0001)

Comparing patients with Co-morbidities, both group showed poor outcome in the high risk patients.

In Group A those with co-morbid illness had 1.883 times higher risk of death (p value 0.008) as compared to 3.049 times higher risk in Group B (p value <0.001)

Mean duration of hospitalization was higher (10.01 days) in group A compared to (7.47 days) Group B (p value <0.0001).

Mean duration of ICU stay was higher (4.29 days) in group A compared to (3.33 days) Group B (p value <0.0002).

The mean days of viral clearance (number of days from first swab till day of RTPCR Negative) in Group A is found to be 12.9 days (12.2-13.5, 95% CI) as compared to Group B which is 15.1 days (13.3-16.8, 95% CI).

Applying Unpaired T Test with Welch Correction, the mean difference of the two groups is found to be 2.185 (0.31-4.1). Two Tailed p Value is 0.0224, considered significant. This implies that the mean days of virological response in Group A is nearly 2.2 days earlier than those in Dual Therapy, which is found to be statistically significant.

Adverse events :

A total of 82 patients reported adverse events. The most common were elevated hepatic transaminases, hyperglycemia and altered renal function. We noted increase of AST and ALT upto 3 to 4 times upper limit of normal in 26.6% of patients receiving Remdesivir and in 6.7% in those not receiving Remdesivir. However, none of the patients required discontinuation of Remdesivir and the levels of transaminases stabilized towards day 14.

The blood sugar levels showed increasing trend in both Group A and B, with mean values of 201.2 mg/dl on day 5 and 194.0 mg/dl on day 14 in Group A and Group B showed a mean value of 205.8 mg/dl on day 5 and 196.4 mg/dl on day 14.

The Serum Creatinine levels increased by a margin of 8-12% in both Group A & B with a mean of 1.42 mg/dl on day 5 and 1.40 mg/dl on day 14, whereas Group B recorded a mean of 1.41 mg/dl on day 5 and 1.33 mg/dl by day 14 (Table 2)

Discussion

The overall mortality in our study was 21.5% (103). 41 patients died in Group A (18%) and 62 died in Group B (24.6%). Although not statistically significant, the survival was better in patients receiving three drugs (Remdesivir + Steroid + Heparin) compared to those receiving only Steroid and Heparin (Table 3).

This finding is consistent with other studies which showed reduction of mortality in patients treated with Remdesivir with or without use of other drugs in combination[6].

Beigel, *et al* found that their results from the 1059 patients (538 assigned to Remdesivir and 521 to Placebo) with data available after randomization indicated that those who received Remdesivir had a median recovery time of 11 days (95% confidence interval [CI], 9 to 12), as compared with 15 days (95% CI, 13 to 19) in those who received placebo (rate ratio for recovery, 1.32; 95% CI, 1.12 to 1.55; P<0.001). The Kaplan Meier estimates of mortality by 14 days were 7.1% with Remdesivir and 11.9% with placebo

Table 5 — *Cox regression analysis showing effect of gender and presence of Co-morbidities on outcome*

		HR	95.0% CI for Exp(B)		Signifi-cance
			Lower	Upper	
Gender :	Male	Ref			
	Female	0.886	0.652	1.204	0.439
Co-morbidity :	No				
	Yes	1.64	1.244	2.161	<0.0001
Remdesiver used+ Male	Group A (Male)	Ref			
Remdesiver used+Female	Group A (Female)	0.986	0.586	1.658	0.957
Remdesiver Not used +Male	Group B (Male)	1.971	1.399	2.777	<0.0001
Remdesiver Not used+Female	Group B (Female)	1.554	1.019	2.37	0.041
Remdesiver Used (Co-mrobidity-absent)	Group A (Co-mrobidity-No)	Ref			
Remdesiver Used (Co-mrobidity-present)	Group A (Co-mrobidity-Yes)	1.883	1.181	3	0.008
Remdesiver Not Used (Co-mrobidity-absent)	Group B (Co-mrobidity-No)	2.041	1.349	3.088	0.001
Remdesiver Not Used (Co-mrobidity-present)	Group B (Co-mrobidity-Yes)	3.049	2.006	4.634	<0.001

(hazard ratio for death, 0.70; 95% CI, 0.47 to 1.04)[6].

A statistically significant difference in survival status based on the Remdesivir starting day after symptom onset was observed. For those who survived, the mean day of starting Remdesivir after onset of symptoms is 6.4 days compared to those who did not survive when Remdesivir was used at 8.2 days, p=0.003 (Table 4 and Fig 1).

We observed that starting Remdesivir early in the course of the disease, leads to significant reduction in risk of death in comparison to starting late after onset of symptoms. This data is consistent with the fact that Remdesivir has shown both as antiviral and clinical effects both *in vitro* and *in vivo* and also early administration of Remdesivir have shown better clinical outcomes (M Wang, *et al* 2020; Williamson, *et al* 2020; Pizzorno, *et al* 2020)[4,7,8].

Williamson, *et al* 2020., found that therapeutic Remdesivir treatment initiated early during infection has a clear clinical benefit in SARS-CoV-2 infected Rhesus Macaques. This data supports early Remdesivir treatment initiation in COVID-19 patients to prevent progression to severe pneumonia[4].

In the study by Wang, *et al* in 2020, however, the primary outcome, time to clinical improvement was 21 *versus* 23 days with Remdesivir and placebo, respectively (HR 1.23, 95% CI 0.87 to 1.75). 28-day mortality was similar 14 *versus* 13%, -1.1% (95% CI -8.1 to 10.3%). The authors conclude that 'intravenous Remdesivir did not significantly improve the time to clinical improvement, mortality or time to viral clearance in patients with serious COVID-19, compared with placebo[7].

Goldman, *et al* noted that discharge rates were higher in the overall population among patients who had had symptoms for less than 10 days before receiving the first dose of Remdesivir (62%) than among those who had had symptoms for 10 or more days before receiving the first dose (49%)[9].

It was found that those with Co-morbid conditions had increased mortality (HR 1.64, 95% CI, p value <0.0001). Both group showed poor outcome in the high risk patients. In Group A those with Co-morbid illness had 1.883 times higher risk of death (p value 0.008) as compared to 3.049 times higher risk in Group B (p value <0.001) (Table 5, Fig 2).

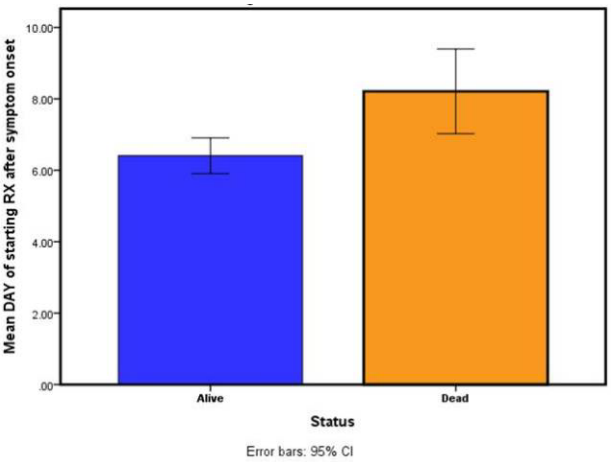

Fig 1 — Mean duration of starting Remdesivir and outcome

Co-morbidity and age (above 65 years) with COVID-19 are one of the greatest risk factor of increased mortality[10]. In our study consistent data have been

Table 6 — *Mean duration of hospitalization and ICU stay*

	Group A			Group B			
	N	Mean	Std. Deviation	N	Mean	Std. Deviation	P Value
DoH	226	10.01	5.24	252	7.47	4.06	<0.0001
DolCU	119	4.29	2.90	175	3.33	2.58	<0.0002

Table 7 — *Mean duration of Viral Clearance in the study population*

Viral Clearance	Group A	Group B	P Value (T-test/Chi Square Test with Welch Correction)	P Value
Days	12.8 ± 4.31	15.06 ± 9.02	0.0224	0<0.0001

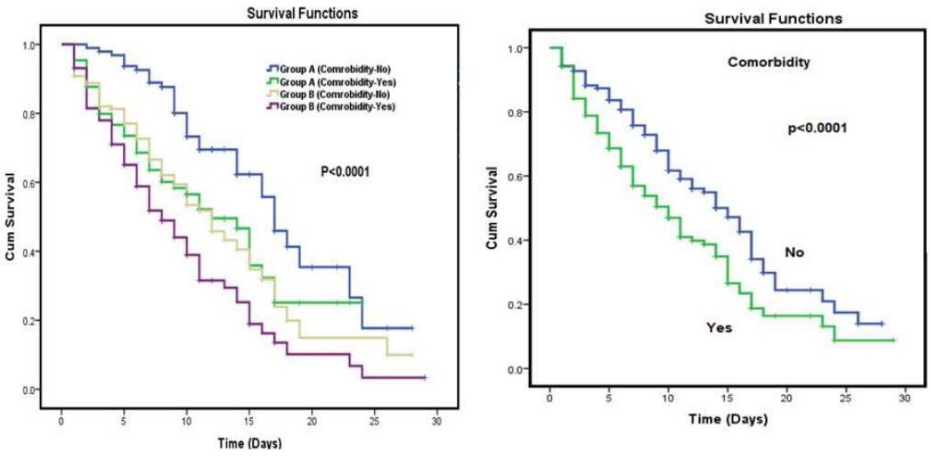

Fig 2 — Kaplan Meier survival curve showing survival benefit in patients without Co-morbidity

found in cases having Co-morbid conditions, the percentage survival decreased significantly (P< 0.0001) as expected. The percentage of survival in co-morbid cases was 56.90% whereas it was 75.80% in persons without Co-morbidity in 7 days. Median survival days in comorbid cases is 10 days whereas in others without Co-morbidity is 15 days.

Yang, *et al* in 2020 concluded that older patients (>65 years) with comorbidities and ARDS are at increased risk of death[10].

Mean duration of hospitalization was higher (10.01 days) in group A compared to (7.47 days) Group B (p value <0.0001). Mean duration of ICU stay was higher (4.29 days) in group A compared to (3.33 days)Group B (p value <0.0001)(Table 6).

The viral clearance in Group A was found to be 2.2 days earlier (mean 12.9 days) as compared to Group B (mean 15.1 days)(Table 7).

We observed that use of Remdesivir with standard supportive treatment leads to quicker virologic response as compared to Dexamethasone and Enoxaparin which signifies Remdesivir being an effective antiviral in addition to the baseline drugs used.

Williamson, *et al* found that 12 hours after the first Remdesivir treatment was administered, the infectious virus titer in BAL was ~100-fold lower in Remdesivir-treated animals than controls. By 3 dpi (day post inoculation), infectious virus could no longer be detected in BAL from Remdesivir-treated animals. However, despite this reduction in virus replication in the lower respiratory tract, neither viral loads nor infectious virus titers were reduced in nose, throat or rectal swabs collected from Remdesivir-treated animals, except a significant difference in virus titer in throat swabs collected on 1 dpi and in viral loads in throat swabs collected on 4 dpi[4].

Our patients demonstrated 3-4 fold rise in hepatic transaminases in both the groups, more so in the Remdesivir treated group. However, none were severe (Table 8).

Table 8 — *Mean values of laboratory parameters*

	Group A				Group B			
	N	Mean D0	Mean D5	Mean D14	N	Mean D0	Mean D5	Mean D14
RBS	97	179.6	201.2	194.0	36	124.08	205.8	196.4
Creat	143	1.38	1.42	1.40	83	1.54	1.41	1.33
AST	139	85.53	151.2	100.3	70	65.89	146.9	82.7
ALT	139	90.14	163.3	106	61	60.18	139.4	72

Conclusion

Our study showed improved survival in patients treated with Remdesivir along with Steroids and Heparin. We also noted that early initiation of Remdesivir offered greater clinical benefits. The Remdesivir treated group also demonstrated early viral clearance. However, no favorable effect on duration of hospitalization was found with use of Remdesivir.

Our study however, was an observational retrospective analysis involving a relatively small sample size. To comment on the positive effects Remdesivir noted in our study, a randomized prospective study involving larger cohort in multiple centres across the state or country would be required.

However, this is the first of its kind study conducted in the entire North East India looking into the therapeutic efficacy of Remdesivir.

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Original Article

Clinico-epidemiological Profile of MIS-C Temporally Associated with COVID-19 — A Hospital Based Retrospective, Cross Sectional, Observational Study. What is new ?

Abhilash Chatterjee[1], Tapan Kumar Kundu[2], Mitali Bera[3], Aditi Chowdhury[4], Imran Khan[4]

Background : Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) related Multisystem Inflammatory Syndrome in Children (MIS-C) is an acute illness accompanied by hyper-inflammatory syndrome and may require ICU admission and can lead to multi organ failure and shock. The objective of this study was to study the Clinico-epidemiological profile and outcome of children with MIS-C treated with methylprednisolone alone or combined methylprednisolone and Intravenous Immunoglobulin (IVIG)

Materials and Methods : This retrospective, observational, cross-sectional study was conducted in children who were admitted from May, 2021 to April, 2022 satisfying WHO MIS-C criteria. Clinico-epidemiological data were obtained and treatment outcomes were compared between children who received methylprednisolone alone and those who received combined methylprednisolone and IVIG.

Results : Study included 53 children with MIS-C with majority patients ie, 22(41.5%) were infants. Respiratory symptoms were present in 12(22.6%) patients.Gastrointestinal symptoms were present in 19(35.8%) patients. Cardiovascular symptoms were present in 13(24.5%) patients. Neurological symptoms were present in 18(34%) patients. Mucocutaneous symptoms were present in 28(52.8%). Methylprednisolone and IVIG were used as immunomodulator therapy. 31(96.9%) patients who received methylprednisolone alone and 21(100%) patients who received combined methylprednisolone and IVIG got discharged. ICU stay for more than 14 days and invasive ventilation requirement were significantly less in methylprednisolone group (p value 0.011438; p value 0.011993).

Conclusion : Both treatment with methylprednisolone alone and methylprednisolone and IVIG combined showed favourable and comparable outcomes in both the groups.

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Key words **: MIS-C, Methylprednisolone, IVIG, COVID-19, SARS-CoV-2.**

The COVID-19 pandemic is far from over and it will not be over anywhere until it's over everywhere[1]. Multisystem inflammatory Syndrome in Children (MIS-C) is an acute illness accompanied by hyper-inflammatory syndrome and may require ICU admission and can lead to multi organ failure and shock[2-5]. There are certain findings that distinguish MIS-C from severe COVID-19[6]. Occurence of MIS-C also has some racial differences[7]. There is therefore an urgent need for collection of standardised data describing clinical presentations, severity, outcomes and epidemiology[2,8]. Early diagnosis is important for favourable outcomes[9]. So, it is important to know the clinical profile of MIS-C temporally associated with COVID-19 of the children in this geographical area.

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Editor's Comment :

- Favourable and comparable outcomes were seen with both treatment with methylprednisolone alone and combined methylprednisolone and IVIG.
- Use of methylprednisolone alone without IVIG for treatment of MIS-C patients in resource constraint setups needs to be determined through larger multicentric studies.

There is a continuous evolution of our understanding of SARS-CoV-2 related syndromes in children[4,10]. Robust information about long-term outcomes needs further study along with immunologic data to improve diagnostic and therapeutic strategies[11]. Various guidelines have already come up which are progressively being upgraded. Further studies are needed urgently to define the real impact of MIS-C on child health and to elucidate the best clinical and therapeutic approach and true prognosis[12,13].

Materials and Methods

This retrospective, observational, cross sectional study was conducted in a peripheral resource constraint Tertiary Care Medical College & Hospital in

India. Ethics Committee clearance for biomedical research involving human participation was obtained before the start of the study from the institutional ethics committee. It was conducted for the period from May, 2021 to April, 2022.

Diagnosis of MIS-C was made on the basis of WHO criteria[2]. Children admitted with MIS-C upto 12 years of age were included. Exclusion criteria were infection with dengue, scrub typhus and bacterial sepsis.

SARS-CoV-2 reverse transcriptase polymerase chain reaction (RT-PCR) was done and SARS-CoV-2 antibody test were done using Electro-chemiluminescence Immuno-assay Analyser (ECLIA). Contact with SARS-CoV-2 patient in past was also documented in all patients. Treatment guideline included methylprednisolone alone and methylprednisolone and IVIG combined as immuno-modulator. Availability of IVIG was an issue. In its absence, necessary modification was made. Study population had no choice of the treatment they received. Echocardiography was done during admission and was followed up after 4-6 weeks or frequently in some cases as per guidelines. Shock was identified in presence of clinical features as per standard guidelines.

Data extraction sheet with pre-designed proforma was used to collect data on demographic, clinical symptoms and signs, type of supportive treatment and immunomodulation. Data were entered in statistical analysis software. Chi square test was used for statistical analysis.

Results

This study included total 53 patients. Males were 38(71.7%). 53(100%) patients had positive SARS-CoV-2 IgG antibodies and temporal association with SARS-CoV-2 contact was present in 10(18.9%) patients. Clinical characteristics as shown in Table 1 are maximum number of patients were infants ie, 20(41.5%), 11(20.8%) were of 1-3 years age, 10(18.9%) were of 3-6 years age, 5(9.4%) were of 6-9 years age and 5(9.4%) were of 9-12 years age. The mean age was 2.62 years(SD 3.43). Associated condition such as diabetes was present in 2(3.8%) patients and neurological disease was present in 7(13.2%) patients. Symptom duration before admission was 5 days (IQR 3-7). Respiratory symptoms were present in 12(22.6%) patients which included cough in 10(18.9%), wheezing in 5(9.4%) and respiratory distress in 3(5.7%) patients. Gastrointestinal symptoms were present in 19(35.8%) patients which included diarrhoea in 15(28.3%), vomiting in 10(18.9%) and abdominal pain in 12(22.6%) patients. Cardiovascular symptoms were present in 13(24.5%) patients which included hypotension in 6(11.3%), shock in 3(5.7%) and heart failure in 4(7.5%) patients. Neurological symptoms were present in 18(34%) patients which included convulsion in 6(11.3%), unconsciousness in 10(18.9%), acute flaccid paralysis in 1(1.9%) and Ophthalmoplegia in 1(1.9%) patient.Mucocutaneous symptoms were commonest in our study in 28(52.8%). Skin rash was present in 20(37.7%) patients. Hand/foot involvement was present

Table 1 — *Epidemiological and clinical profile of MIS-C children*

Characteristics	No of patients (%) (n=53)
Age 0-1 year	22 (41.5)
1-3 years	11 (20.8)
3-6 years	10 (18.9)
6-9 years	5 (9.4)
9-12 years	5 (9.4)
Gender	
Male	38 (71.7)
Associated condition	9(17)
Metabolic disease	2 (3.8)
Neurological disease	7 (13.2)
Symptom duration before admission	Median(5),IQR(3-7)
Respiratory symptoms	12 (22.6)
Cough	10 (18.9)
Wheezing	5 (9.4)
Respiratory distress	3 (5.7)
Gastrointestinal symptoms	19 (35.8)
Diarrhoea	15 (28.3)
Vomiting	10 (18.9)
Abdominal pain	12 (22.6)
Cardiovascular symptoms	13 (24.5)
Hypotension	6 (11.3)
Shock	3 (5.7)
Heart failure	4 (7.5)
Neurological symptoms	18 (34)
Convulsion	6 (11.3)
Unconsciousness	10 (18.9)
Acute flaccid paralysis	1 (1.9)
Ophthalmoplegia	1 (1.9)
Mucocutaneous symptoms	28(52.8)
Skin rash (Erythematous, maculopapular, blanchable)	20 (37.7)
Hand/foot (Rash, Edema, desquamation)	5 (9.4)
Erythematous lips/Red tongue/congested oral mucosa/eyes (congestion, discharge)	3 (5.7)
Musculoskeletal symptoms (Myalgia, arthralgia)	5 (9.4)
Haematological symptoms (Mucosal bleeding, petechiae)	2 (3.8)
Metabolic derangements (metabolic acidosis, hyperglycemia)	2 (3.8)
Raised temperature	52 (98.1)
Palpable lymph nodes	5 (9.4)
Chest auscultation - crepitations, wheezing	11 (20.8)
Heart - Murmur	1 (1.9)
Hepatomegaly	5 (9.4)
Splenomegaly	2 (3.8)
Serology positive	53 (100)
History of contact with SARS-CoV-2 patient	10 (18.9)

in 5(9.4%) patients. Lips, Tongue, Oral mucosa and eye involvement was present in 3(5.7%) patients. Musculoskeletal involvement was present in 5(9.4%) patients. Haematological symptoms and signs were seen in 2(3.8%) patients. Metabolic derangements were present in 2(3.8%) patients. Temperature was raised in 52(98.1%) patients. Hypothermia on examination was present in one patient and this patient had history of fever for four days at the onset. Lymph nodes were palpable in 5(9.4%) patients. Wheezing and crepitations on chest auscultation was present in 11(20.8%) patients. Murmur on auscultation of heart was present in 1(1.9%) patient. Hepatomegaly was present in 5(9.4%) patients. Splenomegaly was present in 2(3.8%) patients.

Among the laboratory parameters, mean Total Leucocyte Count was 15935 cells/mm^3 (SD 8338), mean platelet count was 209100/mm^3 (SD 165194). Mean CRP was 34 mg/L (SD 26). Mean ESR was 48 mm/h (SD 39). Mean Ferritin level was 763 ng/mL (SD 960). Mean D-dimer level was 2746 ng/mL (SD 2506). Mean serum LDH level was 508 U/L (SD 224) (Table 2).

Table 3 shows differences in clinical, treatment measures and outcome in children who received methylprednisolone alone (n=32) or methylprednisolone and IVIG combined (n=21). Coronary artery aneurysm was seen in 1(3.1%) patient in the methylprednisolone group. Multiorgan involvement was seen in 2(6.3%) patients in the methylprednisolone group. Inotrope requirement was seen in 2(6.3%) patients in the methylprednisolone group and 3(14.3%) patients in combined methylprednisolone and IVIG group. ICU stay for more than or equal to 14 days was seen in 9(28.1%) patients in methylprednisolone group and 10(47.6%) patients in combined pulse methylprednisolone and IVIG group. Among respiratory support requirement, 10(31.3%) patients in the methylprednisolone group and 3(14.3%) patients in combined methylprednisolone and IVIG group required oxygen via nasal prong/face mask. 4(12.5%) patients in the methylprednisolone group and 9(42.9%) patients in combined methylprednisolone and IVIG group required invasive ventilation. 31(96.9%) patients in the methylprednisolone group and 21(100%) patients in combined methylprednisolone and IVIG group got discharged. Death occurred in one (3.1%) patient in the methylprednisolone group within a short period after admission due to uncorrected shock and metabolic acidosis.

Applying chi square test to requirement of ICU stay for 14 days or more to the two treatment groups, it was significantly less in methylprednisolone group (p value 0.011438). Applying chi square test to requirement of invasive ventilation between the two treatment groups, it was significantly less in methylprednisolone group (p value 0.011993). When chi square test was applied to other parameters mentioned in Table 3, no statistically significant difference was obtained.

Discussion

We report low case fatality from a resource limited peripheral Medical College & Hospital in India. We could not afford to provide IVIG to all patients though we had intention to do so as has been suggested by the WHO protocol. It was not possible largely due to unavailability of IVIG. Total number of cases was 53. Majority patients ie, 22(41.5%) were infants. The mean age was 3.2 years (SD 3.4). In a study done by Manem, *et al*[14] in India, mean age at presentation was 6.7 years (SD3.5). In a study by Sugunan, *et al*[15] median (IQR) age was 7.5 (5-9.5) years. In a study by Dhanalakshmi, *et al*[16] median (IQR) age was 6 years (13 months-16

Table 2 — *Laboratory parameters of MIS-C children*

Laboratory parameters	Mean (SD)
Total Leucocyte count(cells/mm^3)	15935 (8338)
Platelet count (/mm^3)	209100 (165194)
CRP (mg/L)	34 (26)
ESR (mm/h)	48 (39)
Ferritin (ng/mL)	763 (960)
D-dimer (ng/mL)	2746 (2506)
LDH (U/L)	508 (224)

Table 3 — *Difference of clinical, treatment measures and outcome in the treatment groups*

Characteristics	Methylprednisolone group (n=32)	Combined methylprednisolone and IVIG group (n=21)	p value
Age	2.62 years (SD 2.97)	4.15 years (SD 3.98)	
Shock	6 patients (18.8%)	3 patients (14.3%)	
CRP (mg/L)	33.8 (SD 26.58)	43.42 (SD 28.78)	
D-dimer (ng/mL)	2682.56 (SD 2339.22)	2571.89 (SD 2119.84)	
Coronary Artery Aneurysm (CAA)	1 patient (3.1%)	0	
Multiorgan involvement	2 patients (6.3%)	0	
Inotropes required	2 patients (6.3%)	3 patients (14.3%)	
ICU stay for 14 days or more	5 patients (15.6%)	10 patients (47.6%)	0.011438
Respiratory support :			
Oxygen via nasal prong/face mask	10 patients (31.3%)	3 patients (14.3%)	
Invasive ventilation	4 patients (12.5%)	9 patients (42.9%)	0.011993
Outcome :			
Discharge	31 patients (96.9%)	21 patients (100%)	
Death	1 patient (3.1%)	0	

years). In a study done at South Africa, median age was 7 years[17]. In a study done in US children, median age was 8 (4-13 years)[18]. In a study done by Nunez, *et al* median age was 8 years[19].

Seropositive cases were 53(100%) in our study. History of contact with SARS-CoV-2 patient was present in 10(18.9%) patients. In a study by Dhanalakshmi, *et al* 7 children (47%) had positive serological assay[16]. In a study by Manem, *et al* seropositivity was seen in 87(84.3%) cases and history of contact with SARS-CoV-2 patient was present in 16(15.6%) cases[14]. In a study in South Africa, 29(30%) children had positive serology[17]. Males were 38(71.7%) in our study. In various studies in India, number of males were 55(53%)[14], 21(66%)[15], 8(42%)[16]. In a study in South Africa, males were 52.9%[17]. In a study in US, 133(53.6%) patients were male[18]. Associated conditions and co-morbidities were present in 9(17%) cases in our study. In various studies in India, underlying medical condition was present in 12.5% cases[15] and 5.2% cases[16].

Mucocutaneous symptoms were commonest in our study in 28(52.8%). In various studies in India, it was 90.6%[15] and 74%[16]. In a study in South Africa, mucocutaneous involvement was seen in 85% patients[17].In our study, gastrointestinal system involvement was present in 19(35.8%) patients. In other Indian studies, 84% in one study and 42% in another study presented with gastrointestinal symptoms[15,16]. In a study in South Africa, 85% patients presented with gastrointestinal symptoms[17]. Respiratory symptoms were present in 12(22.6%) patients in our study. In other Indian studies, respiratory system involvement was seen in 43.7% in one study and 42% in another study[15,16]. In a study in South Africa, respiratory symptoms were present in 30% cases[17].

Cardiac involvement was seen in 13(24.5%) cases. It is the most frequently reported organ dysfunction in MIS-C. In other Indian studies, study by Sugunan, *et al* showed cardiac involvement in 90% patients with coronary artery aneurysms being present in 34.4% patients[15]. Study by Dhanalakshmi, *et al* showed cardiac involvement in 63% patients with commonest symptom being hypotension in 52.6% cases[16]. In a study in South Africa, cardiac involvement was seen in 71% patients which included pericardial effusion (17.6%), mitral regurgitation (36.8%) and coronary artery aneurysms (5.9%)[17]. Neurological involvement was seen in 18(24%) patients in our study. In a study by Dhanalakshmi, *et al* neurological involvement was seen in 31% patients[16]. In a study in South Africa, neurological involvement was seen in 29% patients[17].

Treatment with IVIG was a challenge due to unavailability and unaffordability. In our study, children who received methylprednisolone alone had coronary artery aneurysm in 3.1% cases and multiorgan involvement in 6.3% cases. Less number of coronary artery aneurysms in our study might be due to early initiation of therapy with methylprednisolone through its anti-inflammatory activity. Prolonged ICU stay and invasive ventilation requirement were significantly less in patients who received methylprednisolone alone as compared to combined methylprednisolone and IVIG. Favourable outcome was seen in all patients in combined methylprednisolone and IVIG group (100%) and almost all in methylprednisolone group (96.9%) except one (3.1%) patient who presented very late died after a very short period of time after admission due to uncorrected shock and metabolic acidosis in the methylprednisolone group.Early presentation might have improved prognosis.

Small sample sizes, single centred are the main limitations of our study. Though it is a retrospective study, this study can form the basis on which prospective studies can be planned[20].

Conclusions

Majority of our patients (63%) were below the age of 3 years. 100% of our cases were seropositive. Among that, 41.5% were infants. Cardiac involvement was less common in our study reported only in 24.5% cases. Both treatment with methylprednisolone alone and combined methylprednisolone and IVIG showed favourable and comparable outcomes. Only one death occurred in the methylprednisolone group which was not statistically significant. Through multicentric and larger studies, it remains to be determined whether a low cost therapy with methylprednisolone alone without IVIG can be used for treatment of MIS-C patients in resource constraint setups.

Prior publication : Nil

Support : Nil

Conflicts of interest : Nil

Permissions : Ethical Committee approval was taken.

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Original Article

Incidental Cytological Findings of Microfilaria at Unusual Sites with Varied Clinical Presentation : A Retrospective Study

Binod Kumar Sahu[1], Sunanda Nayak[2], Chandrasekhar Panigrahi[3]

Background : Filariasis is one of the major health concerns of tropical country like India, where it remains undiagnosed in conventional test but accidently detected in routinely advised Fine Needle Aspiration Cytology (FNAC) and fluid analysis test for different clinical diseases. Peripheral blood smear examination is usually done to detect Microfilaria, but it is difficult to detect it in routine peripheral blood smears. This study aims to highlight the importance of cytology as very effective diagnostic tool for diagnosis of Microfilaria.

Material and Methods : The study was conducted in Department of Pathology, VIMSAR Burla Sambalpur, Odisha from June, 2020 to June, 2022. FNAC smears from superficial swelling, body fluid cytology and bone marrow smears were encountered in this study. FNAC and centrifused deposit of body fluid smears were stained with Diff Quik, PAP stain. Bone marrow smears were stained with Leishman stain.

Results : A total of ten cases were diagnosed with Microfilaria on microscopic examination. Out of these, maximum (4 cases) of Filariasis were from breast swelling.

Conclusion : The study highlights the importance of cytology as a cost effective tool for diagnosis of Microfilaria in endemic zones.

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Key words **: Microfilaria, FNAC, Pleural fluid, Peripheral Blood smear, Bone marrow.**

Filariasis is an endemic disease in many tropical and subtropical countries, it is endemic in India especially in states of Bihar, Jharkhand, West Bengal and Odisha, where it is regarded as major public health problem[1]. Out of 8 species of filarial worm which infects human, Wuchereria bancrofti, Brugia malayi are responsible for most of the cases in India. It spreads in human through Culex mosquito bites. In spite of high incidence and prevalence in Odisha Microfilariae are rarely found in cytology smear of fine needle aspiration cytology and body fluid. The literature shows a few report of Microfilariae found in swellings of body parts that includes skin, soft tissue, lymph node, breast, epididymis, bone marrow and pleural fluid[2-4]. Here we report a cytology study of ten cases which were diagnosed with microfilaria in Fine Needle Aspiration Cytology (FNAC) smears, pleural fluid cytology and bone marrow aspiration study. Most of the cases were associated with inflammatory reaction. The objective of this study was to assess the role of cytology in diagnosis of filariasis at different possible sites.

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Editor's Comment :

- Screening of all types of Cytological and Bone marrow aspiration smears play a significant role for identifying microfilaria in endemic areas. Thus, it helps in prompt diagnosis and early treatment to prevent chronic manifestation and further complication.

Materials and Methods

The study was conducted in Department of Pathology, VIMSAR Burla, Sambalpur, Odisha during a period of 2 years from June, 2020 to June, 2022. A total of ten cases were diagnosed with microfilaria on microscopic examination by FNAC, Pleural Fluid Cytology and Bone Marrow Smears. FNAC slides were stained with Diff Quik, PAP stain. Body fluid were centrifused at 3000 RPM for 20 minutes and smears were prepared from sediment and then stained with Diff Quik, PAP stain. Bone marrow smears were stained with Leishman stain.

Stastical Analysis : Statistical analysis was done and data were presented as frequencies

Ethical Clearance : Taken from Institutional Research &Ethics Committee as per memo no.025-2022/I.F.O/51/Dt.17.05.2022

Observations

Ten cases of Filariasis were diagnosed on microscopic examination from various sites (Table 1). Out of these ten cases maximum number were from

Table 1 — *Clinical symptoms and Microscopic finding*

Age/Sex	Site	Size/Consistency	Duration	Fever	Aspirate	Microscopic finding
36/F	Rt breast	2x2cm/firm	1 month	A	Pus	Inflammation with MF
37/F	Lt breast	2x3cm/firm	3 months	A	Scanty fluid	Inflammation with MF
48/M	Rt breast	3x4cm/firm	2 months	A	Blood mixed	Inflammation with MF
25/F	Rt breast	2x1cm/firm	2 months	A	2ml fluid	Fibrocystic disease with MF
23/M	Rt arm	2x3cm/firm	1 year	A	Thick fluid	Inflammation with MF
59/M	Rt hand	2x1cm/firm	7 months	A	0.5 ml fluid	Inflammation with MF
40/F	Lt cervical LN	2x1cm/firm	1 month	P	Scanty fluid	Granuloma with MF
15/M	Penis	1x2cm/firm	1 month	A	Thick fluid	Inflammation with MF
54/M	Pleural fluid	-	-	P	Hemorrhagic	Inflammation with MF
43/M	Bone marrow	-	-	A	-	Hypoplastic marrow with MF

M = Male, F = female, Rt = Right, Lt = Left, A = Absent, P = Present, MF = Microfilaria

breast. One of the cases was from male breast. The age of the patient range from 15 years to 59 years. The duration of symptoms, mostly swelling at various sites varied from days to months. The size of the swelling ranges from 1 cm to 4 cm. The aspirates were mostly fluid. Pleural fluid was haemorrhagic and the bone marrow aspirate was bloody. On microscopic examination, all microfilaria had sheaths, blunt head, curve and pointed tail which were free of nuclei at the tip of the tail (Figs 1-3). All the cases of the swelling showed microfilaria with inflammatory reaction except one case of breast showed microfilaria in a fibrocystic disease. Pleural fluid cytology smear had microfilaria with reactive mesothelial cells, lymphocytes and histiocytes (Fig 4). Bone marrow smear showed microfilaria in hypoplastic marrow (Fig 5).

Discussion

Filariasis is a major health problem in many tropical countries including India. Eight known filarial worms have humans as a definitive hosts. These are divided into three groups according to the part of the body they affect : Lymphatic filariasis (caused by *Wuchereriabancrofti, Brugiamalayi, Brugiatimori),* Subcutaneous filariasis (caused by *Loa loa, Mansonella Streptocerca, Onchocerca volvulus*), Serous cavity filariasis (caused by *Mansonella perstans* and *Mansonellaozzardi*).

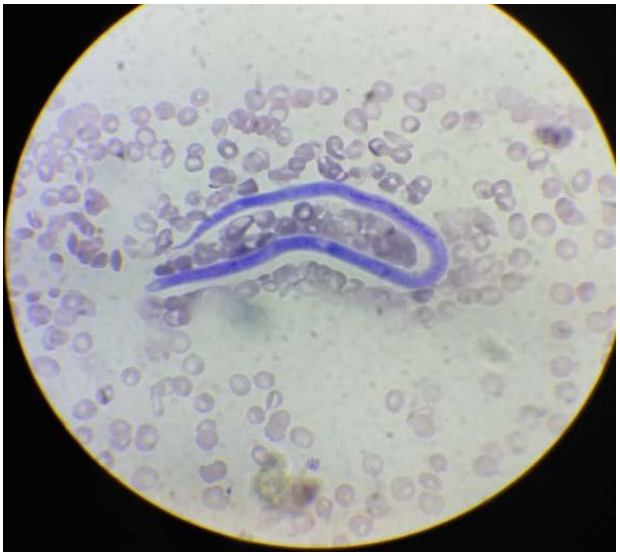

Fig 2 — Sheathed Microfilaria of wucheria bancrofti in Peripheral Blood smear Leishman (X500)

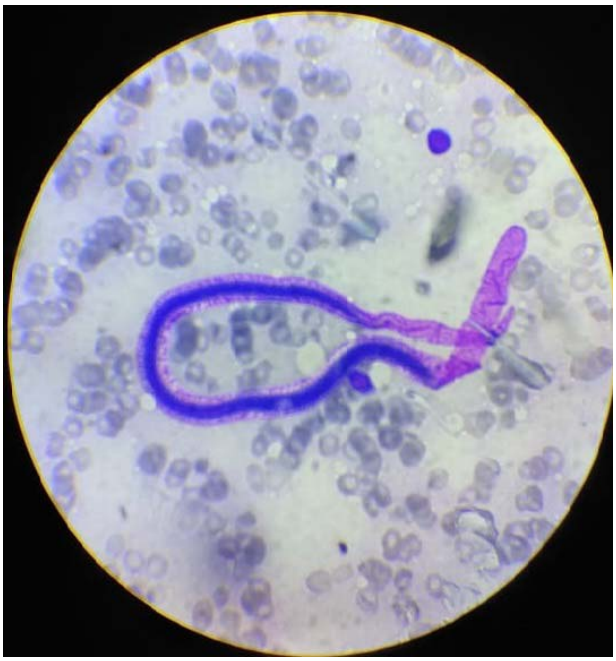

Fig 3 — Microfilaria in Peripheral Blood smear Leishman (X200)

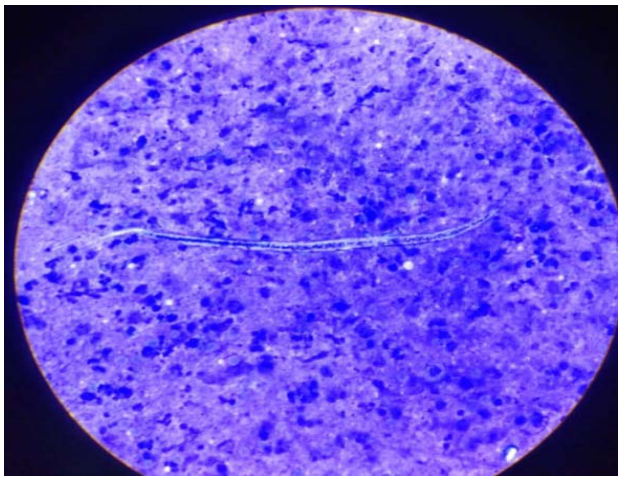

Fig 1 — Microfilaria in Cytology of Breast lump Diff Quik (X200)

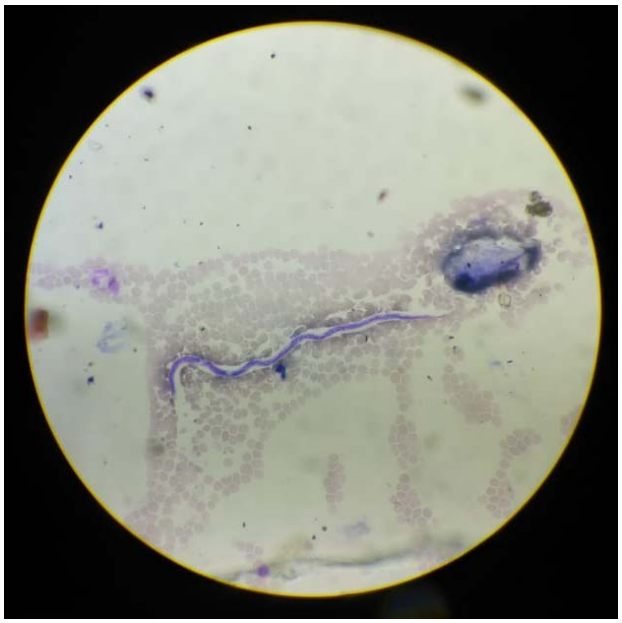

Fig 4 — Microfilaria in Hypoplastic marrow Leishman (X200)

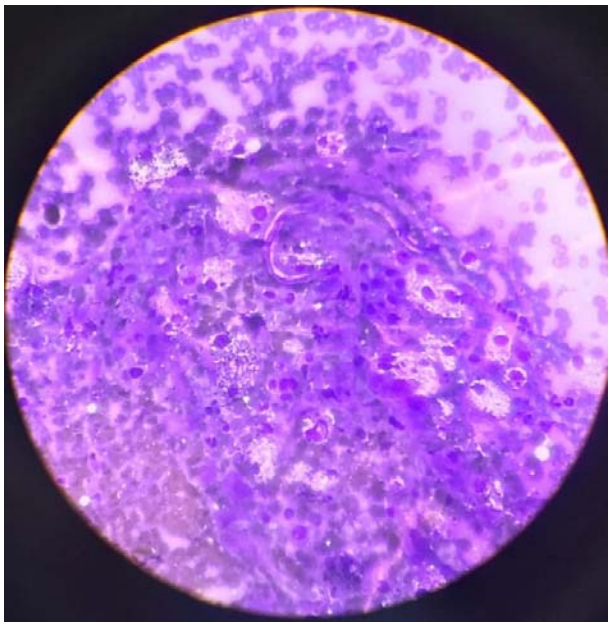

Fig 5 — Microfilaria in Pleural fluid showing histiocytes ,reactive mesothelial cells Diff Quik (X200)

In India, most of the Filariasis is caused by *W Bancrofti* (95%) and *Brugiamalayi* (5%)[5]. Most commonly affected organs are lymphatics of lower limbs, retroperitoneal tissue, spermatic cord, epididymis and breast. Adult worms of filaria involve the lymphatics and Microfilariae are released in peripheral blood. Most of the Filariasis cases are asymptomatic but clinically present with lymphangitis, edema of the limbs and genitalia and Eosinophilia[6]. In endemic region, human beings are affected in early life and peak manifestations are found in 15-20 years. Diagnosis of Microfilaria is mostly peripheral blood smear from mid-night sample and detection of filarial antigen and antibody. Despite high incidence of filariasis in the Indian subcontinent, finding of Microfilaria in the cytology smears is unusual and incidental.

We found 4 cases of Microfilariae in breast aspirate showing different clinical scenarios so also different cytological findings. one of our case is a male patient and cytosmear revealed sheathed Microfilariae in a necrotic background comprising of good number of plump fibroblasts, histiocytes, few lymphocytes along with few eosinophils. In second case, smear show Microfilariae, plenty of polymorphs along with lymphocytes, cyst macrophages, foreign body giant cells and degenerating cells in a background of fluid. In third case smear showed Microfilaria, many eosinophils, polymorphs and lymphocytes. In fourth case, cytosmear show good number of Microfilariae along with few benign looking duct epithelial cells showing apocrine changes in a fluid background containing cyst macrophages. Previous worker reported similar finding of breast aspirate in their study[7-9].

Finding of Microfilaria in subcutaneous nodule of upper limb is rare[10,11]. Here, we reported one subcutaneous swelling of right arm and other at first web space of right hand. On microscopy we found Microfilaria in a inflammatory background. Few study of lymphnode aspirate showed Microfilaria in reactive background[12]. In our case we found Microfilaria in granulomatous background. Most of the study have reported testiculoscrotal region for involvement of Microfilaria[13]. We have a case of penis swelling with Microfilariae larva in bundles along with plenty of polymorphs and many fibroblasts.

Pleural fluid is uncommon site for microfilraria in endemic areas[14]. One of our case in pleural fluid cytology, centrifuged deposit smears revealed Microfilariae in a haemorrhagic background along with reactive mesothelial cells, lymphocytes, polymorphs and few histiocytes without the presence of any malignant cells. In few reported cases Microfilaria was demonstrated in the bone marrow. Bone marrow may be aplastc, hypoplastic, hyperplastic with normoblastic or megaloblastic maturation[15]. We have also a case of bone marrow containing Microfilaria in hypoplastic marrow, peripheral blood smear of the same patient showed pancytopenia and no hemoparasites.

Conclusion

In filarial endemic areas careful screening of FNAC smears is helpful in detecting Microfilaria from different body swelling at different unusual site. This helps clinician to provide early treatment and to avoid unnecessary surgical procedure. In hemorrhagic pleural effusion, tuberculosis and malignancy are in list of differential diagnosis, rarely Microfilaria may be found which prove to be of great clinical significance. Presence of Microfilaria in the bone marrow is an incidental finding and it may cause pancytopenia with hypoplastic marrow, which needed further documentation and investigation.

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Original Article

Endometrial Perfusion on day of hCG Trigger in IVF Cycles Directly Correlates with the Dynamically Changing Endometrial Thickness : A Pilot Study Examining Potential Implications for Endometrial Receptivity and the Development of an Integrated Model to Assess Endometrial Function

Biswanath Ghosh Dastidar[1], Sudarsan Ghosh Dastidar[2], Jayshree Majumdar[3], Chandan Chakraborty[4], Kakoli Ghosh Dastidar[5]

Transvaginal Ultrasound (TV-USG) is an indispensable tool for investigation and patient management in infertility and Assisted Reproductive Technology (ART). It provides us with both anatomic and physiologic information about the uterus, endometrium, ovaries and fallopian tubes; apart from facilitating important procedures like Ovum Pick-up (OPU) and Embryo Transfer (ET). Endometrial assessment by sonographic and other means has been advocated as methods to assess endometrial receptivity in IVF cycles to help predict prognosis. TV-USG has been classically used to assess endometrial thickness and pattern. Recent studies have shown the presence of wave like contractions in the sub-endometrial layer. We have previously reported that these contractions result in variations in endometrial thickness and thus a mean value must be used for endometrial assessment in IVF cycles. It is also thought that optimal sub-endometrial spiral artery blood flow might be important to result in a receptive endometrium. We designed this study to evaluate whether sub-endometrial blood flow varies with endometrial thickness. Our results indicate that peak systolic flow in sub-endometrial spiral arteries is positively correlated with endometrial thickness. Future studies should aim to develop an integrated model for endometrial receptivity using these sonographic parameters to facilitate more accurate prediction and management in IVF patients.

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Key words **: Endometrial Thickness (EMT), Sub-endometrial Contractions, Endometrial Perfusion, Color Doppler, Peak Systolic Velocity, Endometrial Receptivity.**

Around 8-12% of couples of reproductive age worldwide are involuntarily infertile[1]. Ultrasonographic (USG) imaging has proven to be an indispensable tool in the field of infertility management and Assisted Reproductive Technology (ART). A trans-vaginal sonography provides us with a vast array of qualitative and quantitative information and guidance in the management of various ART protocols. USG is used to not only obtain detailed anatomic information about the reproductive organs such as the uterus, ovaries and fallopian tubes, but also offers important prognostic information related to the physiologic functioning of ovaries and the uterine endometrium. Color Doppler flow velocimetry studies are particularly useful in assessing endometrial and ovarian physiology.

Despite significant advances in most clinical as well as technical aspects of ART over the last few decades, embryo implantation rates still remain low globally[2]. Thus, there has been much research focus on refining techniques for embryo culture, selection and transfer. Widespread research is also being carried

Editor's Comment :

- The Endometrial Thickness (ET) changes cyclically due to wave-like sub-endometrial contractions and while measuring ET it might be good clinical practise to take an average of multiple readings.
- Endometrial perfusion as measured by Peak Systolic Velocity (PSV) of blood flow in the sub-endometrial spiral arteries shows positive correlation with mean endometrial thickness.
- Further studies are needed to establish whether these parameters may be integrated to develop a prognostic marker for embryo implantation and thus IVF outcome.

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out for the assessment of endometrial receptivity in order to predict chance of implantation. Endometrial thickness and the classic triple line appearance of the endometrium on sonography are thought to be markers for endometrial receptivity. Endometrial Thickness (EMT)<7 mm has been correlated with poor implantation, although there is yet to be conclusive evidence of linear correlation between EMT and implantation potential[3]. Molecular and genetic markers of endometrial receptivity have also been studied by various groups[4-8].

Endometrial Thickness and Pattern :

Multiple studies have tried to correlate endometrial thickness and morphologic pattern with IVF success, with mixed results. Conflicting results have both supported[3,9-12] as well as dismissed[13-15] the role of endometrial thickness to predict prognosis in IVF cycles. Studies on endometrial pattern have also been inconclusive. Three principal endometrial patterns are recognized : Early follicular proliferative, Peri-ovulatory triple-stripe pattern and Luteal secretory pattern (homogeneously hyperechogenic). Studies have shown that patients with triple layer endometrium on day of HCG were more likely to get pregnant, but not across all different endometrial thickness ranges[9,10]. Thus, it appears that more integrated, multi-parameter models are required to more effectively assess the status of endometrial receptivity.

Sub-endometrial Contractility :

Various studies have reported the presence of wave-like contractions in the endometrial-myometrial Junctional Zone (JZ) which propagate in anterograde or retrograde manner through the uterus[16-18]. We reported that these sub-endometrial contractions resulted in changing endometrial thickness over time and were possibly the first group to recommend that mean value of endometrial thickness measured over multiple contractions be used as a more accurate predictor of IVF prognosis[19]. Some groups have shown that an inverse relationship exists between sub-endometrial wave activity and cycle outcome[20]. However, there is yet to be consensus on how these wave-like contractions may affect embryo implantation and thus IVF results.

Endometrial Perfusion :

It seems reasonable to assume that good blood flow to the endometrium would be a pre-requisite for optimal endometrial function and receptivity. Many studies have tried to correlate endometrial blood flow with IVF outcome. Although some of the indices showed some advantages towards predicting implantation[21], others have failed to show any beneficial role[22]. The current call in the field appears to be the development of integrative endometrial scores which would include data about endometrial thickness, sub-endometrial contractility, and endometrial blood flow[23], in order to more accurately predict endometrial receptivity and thus, IVF outcome.

Thus, we designed a study to assess if endometrial thickness correlates with the end-organ blood flow reaching the endometrium, as an initial step towards developing a multi-parameter, integrated model to assess endometrial receptivity.

Materials and Methods

The study was carried out at a tertiary fertility center in India.Institutional ethical committee approval was taken. After informed consent, an initial series of patients undergoing IVF were recruited into the study (n=25). All patients were undergoing Ovarian Stimulation (OS) using long agonist protocol and Human Menopausal Gonadotropin (HMG), with embryo transfer planned in fresh cycle. There were no other inclusion or exclusion criteria. Four patients dropped out of the study at various stages due to cycle cancellations and loss to follow up (Drop-out rate= 16%). Sub-endometrial JZ contractions were observed by transvaginal sonography for each patient on day of hCG (Wipro LogiqPro 500, Wipro-GE, USA) and 3 endometrial thickness values were measured across contractions and the mean value was recorded as the EMT. Simultaneously, endometrial perfusion was measured by color Doppler by measuring the Peak Systolic Velocity (PSV) in spiral artery in the endometrium and JZ upto 10 mm from the endometrial-myometrial interface. Three complete wave forms were recorded over the contractions by Pulsed Doppler with angle correction kept as close to 0 as possible and wall filter at 0.3-0.7. The mean peak systolic flow (cm/sec) over three waveforms of endometrial spiral artery were recorded and their mean value used for data analysis. Data from 5 patients was left out of final data analysis owing to very poor or absent sub-endometrial blood flow and technical difficulty in velocimetry resulting in lack of interpretable PSV data. Sixteen patients completed the study upto data analysis. Data was analysed using Microsoft Excel and SPSS statistical software. Pearson's correlation coefficient (r) was computed to check for possible correlation between sub-endometrial flow and endometrial thickness (Table 1, Figs 1&2).

Results

Analysis of patient demographic and baseline features shows that 81% of patients had presented

Table 1 — *Summary of Study Data*

Age	Type of Infertility	Cause of Infertility	Endometrial Thickness (mm) over 3 contractions	Mean Endometrial Thickness (mm)	Number of contractions (over 1 min)	Mean Peak Systolic Flow (cm/sec)
25	Primary	Tubal	11, 9, 17	12.3	7	3.81
38	Primary	Tubal	11, 7, 9	9	1	3.44
44	Primary	Tubal	7, 8, 9	8	3	5.93
40	Secondary	Male factor	11, 6, 10	9	2	1.68
37	Primary	Unexplained	11, 6, 7	8	3	0
36	Primary	Unexplained	8, 6, 7	7	2	2.37
39	Primary	Unexplained	6.6, 6, 9	7.2	2	1.59
33	Primary	Male factor	5.2, 6, 9	6.7	2	2.19
37	Primary	Male factor	13, 11, 13.5	12.5	2	5.39
28	Primary	Male factor	8, 6, 8.3	7.4	2	1.79
28	Secondary	Tubal	8, 6, 8	7.3	2	4.24
29	Primary	PCOD	6.7, 6, 8.7	7.1	2	3.34
39	Primary	PCOD	9.7, 9, 11	9.9	5	2.66
36	Secondary	Tubal	9.7, 9, 11	9.9	6	4.07
34	Primary	Male factor	9, 7, 8	8	6	3.12
35	Primary	Male factor	7, 6, 8	7	2	3.32

with primary infertility (n=13) and 19% with secondary infertility (n=3). Distribution of cause of infertility was as follows: 6 with male factor (37%), 5 with tubal factor (31%), 2 with anovulatory/PCOD (13%) and 3 patients with unexplained infertility (19%). Mean age of the patient group was seen to be 34.9 years.

Analysis of sonographic data revealed that there was positive correlation (r=0.401) between mean endometrial thickness (mm) and peak systolic flow in sub-endometrial spiral arteries (cm/sec) as seen on Doppler (Fig 3).

Discussion

A well-proliferated, well-differentiated endometrium is believed to be more receptive to embryo implantation. Various different studies have tried to characterize the endometrial anatomy and physiology in order to develop markers for endometrial receptivity. These include measurement of endometrial thickness, endometrial perfusion, endometrial microbiome, endometrial genomic expression, as well as proteomic and metabolomic profiles. Although evidence-based objective measures of endometrial receptivity are yet to be established there is general consensus in the field that endometrial thickness of over 7 mm with good morphological echo-pattern is preferable before embryo transfer in IVF cycles.

In this study we show that due to waves of contraction in the sub-endometrial myometrial layer the endometrial thickness changes over time and we suggest that using a mean of 3 different endometrial thickness values over contractions may represent a more accurate measure of endometrial thickness. Moreover, we show that peak systolic flow in the sub-endometrial spiral arteries is positively correlated to the mean endometrial

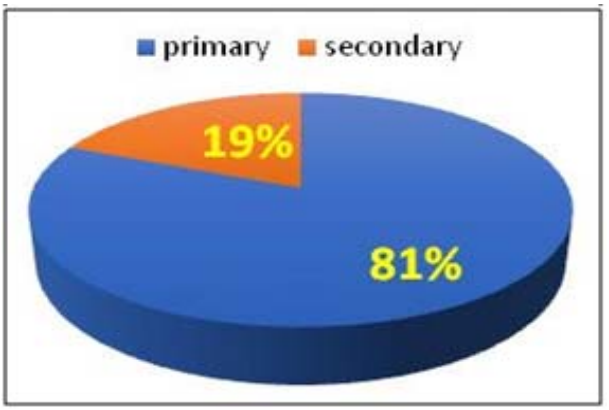

Fig 1 — Distribution of Type of Infertility

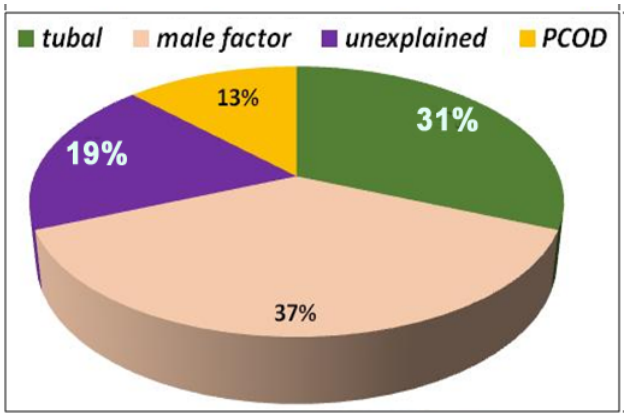

Fig 2 — Distribution of Cause of Infertility

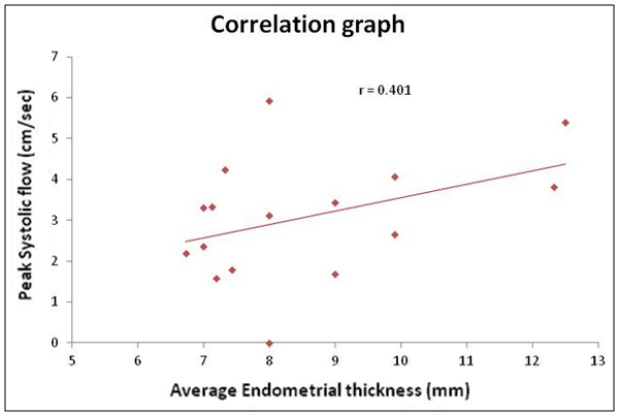

Fig 3 — Positive Correlation (r=0.401) between Endometrial Thickness (mm) and Peak Systolic Flow (cm/sec) in spiral artery

thickness. This finding suggests the very tempting possibility to combine these two markers together to develop a more robust model of endometrial receptivity measurement. Furthermore, we hypothesize that mean endometrial thickness as a function of effective endometrial proliferation and optimal sub-endometrial contractions may be a measure of the innate resistance of the endometrium to blood flow and possibly act as a prognostic marker of endometrial receptivity and IVF outcome.

Limitations :

Measurement of the changing endometrial thickness over time is labor-intensive, time-consuming and hence practically difficult and cost-prohibitive in a busy IVF practice. Moreover, accurate identification and measurement of the blood flow in small spiral arteries is technically challenging and requires patience and a long learning curve. Very low volume flow in many patients also necessitates careful patient recruitment and pre-screening before enrolment into such a study. Even then, it will be technically difficult to achieve multiple measurements of PSV in the small spiral arteries in some patients. Due to these reasons this pilot study presents the data of a modest number of patients and thus these results need to be interpreted with caution. Furthermore, definite conclusions can only be drawn after these findings are correlated with IVF outcomes in larger comparative studies.

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Original Article

To Study Platelet Indices in Alcoholic Liver Disease (ALD) Patients and to Correlate MPV to Platelet Count Ratio with Child Pugh Score to Predict the Severity

Deepti Sharma[1], Anup Kumar Mangal[2], Narendra Fageria[3], Pawan Kumar[4], Gordhan Lal Nagar[4]

Background : Several Non-invasive methods for predecting cirrhosis have been reported, but liver biopsy is only method for definitive diagnosis. However, liver biopsy is invasive and non invasive methods are more desirable. Platelet indices and Mean platelet volume to platelet count ratio can be determined by routine CBC data of blood sample. In the recent years these markers has attracted attention in liver cirrhosis specially due to alcohol.

Objectives : The purpose of this study was to determine platelet indices in alcoholic liver disease patients and to correlate MPV to platelet count ratio with Child-Turcotte-Pugh score.

Methods : This prospective observational case-control study was conducted on 100 patients with alcoholic liver disease. 100 healthy age-matched and sex-matched individuals were taken as controls. The patient and control groups were subjected to detailed history taking, examination and CBC, LFT and PT/INR assessment. Clinical and laboratory examination using the Child-Turcotte-Pugh score was carried out. MPV and platelet count was evaluated within the first 24 hours of admission.

Results : Maximum subjects in our study were in the age range of 40-49 years with 100% males. Mean platelet count of study group was 1.11±0.74 lakh/uL lower than the mean platelets count of control group ie, 3.36±0.87 lakh/uL and the difference between two was statistically significant (p<0.0001). Mean±SD MPV of control was 8.85±0.817 fL and Mean±SD MPV of study subjects was 10.9±0.9 fL and the difference between two was statistically significant with the p value of <0.0001. Mean PDW of study subject 14.88±2.35 fL was higher than mean PDW of control12.08±1.98 fL and the difference between two was statistically significant (p<0.0001).

Mean MPV to platelet count ratio of study subject 16.09±15.17fL/lakh was higher than the control 2.85±0.96 and the difference between two was statistically significant (p<0.0001). The value of MPV to platelet count ratio was also lowest in Child-Pugh class A(6.53±2.74) which gradually increased in Child-Pugh Class B(9.72±4.75) group and Child-Pugh Class C (22.69±17.80) with the highest MPV to platelet count ratio in Child-Pugh Class C group. In this study there was a positive correlation between MPV to platelet count ratio and Child-Turcotte-Pugh Score (r value=0.5241) and p-value was statistically significant (p<0.0001).

Conclusion : MPV to platelet count ratio were significantly higher in patients with Alcoholic Liver Disease than in controls. MPV to PC ratio increased with increasing severity of ALD.

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Key words **: Alcoholic Liver Disease, Platelet Indices, Mean Platelet Volume.**

Liver injury caused by the alcohol abuse is called Alcoholic Liver Disease (ALD) and it is classified into alcoholic steatosis (fatty liver), alcoholic hepatitis, and alcoholic liver cirrhosis. Alcohol can cause a significant alteration of cells, tissues, and organs. In particular, ethanol exposure induces cell membrane remodeling in different cells and lipid vesicles including membrane fluidization[1].

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Editor's Comment :

- Increased MPV is the predictor of liver injury in alcoholics.
- Decreased platelet count is indicator of liver injury with portal hypertension in alcoholics.
- Increased MPV to platelet count ratio is the strong indicator of liver injury in alcoholics.

Thrombocytopenia is the most common hematological abnormality encountered in patients with Chronic Liver Disease (CLD),[2] occurring in 64%-84% of patients with cirrhosis or fibrosis[3]. Among patients undergoing bone marrow biopsies for thrombocytopenia of unknown etiology, the prevalence of cirrhosis is as high as 35%[4]. In addition to being an indicator of advanced disease[5], thrombocytopenia is associated with a poorer prognosis and it frequently prevents patients from receiving crucial interventions

such as medications, as well as invasive diagnostic or therapeutic procedures[6].

Alcohol's adverse effects on the blood building, or hematopoietic system are both direct and indirect. The direct consequences of excessive alcohol consumption include toxic effects on the bone marrow; the blood cell precursors; and the mature Red Blood Cells (RBC's), White Blood Cells (WBC's), and Platelets. Alcohol's indirect effects include nutritional deficiencies that impair the production and function of various blood cells. These direct and indirect effects of alcohol can result in serious medical problems for the drinker. For example, anemia resulting from diminished RBC production and impaired RBC metabolism and function can cause fatigue, shortness of breath, lightheadedness, and even reduced mental capacity and abnormal heartbeats. A decrease in the number and function of WBC's increases the drinker's risk of serious infection and impaired platelet production and function interfere with blood clotting, leading to symptoms ranging from a simple nosebleed to bleeding in the brain (ie, hemorrhagic stroke).

Aims and Objectives

The aim of this study was to determine MPV to platelet count ratio in alcoholic liver disease patients and its correlation with Child-Turcotte-Pugh score.

Materials and Methods

After obtaining approval from Institutional Ethical Committee, a hospital based prospective and observational study was conducted on 100 patients of alcoholic liver disease admitted in Department of Medicine, Government Medical College and Associated MBS Hospital, Kota from 2021 to 2022 and compared with 100 equal number of age and gender matched controls. All Patients of Age >18 years diagnosed with liver disease with history of excessive alcohol intake with exclusion of other etiologies such as viral hepatitis and non-alcoholic steato-hepatitis and had given written informed consent to participate were included in our study whereas Patients of Age <18 years, Viral hepatitis, Non-alcoholic steato-hepatitis, Renal disease, Known thyroid disease, Hematological malignancy, History of drug intake that alter hematological profile, Immuno-suppressed individual, Systemic acute or chronic inflammatory or autoimmune or infectious disease, connective tissue diseases or prior myocardial infarction, Pregnant patient, History of recent blood transfusion, History of recent gastro-intestinal bleeding, History of vitamin supplementation, hematinics or drugs known to interfere with folate metabolism and patient refusing to give informed consent for the study were excluded. The study conducted in patients presented to us with features of Liver disease, Medical history and Ultrasound imaging done to recognize the liver injury and physical examination used in order to determine the definitive diagnosis of Alcoholic Liver Disease. Blood sample was collected from the antecubital vein using a 21-gauge sterile syringe in laboratory. Severity of Alcolic Liver Disease was determined with the Child -Turcotte-Pugh score in all patients at initial presentation. Severity of ALD was grouped in Child-Pugh Class A (5-6), Child-Pugh Class B (7-9), and Child-Pugh Class C (10-15).

Statistical Analysis :

Continuous variables were presented as Mean±SD, categorical variables were expressed in frequency and percentages. Demographic, haematological and clinical parameters were compared between cases and controls by performing independent t- test. Categorical variables were compared by performing chi- square test. Statistical method used was unpaired Student's t-test and chi-square test between MPV to platelet count ratio and severity of ALD including other variables using Graph pad in Stat Version 3. A value of $p>0.05$ was considered as not significant and $p<0.05$ as statistically significant. Correlation coefficient was also assessed between MPV to platelet count ratio and Child-turcotte-pugh Score (Tables 1-3).

Observation and Results

In our study, cases had mean age of 40.46±6.63 years which was comparable with the mean age of control group ie, 39.31±6.71 years and both groups had maximum subjects in the range of 40-49 years ie, 48 and 46 respectively. Out of 100 subjects in the study

Table 1 — *Age distribution of subjects in Case and Control group*

Age	Control Group	Study Group
20-29	10	7
30-39	38	34
40-49	48	46
>49	4	13
Mean age±SD	39.31±6.71	40.46±6.63

Table 2 — *Hematological profile of Case and Control group*

Parameters	Study group (Mean±SD)	Control group (Mean±SD)	P value
Hb	11.27±2.21	13.86±1.15	<0.0001
TRBC	3.51±.0.85	4.39±0.5	<0.0001
MCV	107.86±11.88	87.9±8.35	<0.0001
Platelet Counts	1.11±0.74	3.36±0.87	<0.0001
MPV	10.9±0.9	8.85±0.817	<0.0001
PDW	14.08±2.35	12.08±1.98	<0.0001
MPV to PC ratio	16.09±15.17	2.85±0.96	<0.0001

Table 3 — *Distribution of ALD patients in different Child-Turcotte-Pughscore group*

Child-Turcotte-Pugh class	No of study subjects
A	17
B	27
C	56

group all were males because females were not consuming alcohol in HADOTI region and this is why 100 males control were considered for study. Maximum number of patients was in Child-Pugh class C (56%) followed by 27% in Child-Pugh class B and 17% in Child-Pugh class A. In study population 43% had hepatic encephalopathy, 69% had ascites and out of which 21% had significant ascites, 36% of the patients had jaundice. Anaemia was present in 58% of the cases, haematocrit was low in 58% of the cases, Total RBC count was low in 48% of the cases, Macrocytosis was present in 74% of the cases, Thrombocytopenia was present in 76% of the cases, MPV was raised in 54% of the cases and PDW was raised in 13% of the cases in study (Tables 4-6).

When MPV of the study subjects compared with controls we found that among the study subjects 54% had MPV more than 11 fL and among the control 3% had MPV more than 11 fL. Mean±SD MPV of control was 8.85±0.817 fL and Mean±SD MPV of study subjects was 10.9±0.9 fL, and the difference between two was statistically significant with the p-value of <0.0001. In the study group the value of MPV was lowest ie, 10.14±0.47fL in cases with Child-Turcotte-Pugh score group 5-6 (Child Pugh Class A) which increased to 10.38±0.56fL in Child-Turcotte-Pugh Score group 7-9 (Child Pugh Class B) and 11.32±0.85fL in Child-Turcotte-Pugh Score group 10-15 (Child Pugh Class C). In this study there was a positive correlation between MPV and Child-Turcotte-Pugh Score (r-value=0.7316) and p-value was statistically significant (p<0.0001).

Table 4 — *MPV and Child-Turcotte-Pugh score*

Child-Turcotte-Pugh Class	MPV in Study Group	
	Mean	Standard Deviation
A	10.14	0.47
B	10.38	0.56
C	11.32	0.85
P value	<0.0001 (ANOVA test)	
R (linear regression)	0.7316	

Table 5 — *Platelet Count and Child-Turcotte-Pugh Score*

Child-Turcotte-Pugh Class	Platelet Count in Study Group	
	Mean (lakh/Ul)	Standard Deviation
A	1.78	0.65
B	1.40	0.81
C	0.77	0.51
P value	<0.0001(ANOVA test)	
R (linear regression)	0.4351	

Table 6 — *MPV to Platelet Count Ratio and Child-Turcotte-Pugh Score*

Child-Turcotte-Pugh Class	MPV to platelet Count Ratio in Study Group	
	Mean	Standard Deviation
A	6.53	2.74
B	9.72	4.75
C	22.69	17.80
P value	<0.0001(ANOVA test)	
R(linear regression)	0.5241	

Among the study subjects three fourth (76%) had platelets less than 1.5 lakh/uL, out of which 15% had platelets less than 50,000/uL, 42% had platelets 50,000-100,000/uL and 19% had platelets 1-1.5 lakh/uL and 24% have >1.5 lakh/uL. In control group 1% had 1-1.5 lakh/uL and 99% had >1.5 lakh/uL. When compared Mean±SD values, mean platelet count of study group was 1.11±0.74 lakh/uL lower than the mean platelets count of control group ie, 3.36±0.87 lakh/uL and the difference between two was statistically significant with the p-value of <0.0001. Among the study population, platelet count was lowest ie, 1.78±0.65 lakh/uL in cases with Child-Turcotte-Pugh Score group 5-6 (Child Pugh Class A) which increased to 1.40±0.81 lakh/uL in Child-Turcotte-Pugh Score group 7-9 (Child Pugh Class B) and 0.77±0.51 lakh/uL in Child-Turcotte-Pugh Score group 10-15 (Child Pugh Class C). In this study there was a positive correlation between platelet count and Child-Turcotte-Pughscore (r value=0.4351) and p-value was statistically significant(p<0.0001).

Mean±SD MPV to platelet count ratio of control was 2.85±0.96 and study subjects was 16.09±15.17, and the difference between two was statistically significant with the p-value of <0.0001. On comparing MPV to platelet count ratio it was found to be lowest ie, 6.53±2.74 in Child-Turcotte-Pugh score group 5-6 (Child Pugh Class A) which increased to 9.72±0.4.75 in Child-Turcotte-Pugh Score group 7-9 (Child Pugh Class B) and 22.69±17.80 in Child-Turcotte-Pugh Score group 10-15 (Child Pugh Class C). The highest MPV to PC ratio was present in Child Pugh Class C. In this study there was a positive correlation between MPV to platelet count ratio and Child-Turcotte-Pughscore (r-value=0.5241) and p-value was statistically significant (p<0.0001). When we correlate MPV to platelet count ratio as a predictor of severity of Alcoholic Liver Disease it is more powerful indicator and prognostic tool as compare to individual MPV and platelet count.

Discussion

Our study included 100 patients of Alcoholic Liver Disease and 100 age and sex matched control

subjects. The control subjects were free from alcohol intake. In our study all the cases were males because in *HADOTI* region the females are not consuming alcohol. Studies conducted by 2003 E Giannini, *et al*[7] and 2010 Demriel, *et al*[8] included 29% and 32% females respectively but geographical region was different. In our study, maximum no. of cases (46%) and control (48%) were in the age group of 40-49 years and the mean age was 40.46±6.63 and 39.31±6.71 respectively. In a study conducted by Etesar H Fshaqawy, *et al*[9], it had been observed that mean age in Alcoholic Liver Disease was 49.84±7.28. Also a study by Mona, *et al*[10] had mean age of 45 years with similar results. In the present study, the mean age of cases and controls were comparable with 40.46±6.63 years and 39.31±6.71 years respectively. This confirms that younger age group are more to develop Alcoholic Liver Disease.

In our study MPV of control was 8.85±0.817 fL and MPV of study subjects was 10.9±0.9 fL, Thus MPV in cases were significantly higher (p<0.0001). In study conducted by Das SK, Mukherjee S, *et al*[11] found that MPV in ALD patients was ALD 8.9 ± 1.46 fL (n=40) and in non-alcoholic was Control 8.5 ± 0.97 (n=77) (p<0.001), result was similar to the present study. In our study we noticed that when Child-Turcotte-Pugh score increased, the value of MPV also increased proportionately. The value of MPV was lowest ie, 10.14±0.47 fL in cases with Child-Turcotte-Pugh Score group 5-6 (Child Pugh Class A) which increased to 10.38±0.56 fL in Child-Turcotte-Pugh Score group 7-9 (Child Pugh Class B) and 11.32±0.85 fL in Child-Turcotte-Pugh score group 10-15 (Child Pugh Class C). Our study highlighted that there was a positive correlation between MPV and Child-Turcotte-Pugh score (r value=0.7316) and p value was statistically significant (p<0.0001). Study conducted by Edoardo G Giannini, *et al*[7] showed a similar finding such that the groups of Alcoholic Liver Disease with low Child-Turcotte-Pugh score had low MPV and those with high Child-Turcotte-Pugh score had high MPV values which were statistically significant. Mohamed S Mohamed, *et al*[12] study in 2018 also demonstrated the positive correlation between MPV values and PT/INR, serum bilirubin, lower serum albumin in ALD patients. Also, the MPV values were significantly higher in patients with more severe liver disease according to the model for end-stage liver disease (r=+0.424, P=0.008) and CTP scores (r=+0.353, P=0.03).

In our study among the study subjects 76% had thrombocytopenia, out of which 15% have platelets less than 50,000/uL, 42% have platelets 50,000-100,000/uL and 19% have 1-1.5 lakh/uL and 24% have >1.5 lakh/uL. In control group 1% have 1-1.5 lakh/uL and 99% have >1.5 lakh/uL. When compared mean values, mean platelet count of study group is 1.11±0.74 lakh/uL that was lower than mean platelet count of control group ie, 3.36±0.87 lakh/uL, which was statistically significant (p=<0.0001). Dr G Balasubramanian, *et al* 2007[13] also found platelets less than 1.5lakh/uL in 73% patients of Alcoholic Liver Disease with sample size of 200 patients as compare to control and was significant with p(0.0001), result of this study was closely similar to present study. 2011 Das S K, Mukherjee S, Vasudevan D M, Balakrishnan, *et al* found that Platelet count in control was 237.9 ± 51.30k/uL and ALD patients was 142.2 ± 73.80k/uL and the result was in accordance with present study. Bibhu Prasad Behera, *et al*[14] study found that among the 69 ALD patients 47 patients had platelets less than 1.5lakh/uL, 21 patients had platelets 1.5-4.5lakh/uL and 1 patient had platelets >4.5lakh/uL. Deepak Jain, H K Aggarwal, *et al*[15] concluded that Median platelet count among the study subjects was 150×103/µl. Median platelet count in the individual MELD score groups was as follows; in group 1 it was 380×103/µl, in group 2 it was 315×103/µl, in group 3 it was 130×103/µl, in group 4 it was 105×103/µl and in group 5 it was 100×103/µl. Among 88 study subjects, 43 had thrombocytopenia. MELD score group 1 and 2 patients did not have thrombocytopenia. Of 27 patients in group 3, 20 (74.1%) patients had thrombocytopenia. All the patients in group 4 and 5 had thrombocytopenia. The variation of thrombocytopenia among different groups was statistically significant with p value of <0.01. In study done by 2021 E Halleys Kumar, A Radhakrishnan, *et al*[16] thrombocytopenia is seen in 38 males and 18 females with (22.9 percent) of the males and (22 percent) of the females has thrombocytopenia.

In our study MPV to Platelet Count (PC) ratio of control was 2.85±0.96 and study subjects was 16.81±15.17. Thus MPV to PC in cases were significantly higher (p<0.0001). In our study we noticed that when Child-Turcotte-Pugh Score increased, the value of MPV to platelet count ratio also increased proportionately. The value of MPV to PC ratio was lowest ie, 6.53±2.74 in cases with Child-Turcotte-Pugh score group 5-6 (Child Pugh Class A) which increased to 9.72±4.75 fL/lakh in Child-Turcotte-Pugh Score group 7-9 (Child Pugh Class B) and 22.69±17.80 in Child-Turcotte-Pugh Score group 10-15 (Child Pugh Class C). Our study highlighted that there was a positive correlation between MPV to platelet count ratio

and Child-Turcotte-Pugh Score (r value=0.5241) and p-value was statistically significant (p<0.0001).

When we correlate MPV to platelet count ratio as a predictor of severity of alcoholic liver disease it is more powerful indicator and prognostic tool as compare to individual MPV and platelet count.

Conclusion

MPV to platelet count ratio is a simple, cost-effective marker that may help in diagnosis of alcoholic liver disease, predicting the severity of disease and prognosis in terms of functional outcome as evidenced by its raised value in alcoholic liver disease patients as well as its linear positive correlation with Child-Turcotte-Pugh Score. Though, more studies are needed to validate our results.

Limitation of Study :

Despite our best efforts our studies had few limitations

(1) The sample size of our study was small involving only single centre patients of acute ischemic stroke.

(2) Owing to lack of long term follow up for our patients, we cannot comment whether platelet indicesarethe useful predictor of long-term prognostic outcome in Alcoholic Liver Disease patients or not.

(3) Our study was carried out in a tertiary centre where the cases are either serious or referred. Our study may thus be biased towards more serious cases.

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Original Article

Are Dengue Patients Aware Enough ? — A Cross-sectional Study among Dengue In-patients in a Rural Based Tertiary Hospital in West Bengal

Indranil Thakur[1], Somak Majumdar[2], Sanat Kumar Jatua[3], Moloy Kanti Makhal[1], Santanu Saha[4]

Background : Dengue fever is endemic in many parts of South-east Asia and the tropical countries including India. It takes a huge toll on lives every year during the rainy season due to the upsurge of the vector mosquitoes. Numerous studies have been performed on the Knowledge, Attitude and Practice (KAP) about Dengue prevalent in the community but very few have been performed among admitted patients.

Aims and Objectives : To find out the Socio-demographic profile, predictors of KAP and the correlation among KAP parameters among in-patients of dengue.

Results : In 50.7% patients had a good KAP score. Age, Sex and Floor of residence had significant associations with KAP and there was a good correlation between Knowledge, Attitude and Practice.

Conclusions : The KAP scores were not satisfactory enough even though the subjects were going through the suffering of dengue which potentiates the need for a robust Information, Education and Communication (IEC) campaign for the admitted patients from the authorities. [*J Indian Med Assoc* 2024; **122(2):** 39-44]

Key words **: Dengue, In-patients, KAP, Correlation, Predictors.**

Dengue fever is endemic in various parts of India including West Bengal. Many regions of the world for example the South-east Asian region and the islands of the Western pacific represent a significant proportion of the Dengue global burden. It is endemic in some parts of India. The number of Dengue cases has currently been on a rising trend in India[1]. Recently after the COVID pandemic managing Dengue patients has become a real challenge to healthcare professionals. During the indoor rounds in hospitals, it has been noticed that indoor patients and their relatives lack knowledge about Dengue and other mosquito-borne infections endemic in the community. This knowledge deficiency was noticed even among the patients suffering from dengue. Even on the day of discharge, they remain sternly ignorant about the facts.The global incidence of Dengue fever and its complications are increasing at an alarming pace and it poses a threat to almost more than a half of the world's population. An estimated 100-400 million infections occur each year worldwide[2]. Dengue/Dengue Haemorrhagic Fever (DHF) is a fast upcoming disease in India. It is a major contributor of sporadic outbreaks in the country and finds its place among the many endemic diseases of the country[3]. A survey on 625 Bangladeshi University students reported 66.67% of students had exemplary knowledge of Dengue with 89% good attitude and 68% good practice[4]. Though there is adequate KAP related to Dengue still there is increased requirement for awareness activities[5]. Prevention may be the only way to combat any emergent situation in Dengue, as an effective prophylaxis or working vaccine is not known till date[6]. Certain health behaviors like bearing a positive attitude towards Dengue, possessing adequate knowledge and proper preventive procedures may only help to reduce Dengue fever in the community[7,8]. Our study is thus intended to assess the Knowledge, Attitude and Practice (KAP) related to Dengue infection amid indoor admitted patients suffering from Dengue fever, their predictors and the correlation between the different parameters. Numerous community based surveys are

Editor's Comment :

- Lack of awareness regarding Dengue Fever symptomatology and prevention is quite widespread in the community as is evident by a lot of studies. But the situation remains the same or even worse in those who have suffered from it and similar assessments are scarce. Thus active IEC campaigns, as done outdoors, are also required indoors to educate the sufferers as they may turn out to be a useful resource for experience sharing with the community after their discharge. A lot of administrative efforts need to be kickstarted to support this beneficial purpose.

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being conducted related to the same issue in various parts of the world but KAP surveys on patients already suffering from Dengue ie, indoor admitted patients is intended to give an impression of the burden of reluctance related to disease prevention. This study may also provide an imprint of the requirement of an active hospital indoor Awareness program during the admission period which finally can lead to behavioral change.

Materials and Methods

An Observational, Descriptive and Cross-sectional study was conducted among Dengue fever patients admitted at Diamond Harbour Government Medical College & Hospital for 3 months from September, 2022 to November, 2022 after proper ethical approval. The prevalence of awareness about Dengue was taken from a previous study to be 90% where it was noticed that almost 82% of the population was aware of Dengue fever as a Mosquito-borne disease[9]. This information was also supported by another study conducted by Podder D from West Bengal, Kolkata[10]. Contemplating the value of Z as 1.96 (at 95% confidence interval) and an absolute error of 5%, the desired sample size was calculated as 138. Also approximating a denial rate of 10% the final sample size came out to be 152. All the adult patients suffering from Dengue infection were included in the study. Population below 18 years of age were excluded from the study. A questionnaire related to Knowledge, Attitude and Practice on Dengue was prepared and a set of 20 questions were made. The internal validity of the total questionnaire set was calculated with resultant value of Cronbach's Alpha as 0.7, on the basis of a pilot testing on 20 patients different from the study sample. Questionnaire was administered by face-to-face interview to only those subjects who gave a verbal informed consent and the whole process was monitored by an independent observer for quality control purpose. The data after collection were entered into Microsoft Excel version 2016 and were collated and corrected for incorrect entries. They were then transferred to SPSS version 23 for further exploration. Descriptive analyses were performed using frequency distribution tables and mean, numbers and percentages of each variable was found out and recorded. The mean of each of the Knowledge, Attitude and Practice scores were established and compared using correlation coefficients and p values. Multivariate regression analyses were then performed to find out the predictors of Knowledge, Attitude and Practice about Dengue and were represented in the form of the table showing the adjusted odds and the p-values. A p-value of <0.05 was deliberated as statistically substantial at a 95% confidence interval.

Analysis and Results

The study was conducted on 152 patients admitted in the indoor unit of the General Medicine Department of Diamond Harbour Government Medical College and Hospital. Table 1 illustrates the study population demographic characteristics. The subjects are mostly equally distributed between females and males with females being a majority (50.7%). The subjects mostly consisted of a young population, married and Hindu in religion. 86.8% of the subjects were literate and 97.4% of the population were affected for the first time. The subjects were residents mostly of the rural areas so 69.1% of them stayed on the ground floor.

Table 2 summarizes the correct responses given by the study subjects on the questions on Knowledge, Attitude and Practice regarding Dengue. 48.7% of the subjects had a good knowledge, 54.6% had a good attitude while only 34.9% of the subjects converted the Knowledge and Attitude to a good Practice. Overall, 50.7% of the subjects had a good KAP score. Most of the people knew that Dengue is caused by a mosquito (94.7%), Dengue is deadly (67.8%) and the principal symptoms are fever and joint pain (72.4%). But the causative agent of Dengue as a virus (32.2%) and as Aedes mosquito (24.3%) was only known to few. Also, causative agent of Dengue needs clean water for breeding, bites mostly during the late night and early morning, Dengue causes bleeding and is transmitted during rainy season was known by 47.4%, 57.2%, 50.7% and 55.9% respectively. Only age was associated with knowledge (p=0.018) where younger people showed lower levels of overall knowledge than older people as shown by Table 3.

About questions on attitude, maximum people (89.5%) wanted Dengue case reduction in their areas and wished to consult a doctor when suffering from fever (75.7%). But only 30.3% and 34.9% of the people thought that it's a collective responsibility to reduce Dengue and were aware of the various IEC materials in their surroundings. Most of the people understood it as an individual responsibility to reduce Dengue (67.1%). People living on the ground floor had a positive association with good attitude (p=0.005) towards Dengue as shown in Table.

The overall practice of the study subjects for prevention of Dengue was poor. The only good practice was use of mosquito nets by 72.4% of the people. Practice towards Dengue prevention had a positive association with male subjects (p=0.014) and living on the ground floor (p=0.016).

Table 1 — *Distribution of the Study Population according to their Socio-demographic Characteristics*

Socio-demographic Variables		Frequency (%)
Age	< Mean	87 (57.2)
	> Mean	65 (42.8)
Gender	Male	75 (49.3)
	Female	77 (50.7)
Religion	Hindu	90 (59.2)
	Muslim	62 (40.8)
Marital Status	Married	115 (76.3)
	Single	32 (20.4)
	Widow	5 (3.3)
Educational Status	Illiterate	20 (13.2)
	Literate	132 (86.8)
Occupation	Employed	70 (46.1)
	Housewife	63 (41.4)
	Unemployed	19 (12.5)
Floor of Residence	Ground Floor	105 (69.1)
	1st Floor	29 (19.1)
	2nd Floor	15 (9.9)
	3rd Floor	3 (2.0)
Past History of Dengue	No	148 (97.4)
	Yes	4 (2.6)

Further on conduction of the correlation test, there was a significant positive correlation between knowledge-attitude ($r_s = 0.517$, $p < 0.000$), knowledge-practice ($r_s = 0.498$, $p < 0.000$) and attitude-practice ($r_s = 0.445$, $p < 0.000$). the degree of correlation can be considered to be good ($r_s < 0.55$). It was also seen that subjects who had a good knowledge were 3.5 times likely to have a good attitude (OR 3.527, 95% CI:1.718-7.244) and 3.2 times likely to have a good practice (OR:3.289, 95% CI:1.535-7.051). Similarly reciprocating the fact participants with a good attitude were 4 times likely to have a good practice (OR:4.007, 95% CI: 1.909-8.409).

Table 2 — *Distribution of the Study Population According to their Correct Knowledge, Attitude and Practice towards Dengue*

Questions	Correct Responses (%)
Knowledge :	
Is Dengue caused by a mosquito bite?	144 (94.7)
Is Dengue caused by a virus?	49 (32.2)
Is Dengue caused by aedes mosquito?	37 (24.3)
Do you know that a small amount of accumulated clean water is a good breeding space for aedes mosquito?	72 (47.4)
Do you know that fever and joint pain are the principal symptoms of Dengue?	110 (72.4)
Can Dengue cause bleeding?	77 (50.7)
Can Dengue cause death?	103 (67.8)
Is Dengue transmitted mostly during the rainy season?	85 (55.9)
Can Dengue be transmitted from mother to fetus?	106 (69.7)
Does aedes mosquito bite mostly in late night and early morning?	87 (57.2)
Attitude :	
Do you want Dengue cases to reduce in your area?	136 (89.5)
Do you check the existence of possible mosquito breeding sites around your area?	72 (47.4)
Do you wish to consult a doctor early if you suffer from fever?	115 (75.7)
Do you feel responsible to prevent and reduce Dengue cases in your locality?	102 (67.1)
Do you think all of us should own the responsibility to control Dengue?	46 (30.3)
Are you aware of the various IEC materials displayed in the hospital around you?	53 (34.9)
Practice :	
Do you have the practice to call authorities for spraying?	48 (31.6)
Do you contact the health authorities for fogging?	68 (44.7)
Do you regularly use mosquito net?	110 (72.4)
Do you take over the counter medications to treat your fever usually?	71 (46.7)

Discussion

The study was conducted on 152 patients admitted with dengue fever in the in patient unit of the General Medicine Department of Diamond Harbour Government Medical College and Hospital, a rural based Tertiary Hospital in West Bengal, India. The subjects are mostly equally distributed between females and males with females comprise a slight majority (50.7%). Similar studies conducted in Tanzania showed female preponderance[11]. However, males constituted the majority of the study subjects in studies conducted by Prof Oche OM in Nigeria[12] and Tan, *et al* in Taiwan[13]. The subjects mostly consisted of a young population in present study. This observation was similar to the studies conducted by Prof Oche OM[12] in Nigeria in 2021 and Kazaura M in Tanzania in 2019[14].

Most of the people in our study knew that Dengue is caused by a mosquito bite (94.7%). Similar observations of higher knowledge among the subjects regarding the fact that transmission of Dengue fever occurs by the bite of mosquito were reported by Oche OM study[9] and the study conducted by Huong Van Nguyen in Vietnam[15]. But only 32.2% subjects in our study knew that the causative agent of Dengue fever is a virus. In the study conducted by Farizah H in Malaysia,only 2.5% of the respondent knew that Dengue is caused by Dengue virus[16].

In the present study, 24.3% of the subjects knew that Dengue is spread by Aedes mosquito. Similar observation was also made by Oche OM in Nigeria[9]. This contrasted with studies conducted by Rahman MM among University Students of Dhaka City (88.96%), Bangladesh and Mohammed Ali Saghir in Shabwah Governorate, Yemen (75%)[4,5]. Also,the causative agent of Dengue needs clean water for breeding was known by 47.4%. This finding is

Table 3 — *Predictors of KAP About Dengue through Multivariate Analysis*

Variables		Knowledge		Attitude		Practice	
		AOR	P	AOR	P	AOR	P
Age	<mean	0.396 (0.183-0.855)*	0.018	1.260 (0.584-2.721)	0.556	0.688 (0.309-1.529)	0.359
	>mean	1		1		1	
Sex	Male	1.138 (0.386-3.358)	0.815	2.099 (0.706-6.235)	0.182	5.219 (1.401-19.451)*	0.014
	Female	1		1		1	
Religion	Hindu	1.038 (0.513-2.097)	0.918	1.434 (0.709-2.902)	0.316	1.857 (0.882-3.910)	0.103
	Muslim	1		1		1	
Marital status	Married	0.626 (0.244-1.609)	0.331	1.200 (0.469-3.070)	0.704	0.503 (0.184-1.376)	0.181
	Single	1		1		1	
Education	Illiterate	2.111 (0.645-6.903)	0.217	1.945 (0.627-6.036)	0.250	0.537 (0.174-1.654)	0.278
	Literate	1		1		1	
Occupation	Employed	0.628 (0.221-1.786)	0.383	1.213 (0.435-3.382)	0.712	0.393 (0.110-1.405)	0.151
	Unemployed	1		1		1	
Floor of residence	Ground floor	1.836 (0.855-3.939)	0.119	3.088 (1.395-6.838)*	0.005	2.772 (1.210-6.352) *	0.016
	Upper floors	1		1		1	
Other family members	Unaffected	1.910 (0.205-17.749)	0.570	2.809 (0.244-32.364)	0.408	0.946 (0.071-12.682)	0.966
	Affected	1		1		1	

*denotes significant values at p<0.05, 1 is taken as referend value for multiple logistic regression.

analogous with the study conducted by Rahman MM in Bangladesh (54.24%)[4]. Our study reported that 57.2% people know about the biting behaviours of Aedes mosquito in early morning and late night, whereas the study conducted by Rahman MM in Bangladesh reported that 74.08% students were aware of the fact[4]. The principal symptoms of Dengue as fever and joint pain were known by 72.4% people. They were similarly identified by 87.52% of subjects in a study conducted by Rahman MM[4]. Similar finding was also reported by Oche OM in Nigeria where fever was identified by 94.7% and muscular pain was identified by 93.5% subjects as symptoms of Dengue fever[12]. This contrasted with the study by Kazaura M in Tanzania where symptoms of Dengue fever were identified by only 14.3% of subjects[14]. The fact that Dengue is deadly was known among 67.8% cases in present study. 74.6% of people strongly agreed that Dengue is a serious disease in study conducted by Mohammed Ali Saghir in Yemen[5]. Rahman MM reported that 93.12% subjects were aware of the fact that Dengue causes death in study among students of Dhaka city in Bangladesh[4].

Overall, 48.7% of our respondents had sufficient knowledge of the cause, transmission, principal symptoms of dengue fever. The study conducted by Oche OM revealed that most of the respondents had good knowledge of causes, spread and Dengue fever symptoms with a score of 75% and above[9]. A similar study by Farizah H showed that a good knowledge of both Dengue and Aedes was possessed by 68.5% of the respondents[16]. In another study by Rahman MM, around 80% of the students who participated in the study reported correctly about the symptoms, effect, mosquito type, phenotype and cleanliness[4]. Kazaura M in his study in Tanzania reported that low knowledge about Dengue transmission, symptoms and preventive mechanisms was present in more than three quarters of the adult communities[14]. It was found that a good level of knowledge about DF was possessed by only 53.7% of the people in the study by Saghir MA[5].

About questions on attitude, maximum people (89.5%) wanted Dengue case reduction in their areas. But only 30.3% and 34.9% of the people in our study thought that it's a collective responsibility to reduce Dengue and were aware of the various IEC materials in their surroundings respectively. In Rahman MM study 34.08% people strongly expressed their willingness to take part in Dengue fever control[4], whereas 76.2% subjects thought that there should be an active participation by the communities for vector control in Dengue Fever in study of Saghir MA[3]. 86.8% respondents considered themselves as an important to fight Dengue spread in study conducted by Nurul Akmar Ghani in selected hotspot areas of Dengue in Selangor, Malaysia[17]. A substantial portion of the respondents (57.0%) in Farizah H study[16] felt that controlling Aedes mosquito was their own responsibility, while another 9.5% transferred the responsibility on the Government. Another one-third of the responders felt of it as a shared responsibility. 47.4% people checked the existence of possible mosquito breeding sites around their locality in our study. This was comparable to the study conducted by Rahman MM in Bangladesh where around 47.84% respondents were of the opinion of regular mosquito breeding site removal even during non-febrile periods[4].

The overall practice of the study subjects for

prevention of Dengue was poor. Only 34.9% of the subjects in our present study converted the knowledge and attitude to a good practice. 31.6% of subjects had the practice to call authorities for spraying in our present study. 88.1% people used insecticide sprays to reduce mosquitoes populations in study by Saghir MA[5]. 44.7% subjects in our study used to contact the health authorities for fogging.In contrast, Rahman MM reported that only 25.6% of the respondents used to call the municipal authority for fogging[4].

A good practice noted in our study was use of mosquito nets by 72.4% of the people. It was even higher in study done in Yemen(89.2%)[3]. In contrast to this, another study by S Matta in India reported that 20.2% people were using bed nets for personal protection against mosquito bite[18].

Overall, 50.7% of the subjects had a good KAP score. Practice towards Dengue prevention had a positive association with male subjects (p=0.014) and those living on the ground floor (p=0.016). This contrasted with the study by Farizah H that reported no apparent differences between male and female in terms of the practice of Aedes breeding prevention[16]. On the other hand, Female respondents had comparatively better attitudes and practices related to Dengue than their male counterparts in study by Rahman MM[4].

There was a positive correlation between knowledge-attitude ($r_s = 0.517$, $p < 0.000$), knowledge-practice ($r_s = 0.498$, $p < 0.000$) and attitude-practice ($r_s = 0.445$, $p < 0.000$) in our present study which was statistically significant[4,26]. Similar associations between Knowledge, Attitude and Practice were also found in study by Rahman MM in Bangladesh and Dhimal, *et al* in Nepal[4,26]. Saghir MA revealed that inspite of there being a significant correlation between the KAP domains in his study, there was a weak linear relationship[5]. On the other hand statistically significant correlations between the Knowledge, Attitude and Practice domains were totally absent in the study conducted by Phuyal P from Central Nepal. The overall practice score obtained was higher than the overall knowledge score. Similar findings like his study were reported in studies from Sri Lanka[19], Vietnam[20,21] and Malaysia[22] but contrary to other studies of Philippines[23] and Jamaica[24], which reported high levels of knowledge but low level of practices. In another study conducted by Das S from Dhaka, Bangladesh again concluded the importance of mass awareness programs sponsored by the Government[25]. It was seen in our study that subjects who had a good knowledge were 3.5 times likely to have a good attitude and 3.2 times likely to have a good practice. Similarly, a good attitude were 4 times likely to have a good practice.

Conclusion

Respondent's knowledge and attitude concerning Dengue fever and its control were not good enough. It was found that the knowledge and practice were significantly associated just like knowledge and attitude. This absence of knowledge about the illness, its transmission and prevention, made the population highly vulnerable to contract the virus. This provides an impetus to the idea that the health education programmes should be intensified with a focus to improve the knowledge of Dengue fever, its cause, transmission and principal symptoms. A proposal for a holistic preparedness for Dengue fever by the various stakeholders can be drawn up, which can ultimately contribute in reducing frequent Dengue fever outbreaks in the community which has been represented by our study.

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Original Article

Investigating the Multifaceted Aspects that Affect Interns' Competence and Performance in Arterial Blood Gas Sampling Technique in Emergency Department Settings

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Background : Arterial Blood Gas (ABG) sampling is a critical clinical procedure commonly performed by Junior Residents and Interns in teaching hospitals, particularly in the Emergency Department for critically ill patients. Improper technique can lead to a range of complications, such as local hematoma, pain and infection, compromising patient care and outcomes. It is therefore essential for interns to have the necessary skills and expertise to perform the procedure correctly. This descriptive cross-sectional study aims to identify the specific challenges that Interns face when performing ABG sampling and develop targeted training programs to address these challenges. The study results can help develop evidence-based guidelines for ABG sampling in emergency department settings.

Materials and Methods : A validated questionnaire containing questions on the competency and understanding of ABG sampling was distributed to 200 Interns affiliated with our institution. The collected data was analyzed using descriptive statistics in the form of frequencies and percentages. The analysis was performed using SPSS version 21.0 software.

Results : In this study, among 200 interns we found that the radial artery was the preferred site for ABG sampling (91%), with 86.6% preferring a 2 ml heparinized needle. Most recognized local infection (90.5%) and hematoma formation (96.5%) as potential complications. 87.5% of participants had performed the procedure at least once on a patient with 39% being supervised by a nurse during their first attempt. Only 31% of participants expressed confidence in performing and 25% documented the procedure. The majority adhered to aseptic precautions (66% hand washing, 78% skin antisepsis, 74% gloves and 62% sterile towel). Almost all palpated the pulse prior to insertion (89.5%) and applied local pressure for hemostasis (86%) but only 56% properly disposed of the needle. Notably none had received training in the skill lab during the undergraduate programme.

Conclusion : The study revealed significant gaps in the competency and understanding of ABG sampling among interns which underscore the need for a training program before the commencement of the internship to provide adequate knowledge about the technique, complications and management. Such a program could help improve the quality of ABG sampling and minimize complications associated with the procedure.

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Key words **: Arterial Blood Gas, Hand Disinfection, Asepsis, Education Medical Undergraduate.**

Arterial Blood Gas (ABG) sampling is a crucial bedside procedure commonly practiced in the Emergency Room (ER) and critical care settings. It is used to assess acid-base balance, gas exchange and respiratory, metabolic and renal function[1]. The procedure is considered the most reliable determination of ventilation and successful oxygenation and is the only way to determine the alveolar-arterial oxygen gradient[2]. With relatively low complications, ABG sampling has become an essential tool in guiding treatment plans for patients and its demand is increasing due to the rising prevalence of ICU care and ventilator settings.

Editor's Comment :

- This study emphasizes the intricate factors influencing interns' proficiency in arterial blood gas sampling in emergency departments. By addressing both technical skills and contextual elements, healthcare educators can enhance training programs to ensure interns are adept at this critical technique in high-pressure settings, ultimately improving patient care.

Prior knowledge of the technique and potential complications is necessary to select the patient and site of arterial puncture and avoid the risks of local hematoma, arterial occlusion, and laceration[3]. Critical components of ABG sampling include the angle of needle insertion, heparin flush of the syringe and infection control measures to reduce complications.

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In our institute, Interns commonly perform ABG sampling. Therefore, we conducted a study to assess their knowledge and clinical skills based on the training they received during their undergraduate (MBBS) course and their experience practicing on mannequins and patients. The results of this study will help identify the gaps in their training and improve the quality of care provided to patients undergoing ABG sampling.

Materials and Methods

This descriptive study was conducted over a period of twelve months at a tertiary care teaching hospital. Ethical clearance was obtained from the Institute's Ethical Committee and verbal and written consent was obtained from all 200 participants selected using a convenience sampling method among medical interns who had completed their compulsory rotation in Department of Emergency Medicine.

The sample size was calculated using the formula

$$n= (Z^2 \times p \times q) / e^2$$

Where N is the minimum required sample size, Z is 1.96 at 95% Confidence Interval (CI), P is prevalence taken as 50% for maximum sample size, Q is 1-p and E is margin of error, 8%.

Before beginning the study, six experts from various departments of our hospital validated the questionnaires and those with a Content Validity Ratio (CVR) of >0.6 were included in the study. The study participants were provided with a structured, validated, and pre-tested questionnaire in English to evaluate their understanding, practices, and perception of ABG sampling. The principal investigator collected the questionnaires from all participants and the data was later entered in Excel. Statistical analysis was conducted using SPSS version 21.0, and results were expressed in frequencies and percentages.

Results

Assessment of Knowledge of ABG Sampling among Interns :

The preferred arterial sites for ABG sampling among the Interns were the radial artery (91%), followed by the femoral artery (89%) and the brachial artery (66%). The majority of participants (86.6%) preferred a 2ml heparinized needle for sampling. In terms of contraindications, the most commonly recognized was local infection (90.5%), followed by severe peripheral vascular disease (73%). Regarding complications, all participants recognized local pain as a potential adverse event, while infection at the puncture site was recognized by 45% of participants. Hematoma formation (96.5%) was also commonly recognized, while arterial vasospasm/occlusion/laceration (60%) and needle-stick injuries to healthcare personnel (80%) were also acknowledged as potential complications. (Table 1).

Table 1 — *Assessment of Knowledge of ABG sampling*

	Yes n (%)	No n (%)
Site :		
Radial artery	182 (91)	8 (9)
Femoral artery	178 (89)	22 (11)
Brachial artery	132 (66)	68 (34)
Contraindication :		
Abnormal modified Allen test	114 (57)	86 (43)
Local infection	181 (90.5)	19 (9.5)
Arteriovenous fistulas	91 (45.5)	109 (54.5)
Severe peripheral vascular disease	146 (73)	54 (27)
Severe coagulopathy	129 (64.5)	71 (35.5)
Complication :		
Local pain	200 (100)	0 (0)
Local Hematoma	193 (96.5)	07 (3.5)
Arterial vasospasm / occlusion / laceration	120 (60)	80 (40)
Embolism	64 (32)	136 (68)
Infection at the puncture site	90 (45)	110(55)
Vasovagal response	80(40)	120 (60)
Needle-stick injury to healthcare personnel	160 (80)	40(20)

Assessment of Attitude of ABG Sampling among Interns :

Only 25% of the participants documented the ABG sampling procedure. 87.5% of the participants performed the procedure on patients, but none of them had ever performed the procedure on a mannequin (Table 2).

Table 2 — *Assessment of attitude of ABG sampling procedure*

Questions	Yes n (%)	No n (%)
During your MBBS course, was any formal training given on ABG Sampling procedure ?	0 (0)	200 (100)
Have you performed an ABG Sampling on a mannequin ?	0 (0)	200 (100)
Have you ever performed ABG Sampling on a patient ?	175 (87.5)	25 (12.5)
Was the procedure documented ?	50 (25)	125 (75)

Regarding supervision during ABG sampling, 39% of the participants were supervised by a nurse and 35.5% were supervised by postgraduates during their first attempt at the procedure (Fig 1).

31% of the participants were confident, 10.5% were very confident, 28% were neutral, 11% were not confident and 19.5% were not at all confident in performing the procedure (Fig 2).

Assessment of Practice of ABG Sampling among Interns :

The majority of participants reported adherence to

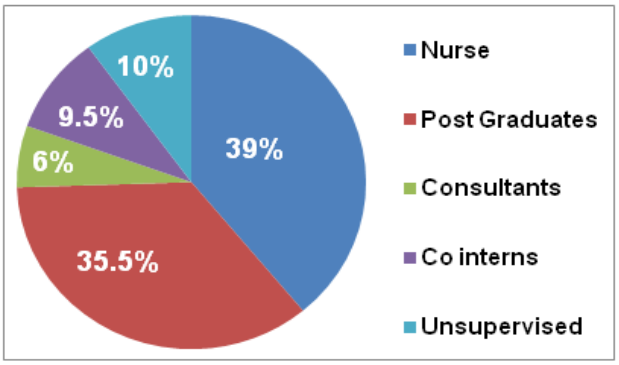

Fig 1 — Supervision during ABG sampling

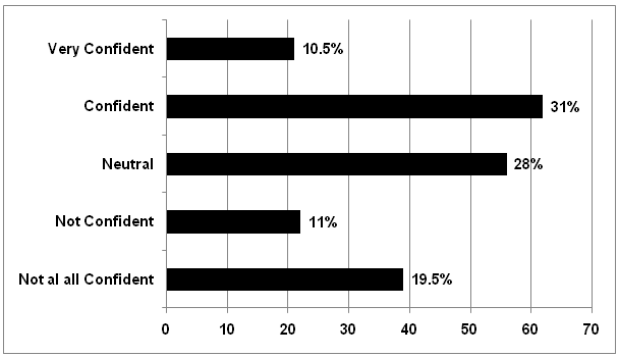

Fig 2 — Level of confidence to perform ABG sampling

aseptic precautions during ABG sampling, with 66% reporting hand washing prior to the procedure, 78% reporting skin antisepsis, 74% using gloves and 62% using a sterile towel.

In terms of the technique used during ABG sampling, 89.5% of participants reported palpating the pulse prior to insertion and 76% reported placing their hand in extension. Additionally, 74.5% of participants reported using proper needle insertion technique, 86% applying local pressure for hemostasis, 66.5% removing air bubbles from the syringe and 56% capping the syringe. Finally, 60% of participants reported properly disposing of the needle (Table 3).

Table 3 — *Assessment of practice of ABG sampling*

	Yes n (%)	No n (%)
Aseptic Precaution :		
Hand wash before the procedure	132 (66)	68 (34)
Skin Antisepsis	156 (78)	44 (22)
Gloves	148 (74)	52 (26)
Sterile Towel	124 (62)	76 (38)
Technique :		
Palpate Pulse	179 (89.5)	21 (10.5)
Placement of hand-in extension	152(76)	48(24)
Needle insertion technique	149 (74.5)	51 (25.5)
Application of local pressure	172 (86)	28 (14)
Removal of air bubbles from syringe.	133 (66.5)	67 (33.5)
Capping of the syringe.	112 (56)	88 (44)
Disposal of needle	120 (60)	80 (40)
2ml syringe	173 (86.5)	27 (13.5)

Discussion

The purpose of this study was to evaluate the level of competency and understanding of Arterial Blood Gas (ABG) sampling technique among Interns. Interns were selected as study participants, as they are responsible for conducting various basic medical procedures, including ABG sampling, securing intravenous cannulas and urinary catheterization, which are commonly performed in healthcare settings.

In our study, we observed that the majority of interns demonstrated a good level of knowledge about the site selection, contraindications and complications associated with ABG sampling. However, their adherence to aseptic precautions and procedural technique was found to be inadequate. This suggests that while Interns possess a good theoretical understanding of the procedure, they may lack the practical skills necessary to ensure the procedure is conducted safely and effectively.

It is worth noting that 91% of the Interns in our study preferred to use the radial artery for ABG sampling, citing its superficial location and relatively lower level of pain compared to other sites. Interestingly, only few of participants opted for the brachial artery, which could be due to the knowledge of increased likelihood of nerve damage and more painful procedure[5].

Furthermore, the use of a heparinized 2ml syringe was preferred by majority of Interns, as it caused less discomfort and was adequately sized for accessing the vessel[6]. However, the majority of Interns in our study were unaware of contraindications, such as abnormal modified Allen's test, arterio-venous fistula in the limb and severe coagulopathy, which could impact the accuracy and safety of the procedure[7,8]. This could be attributed to inadequate formal training during their undergraduate course.

While Interns demonstrated good knowledge of common complications associated with ABG sampling, such as local pain, hematoma, and needle stick injuries, they were less aware of rare complications such as arterial vasospasm, occlusion, laceration, embolism, vasovagal response, and infections. Notably, coagulase-negative staphylococci and Staphylococcus aureus were identified as the most common agents for infection at the puncture site. [9] This suggests that there may be a need for more comprehensive training on the potential risks associated with ABG sampling.

It is worth noting that hand washing remains an essential step before conducting any clinical procedure and the use of sterile gloves, chlorhexidine-based antiseptic solutions, and sterile towels can significantly

reduce the risk of infective-related complications[10]. In our study, the majority of Interns were aware of the importance of aseptic procedures. However, it is worth mentioning that 68% of Interns were not aware of rare complications, such as embolism, when compared with a similar study by Rowling S, *et al* which showed results of 49%[11].

Previous research on ABG sampling technique has mainly focused on the Knowledge, Attitude and Practice of nurses. However, we decided to assess the level of understanding and proficiency of Interns in this procedure and our study aimed to provide an in-depth analysis of Interns' level of competency and understanding related to ABG sampling, which could serve as a foundation for developing effective training programs to improve the quality and safety of this procedure in our Institution. Our findings highlight the need for structured training programs and skill labs to strengthen the procedural skills and knowledge of Interns, ultimately ensuring the safe and effective delivery of patient care.

Conclusion

The results of our study indicate that Interns possessed sufficient theoretical knowledge of ABG sampling, including artery selection and contraindications. However, our findings also revealed a deficiency in their practical skills related to aseptic precautions, technique and complications of the procedure. Based on these results, it is essential to emphasize the need for supervised practice on mannequins before the commencement of the Internship and formal training during the Undergraduate course. Such measures will aid in improving the Interns' clinical skills and ensure the safety and quality of ABG sampling in our Institution.

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Original Article

Pattern of Smartphone Exposure among Children <5 Years of Age Attending Out-patient Department of a Tertiary Care Hospital : A Cross-sectional Study

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Background : Smartphones are becoming widely popular and the number of users is significantly increased over the last decades. In the current era of COVID pandemic, even the school age children must resort to mobile media devices for online learning. But the risk of adverse outcome, both physical and psychological, is more in pre-school children with prolonged exposures as shown by different studies.

Materials and Methods : The study was conducted among parents/ caregivers of under-five children, attending Outpatient Department of a tertiary care hospital.

Result : A total of 387 parents/ caregivers attending the Paediatrics OPD with under 5 children were interviewed for the study over the 6 months period of the study. Among the study participants, 223 (57.6%) parents confirmed use of Smartphone in their children. 81 (36.3%) children are exposed to higher level of usage (>2 hour/Day). The questionnaire also revealed that, majority of parents/ caregivers (174, 78%) perceived no adverse effects from usage of Smartphones to young children.

Conclusion : Paediatricians have an important role in advising regarding the use to smartphones in childhood and it is important to bridge the knowledge gap among parents and caregivers, regarding the misuse of mobile devices by under 5 children.

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Key words **: Pre-schoolers, Smartphone exposure, Under-five children.**

Smartphones have become widely popular and the number of users is significantly increased over the last decades[1]. Mobile phones are indispensable part of today's societies. We cannot think of going about our day without the use of mobile phones. With the great boom in number of Smartphones use, children are invariably becoming exposed to Smartphone devices. Earlier and higher exposure to multimedia is known to have negative effects on children's physical and mental status[1]. Specially, children with electronic media use during early childhood for more than 2 hours per day has been linked to increase weight status and to behavioral problems[2]. Moreover, media usage may interfere with sleep quality through the increase of psychological arousal caused by stimulating content watched or through bright light exposure[3]. Bright light may impact sleep by delaying the circadian rhythm when exposure takes place in the evening and by causing an immediate activation itself[4,5]. In the current era of Global COVID pandemic, even the school age children must resort to mobile media devices for online learning. But the risk of adverse outcome, both physical and psychological, is more in pre-school children with prolonged exposures as shown by different studies[6-8]. Our present study thus, is an endeavor to investigate the pattern of mobile device use among under 5 children.

Editor's Comment :

- There is a facet to the problem as using mobile phones in very young children increases a longer lifetime exposure to Radiofrequency Electromagnetic Fields (RF-EMF) from Mobile Phones.
- Risk to young children from this RF-EMF is very necessary to be focused in future and broader studies.

Materials and Methods

The study was conducted in the Outpatient Department of the Pediatrics Ward of a Tertiary Care Hospital of Eastern India. First, a draft proposal was prepared and a proforma was developed for recording necessary information from the parents/ caregivers accompanying the children, along with, patient

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information brochure and consent form printed in local language. The study proposal was then submitted and presented to the Scientific Review Committee and was subsequently forwarded to the Institutional Ethics Committee. After getting the necessary approval, the pre-validated questionnaire was administered to parents/ care-givers who attended the Pediatrics OPD with under-five children. Data were collected from January, 2021 to June, 2021, for a period of 6 months. After data collection, data were compiled on the Microsoft Excel Software and data were analysed and tabulated.

Results

A total of 387 parents/ caregivers attending the Paediatrics OPD with under 5 children were interviewed for the study over the 6 months period of the study. Among the study participants, 223 (57.6%) parents informed use of Smartphone in their children. Among the Smartphone exposed groups, 129 (57.8%) were males and 94 (42.2%) were females. 23 (10.3%) users of Smartphone were infants (<1 year), 89 (40%) belonged to toddler age group (1-3 year). However, majority of the exposed children belonged to 111 (49.8%) , were from Pre-schooler age groups (3-5 years). All smartphone devices used by these children belonged to either of their parents.

Among the Smartphone user group, 81 (36.3%) children reported high daily usage (>2 hours) of Smartphones, whereas 142 (63.7%) cases reported low daily usage (<2 hours). Among the under -five children using mobile phones, 126 (56.5%) reported frequently using Smartphones to facilitate feeding the child. Moreover, 123 (55.2%) under-five children using Smartphone also used mobile phone at bedtime. Smartphone devices were also used to keep the children calm during daily chores in about 92 (41.3%) cases as reported by the parents/caregivers.

The contents showed to the children varied from watching videos 156 (70%), playing games 122 (54.7%) and watching mixed and varied contents 41 (18.3%), however, these were not mutually exclusive.

The questionnaire also revealed that, majority of parents/ caregivers (174, 78%) perceived no adverse effects from usage of Smartphones to young children, whereas 49 (22%) parents from the user group perceived some adverse effect from exposure of Smartphone devices among young users.

Discussion

Smartphones have become indispensable part of today's life. Moreover, in the current pandemic situation, education in the school aged children has become dependent on usage of Mobile media device as schools have mostly resorted to on-line education for fear of exposing vulnerable children to COVID infection. At this juncture, it has become difficult to protect pre-school children from developing negative effects on children's physical and mental status due to earlier and higher exposure of multimedia devices, particularly, Smartphones, due to their almost universal availability. However, the current magnitude and pattern of Smartphone exposure in under-five children, particularly, during the current COVID pandemic is not yet fully explored. The current study detects that 52.6% of the concerned under-five children are exposed to Smartphones by their parents/caregivers. It is also alarming that even infants are not spared of this practice of mobile device exposure as almost 10.3 % children are exposed to Smartphone, although the rate of exposure increases progressively, as the rate is 40% among the toddler age group and 49.8% among the pre-schooler age group. What is more concerning is that more than one-third of the user of Smartphone devices, use these devices for more than 2 hours in a day. Studies have shown more somatic symptoms, more attention problems, more aggressive symptoms and more withdrawal symptoms among the high exposure groups (ie, with exposure to mobile phones of >2 hours a day)[1].

The current study shows that, in the under-five children, Smartphone exposure occurs more often during feeding. Also, use of mobile phones was high during bedtime. This practice is however, counter-productive, as several studies have reported adverse health effects of using mobile phones during night-time[3-5]. Smartphone devices were also used to keep the children calm during daily chores in 41% cases as reported by the parents/caregivers. This practice has also been reported in other studies[9].

This study has also shown that, there is a huge knowledge gap among parents and caregivers regarding potential negative effects caused by early and prolonged Smartphone exposure in young children, as parents/caregivers perceived no adverse effects from usage of smartphones to young children in the majority of the cases (174, 78%). According to studies only 16% of Paediatricians ask families regarding their media device exposure[10] although, the risk of negative effects on children and to pre-school children seems to be very high.

Apart from all these adverse effects, there is another evil that needs to be addressed, while considering serious adverse effects of mobile phones. A nationwide cross-sectional study was conducted in Taiwan, to

collect information on children's use of mobile phones and the perceived health symptoms reported by their parents. Mobile Phone use was associated with a significantly increased Adjusted Odds Ratio (AOR) for headache and migraine and skin itches. Children who regularly used mobile phones were also considered to have a health status worse than it was 1 year ago. The study in conclusion, suggested a more cautious use of Mobile Phones in children, because, children are expected to experience a longer lifetime exposure to Radiofrequency Electromagnetic Fields (RF-EMF) from Mobile phones[11]. However, this was beyond the scope of this present study.

Conclusion

The current study has picked up the current pattern of exposure of Smartphones, to the vulnerable pre-schoolers, toddlers and even to the infant age groups. However, several large scale and possibly multicentre studies are required to appropriately understand the true magnitude of the problem and at the same time, it is also mandatory to try to bridge the knowledge gap among parents and care-givers, regarding the issue. Paediatricians have an important role in advising against the exposure to Smartphones in childhood. Moreover, there is another facet to the problem as using mobile phones in very young children also increases a longer lifetime exposure to Radiofrequency Electromagnetic Fields (RF-EMF) from Mobile Phones. Risk to young children from this RF-EMF is also a very necessary to be focused in future and broader studies.

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Original Article

A Study of Occurrence of Hypothermia in Newborn in Post Neonatal Ward and Factors Contributing It

Anjali Jagdish Dodiya[1], Khyati Mitesh Kakkad[2], Vaishali Nandkishor Prajapati[3], Hardik Parmar[3]

Research Question : What is the occurrence of Hypothermia in healthy newborn during winter months and what are the factors contributing it ?

Settings : Post Neonatal Ward of tertiary care hospital.

Study Design : Cross-sectional study.

Participants : 675 normal delivered healthy newborn.

Methodology : All participants during month of December 2020 and January 2021 were screened for hypothermia Factors contributing it and Effect of KMC on temperature change were statistically studied.

Results : Incidence of hypothermia was 13%. Preterm (34-37week) were 2 times more prone to have hypothermia compared with term neonates ($p<0.05$). Neonates were 3.8 times more prone to develop hypothermia during early hours of life ($p<0.05$). Hypothermia was observed more in newborns not breast fed within 2 hours (15.5%) and newborns with low birth weight (36%). With the help of paired t-test, effect of KMC in hypothermic newborn was statistically significant (p value <0.05).

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Key words **: Hypothermia, KMC, Post Neonatal Ward.**

India accounts for 21.7 neonatal deaths per 1000 live birth in 2019, which is unacceptably high as compared to developed countries[1]. In order to attain the global development goal of reducing neonatal mortality to under 12 neonatal deaths per 1000 live births by 2030, there is a need to identify and quantify the predictors of neonatal mortality; especially those that are preventable by available low-cost interventions[2,3]. One of the predictors of neonatal mortality that can easily be solved by available low-cost interventions is Neonatal hypothermia[4]. Neonatal hypothermia, defined as an axillary temperature less than 36.5°C, is associated with increased neonatal morbidity and mortality[5,6]. They are susceptible to hypothermia due to physical and environmental factors. Physical factors that pre-dispose neonates to hypothermia include a large surface area to volume ratio, immature skin, low amount of insulating subcutaneous fat, poorly developed metabolic mechanisms for responding to thermal stress and altered skin blood flow[4,7]. Many studies in literature have identified risk factors associated with Hypothermia in low-birth weight, pre-term, sick neonate while studies related to hypothermia in healthy term neonate are few. As a result, there is need to identify factors associated with Hypothermia in healthy term neonate who get easily unnoticed.

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Editor's Comment :

- In this study, the incidence of hypothermia was high (13%). Hence, Screening of all the newborn lying in Post Natal Ward as well as increase sensitivity regarding thermal control among mother has to be emphasized.
- Late Preterm, early hours of life, not breast-fed within 2 hours and low birth weight were the factors significantly associated with the hypothermia. Indicating round the clock monitoring for the thermal care of preterm babies during early hours of life.

Kangaroo Mother Care (KMC) is one of the safe and low cost method available, effective intervention as compared to conventional neonatal care for hypothermic babies. Skin to skin contact is the major component of KMC[8]. Hence, this study was undertaken to identify risk factors associated with Hypothermia in healthy term neonate in Post Neonatal Ward and to study the effectiveness of KMC in them.

Materials and Methods

A cross-sectional study was conducted from December 1, 2020 to January 31, 2021 in Post Neonatal Care (PNC) ward of tertiary care hospital. All Normal delivered neonate with gestational age >34 weeks and >1.8kgs were involved in the study. The data was collected from the mother and the indoor case sheet using a semi structured questionnaire. The axillary temperature of neonate, using digital thermometer was measured at 6'o clock in the morning. Neonate those who were identified as mild Hypothermic (Cold stress) (Temperature in range of 36°C-36.4°C) were given skin to skin contact with mother. Axillary temperature was again measured after

2 hours. Neonates who were moderate to severe hypothermic (Temperature <35.9) were admitted directly in NICU. Multivariate logistic regression analysis was used to assess the association of independent variables with the outcome variable. Odds Ratio (OR) with 95% CI was used as a measure of association and variables that p value less than 0.05 in the multivariate logistic regression were considered as significantly associated.

Observation

Out of total 675 neonates screened, 13% neonates were found to be hypothermic. Out of total hypothermic newborn, 96.7% of neonate were mildly hypothermic, 3.3% were moderately hypothermic while no newborn with severe hypothermia was identified. Out of total 381 male neonates 12.3% developed Hypothermia while out of total 294 female neonates 14.6% developed Hypothermia. In the month of December, total 439 neonates were screened out of which 78 neonates were found Hypothermic (17.7%). In month of December, lowest temperature reached was 10°C. Total 236 neonates were screened in month of January out of which 12 neonates were found Hypothermic (5%). Lowest temperature reached in the month of January was also 10°C. In present study, various pre-disposing factors were Neonate with gestational age 34-37 weeks (18.2%),early hours of life (45%), not breast fed within 2 hours (15.5%), neonates with birth weight <2 kg (36%), those who were night-time delivered (Table 1).

In present study, Preterm (34-37weeks) were 2 times more prone to have hypothermia compared with term neonates (p value-0.001, 95% CI:1.3, 3.4). Neonates were more prone to develop hypothermia during early hours of life. (p value-0.0005) (Table 2). The mean temperature before initiation of KMC was 36.17 (SD 0.14) and the mean temperature after 2 hours of KMC was 37.21 (SD 0.16). The increase in temperature was statistically significant using a paired t-test (t-52.76, p-value- 0.0001).

Discussion

The proportion of Hypothermia was 13% in present study which is in accordance to a study carried out among home delivered healthy neonates in 10 villages of Haryana, India where incidence of hypothermia was 19.1% and 3.1%, respectively in winter and summer, 24 hours after delivery[9,10]. In a study carried out among home delivered neonate in rural Uttar Pradesh, India, incidence of hypothermia in normal birth weight neonate was 43%, which was higher compared to the present study[11,12]. Another such study carried out in Nepal among healthy term neonate, the proportion of hypothermia was 85%[9,14]. Inspite of being tertiary care hospital and not so cold city, occurrence of hypothermia was high.

In the present study, Late preterm (34 week to <37 week) were 2 times more prone to have hypothermia compared with term neonates (p value-0.001, 95% CI: 1.3, 3.4). Similar findings were observed in study conducted by Yibeltal Asmamaw Yitayew, *et al*[21] and F Zayeri, *et al*[9]. The possible reason could be larger surface area to body mass in neonate, less subcutaneous fat stores and limited capacity to generate heat from fat store.

Neonate less than 6 hours were at highest risk of

Table 1 — *Socio-demographic Charecteristics of Mother and their effect on Hypothermia*

Variables/Category	Hypothermic	Normo-thermic	Total
Age of mother :			
<20 years	12(13.3%)	92(86.6%)	104
20-30 years	73(13.8%)	453(86.2%)	526
30-40 years	5(12%)	37(88%)	42
>40 years	0(0%)	3(100%)	3
Religion :			
Hindu	37(41.1%)	252(58.9%)	289
Muslim	53(58.8%)	333(41.2%)	386
Educational status :			
Illiterate	17(13.1%)	92(86.9%)	109
Primary	21(10%)	189(90%)	210
Secondary	26(11.2%)	205(88.8%)	231
Higher secondary	18(20.9%)	68(79.1%)	86
Graduate	8(20.5%)	31(79.5%)	39
ANC visit :			
0	0(0%)	3(100%)	3
1	4(9.7%)	37(90.3%)	41
2	18(15.2%)	100(84.8%)	118
3	38(16%)	200(84%)	238
4	26(10%)	214(90%)	240
5	4(12.5%)	28(87.5%)	32
6	0(0%)	3(100%)	3

Table 2 — *Multivariate Logistic Regression Analysis of Factors associated with Neonatal Hypothermia*

Variables/ Category	Hypothermia Yes	Hypothermia No	COR (95% CI)	P value
Gender :				
Male	47(12.3%)	334(87.7%)	1.078 (0.7,1.7)	0.8
Female	43(14.6%)	251(85.4%)	1	
Time of delivery :				
Night	60(13.6%)	381(86.4%)	3.872 (2.2,6.8)	0.4
Day	30(0.12%)	204(87.2%)	1	
Birth weight (grams) :				
<2500	35(16.3%)	179(83.6%)	0.7740 (0.4,1.3)	0.6
≥2500	55(11.9%)	406(88%)	1	
Gestational age (weeks) :				
35-37	50(18.2%)	224(81.8%)	2.058 (1.3,3.4)	0.001
>37	40(10%)	361(90%)	1	
Initiation of breast feeding within 2 hours :				
Yes	67(12.7%)	460(87.3%)	1.000 (0.6,1.7)	1
No	23(15.5%)	125(84.5%)	1	
Hour of life (hours) :				
<6	55(45%)	67(55%)	1.061(0.6,1.7)	0.0005
≥6	35(6.3%)	518(93%)	1	

hypothermia (45%). Similar results were observed by F Zayeri, *et al* where 53.3% were hypothermic immediately after birth[9]. It is well documented in literature that neonates loses heat immediately after birth by conduction, convection, evaporation and radiation. As age advances occurrence of hypothermia reduces, this may be because by 6 hours, they get clothed, breast fed, counselled for skin to skin contact.

Neonate who were initated with breast feeding within 2 hours were protected for Hypothermia as compared to neonates who were breast fed after 2 hours. Similar findings were proved by Jeffrey Pradeep Raj, *et al*[13] and by Gebresilasea Gendisha Ukke, *et al*[16]. This could be due to the fact that breastfeed babies get adequate calories from the breast milk which protects them from the hypothermia[9,17]. Another reason could be skin-to-skin contact with their mothers' body[9,18,19].

As per Table 2, Neonates delivered at night time were 3.8 times more prone to develop hypothermia compared to neonate delivered at day time (p value-0.4, 95% CI-2.2, 6.8). This finding is comparable to studies conducted in Northest Ethopia by Yibeltal Asmamaw Yitayew, *et al* where Delivery time showed a significant association with neonatal hypothermia. (AOR=2)[15].

In our study the increase in temperature after 2 hours of KMC was statistically significant using a paired t-test (t-52.76, p-value- 0.0001). Effectiveness of KMC has been established in low-birth weight and preterm neonate in an updated Cochrane review (Conde-Agudelo, Diaz-Rossello, Beltzan 2011)[8]. Also, Skin to skin contact immediately after birth prevents Hypothermia, is been very well explained in the study of Yibeltal Asmamaw Yitayew, *et al* where neonates who had no skin-to-skin contact within 1 hour after delivery had a 3.1 times higher odds of hypothermia compared to those who had skin-to-skin contact[15]. While few studies in literature[20], proves the effectiveness of KMC in healthy neonates, this study was undertaken to study effect of KMC in stable term neonate.

Conclusion

Inspite of various research and awareness in the field of hypothermia, the incidence of hypothermia was high in present study. Preterm delivery, early hours of life were the factors significantly associated with the hypothermia in the present study. Hence, there is a need to spread awareness among mothers and nurses in Post Neonatal Ward regarding low-cost early measures like wapping with 2-3 layers, early breast-feeding, use of mitten and socks, regular measurement of temperature and look for signs of hypothermia to prevent occurence of hypothermia.

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Case Series

Congenital Neonatal Colonic Atresias Arising in Watershed Areas of the Colonic Blood Supply

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There are certain junctional weak points in the colonic marginal artery blood supply, known as watershed areas, which result from congenital incomplete development of anastomoses of the marginal arteries. These critical points in the marginal arcade are more vulnerable to consequences of ischemic injury than other parts of the marginal arterial arcade. We report herein the series of five patients who developed colonic atresia well localized in the rectosigmoid region at Sudeck's point in two patients, in the splenic flexure region at Griffith's point in one patient and in the cecum-ascending colon junction in one patient respectively and a very interesting case of wide spread multiple junctions at middle colic and inferior mesenteric artery distribution type 3 atresia in one case. This report and our review of the literature suggest that watershed areas, including Sudeck's point or rectosigmoid junction area, the splenic flexure or Griffith's point and the ileocecal region between ileal and colic branches and combinations thereof, are high-risk regions for the development of colonic atresia and rarely the vascular insult can be major and can involve key branch of marginal arcade leading to short colon syndrome. We have treated all different approaches with one stage, two stage and three stage open, laparoscopic and minimal invasive periumbilical approach. All three approaches and single stage or staged approaches are safe and effective in colonic atresias depending on the case and available resources. An attempt to save ileocecal valve, appendix and cecum with ceco-coloplasty in the initial stage did not work and had to finally perform subtotal resection of the dilated cecum and part of the ascending colon with preservation of the ileocecal valve and the appendix at corrective surgery in the right colonic atresia case. We had motility disorders associated with two of our cases.

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Key words **: Colonic Atresia, Griffith Point, Sudeck Point, Middle Colic Artery, Neonatal Intestinal Obstruction, Left Transverse Colostomy, Laparoscopy.**

Isolated Colonic Atresia in a neonate is exceedingly rare, least common intestinal atresia, poses several diagnostic and therapeutic challenges for successful and safe outcome of ideal treatment which has consequences of life long implications[1-11]. The Colonic Atresias are different from other intestinal atresias as there is a huge disproportion between the proximal and distal segments and hence, more likely to be managed by staged approach rather than single stage repair. Plain radiograph and contrast enema should help establish the diagnosis. Here, we present a series of neonatal colonic atresia cases with its all-associated risks, with a review of the literature focusing on preservation of ileocecal valve, appendix and colon with emphasis on innovative minimal

Editor's Comment :

- The vascular theory of colonic atresia is well supported by occurrence at three critical junctional weak points called watershed areas of marginal colonic artery anastomosis as congenital anomaly between different branches is a new finding and objective evidence.
- Association of Hirschsprung's disease with colonic atresia is well known but we have reported motility disorders as variant Hirschsprung's disease.
- The watershed areas, including Sudeck's point or rectosigmoid junction area, the splenic flexure or Griffith's point, and the ileocecal region between ileal and colic branches and combinations thereof, are high-risk regions for the development of colonic atresia.
- All three approaches (open, periumbilical and laparoscopic) and single stage or staged approaches are safe and effective in colonic atresias depending on the case and available resources.

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invasive surgery and its peri-operative care. We aim to contribute to the awareness of the existence of these rare lesions and safe and successful surgical management.

Case 1

A 2080 grams baby girl was delivered normally at 36 weeks. Two days after birth she developed abdominal distension, failure to pass meconium and bilious vomiting. Physical examination and abdominal X-ray showed bowel obstruction with no gas in the rectum (Fig 1A). Contrast enema confirmed Colonic Atresia at rectosigmoid junction (Fig 1B).

Left transverse colostomy with biopsy at colostomy site and rectal suction biopsies, to rule out associated Hirschsprung's disease, were performed in the neonatal period uneventfully. The histological examination of both biopsies showed immature ganglion cells. At definitive surgery, type 2 rectosigmoid Colonic Atresia was resected and end to end Anastomosis was performed at 4 months after repeat rectal suction biopsy showed normal mature ganglion cells. Postoperative colostogram was normal and Colostomy closure was done at 6 months of age uneventfully. Follow up was uneventful and the patient is now 16 years old with normal feeding and transit.

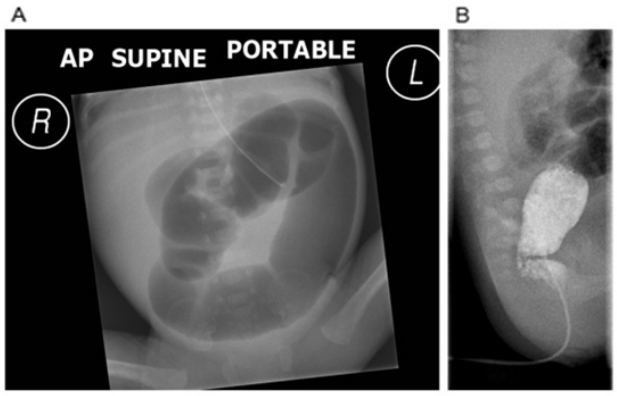


Fig 1 — Plain abdominal radiograph and contrast enema of Case 1

Case 2

A full-term male neonate weighing 3450 grams was delivered by normal vaginal delivery. On the first day of life, he was admitted with bilious vomiting and mild abdominal fullness.Chest radiograph was normal. Plain radiograph showed dilated small bowel and no gas was visualized within the rectum suggesting a distal bowel obstruction (Fig 2A). Bowel atresia, a meconium ileus or long segment Hirschsprung's disease was a probability. Water soluble contrast enema passed easily up to a point probably involving the splenic flexure but without any significant meconium or bowel content present within the lumen of the distal microcolon. It would not pass any further than this and no evidence of caliber change anywhere to suggest Hirschsprung's disease. Appearances would suggest a Colonic Atresia with

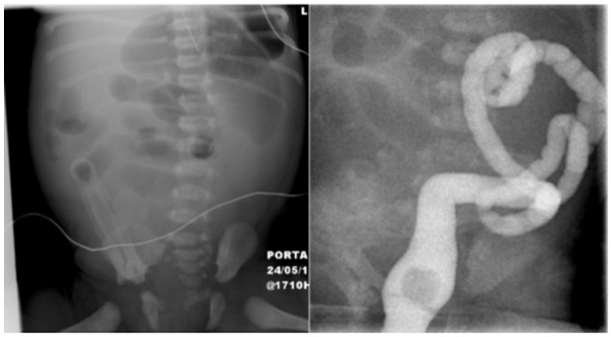


Fig 2 — Plain abdominal radiograph and contrast enema of Case 2

adjacent proximal bowel loops did appear dilated (Fig 2B).

Rectal suction biopsy showed few ganglion cells but no hypertrophy of nerve fibers and normal acetylcholinesterase suggestive of Hypoganglionosis. As there was no significant abdominal distention and good weight term baby, an option for laparoscopic evaluation and exteriorization of the atresia at one of the ports and primary Anastomosis was carried out uneventfully. Postoperative period was uneventful and is doing well at 8 years with micronutrient therapy and laxatives intermittently for associated hypo-ganglionosis.

Case 3

A 36 hours old male term infant weighing 3200 mg. At the 2nd day of life was admitted at local community hospital for failure to pass meconium, no bowel movements despite feeding and no response to glycerin suppository and persistent non-bilious vomiting. Physical examination revealed a distended abdomen, no associated anomalies were found.

Abdominal ultrasound showed normal pyloric canal length of 12 mm and thickness of 2mm and rest of the ultrasound was normal. Chest radiograph showed the tip of the feeding tube was in the stomach. Abdominal radiograph revealed a large dilated viscus lying the right of midline with some dilated loops of further bowel, probably representing an obstructed small bowel and no distal or rectal gas suggesting low bowel obstruction such as bowel atresia, meconium ileus or long segment Hirschsprung's disease (Fig 3 A). He was resuscitated and transferred to our regional Neonatal Care Unit.

A water-soluble enema was performed. The colon was displaced to the left side of the abdomen by a large air-filled loop of bowel seen within the right iliac fossa. No meconium, air passed or anorectum gripping the catheter during the rectal examination. Contrast then passed through rectum, sigmoid colon, the transverse and hepatic flexure without any transition zone. No contrast could be passed further despite repeated attempts even using hand pressure. No meconium was identified during the examination. Ascending colonic atresia with dilatation of the proximal caecum and small bowel was very likely (Fig 3B).

Minimal Invasive Surgery via periumbilical incision revealed upper ascending Colon Atresia type 3 with close loop dilatation of proximal ascending colon and cecum

with competent ileocecal valve and diffuse secondary small bowel dilatation. Resection of both dilated end and atretic ends with ceco-colic anti-mesenteric tapering ceco-coloplasty and end to end Anastomosis was carried out uneventfully. Rectal suction biopsy and excised specimen at surgery showed normal ganglion cells with no evidence of Hirschsprung's disease. Immediate postoperative period was uneventful and discharged home after 6 days.

Postoperatively, a water-soluble contrast was injected through a rectal tube. There is free flow of contrast through the distal colon, which has small caliber into the proximal part of the transverse colon, at the site of the surgical anastomosis of corrected Colonic Atresia. The contrast accumulated gradually in a markedly distended ascending colon and cecum and in turn, refluxed into the terminal ileum through incompetent ileocecal valve. The progressively distended ascending colon and cecum could be related to partial obstruction at the site of surgical Anastomosis or Dysmotility.

However, in few months' time, represented with gradually increasing abdominal distention, anemia and failure to thrive and nasogastric tube culture grew candida. Abdominal ultrasound suggested multiple dilated loops of bowel seen throughout the abdomen. Abdominal radiograph showed small and right sided large bowel with gas in the distal colon suggestive of partial obstruction (Fig 3C). Contrast studies showed partial functional obstruction with hugely dilated previously tapered ceco-coloplasty segment, patent anastomosis and no distal obstruction (Fig 3D).

He underwent re-explanation through the same periumbilical scar cutting incision and the hugely dilated right colon was resected with partial subtotal excision of the cecum, preservation of the appendix and ileocecal valve, appendicostomy with a silastic tube with multiple holes was passed into terminal ileum to decompress it and appendix tip was stitched with lateral abdominal peritoneum to exteriorize and the silastic tube appendico-ceco-ileostomy temporary proximal decompression

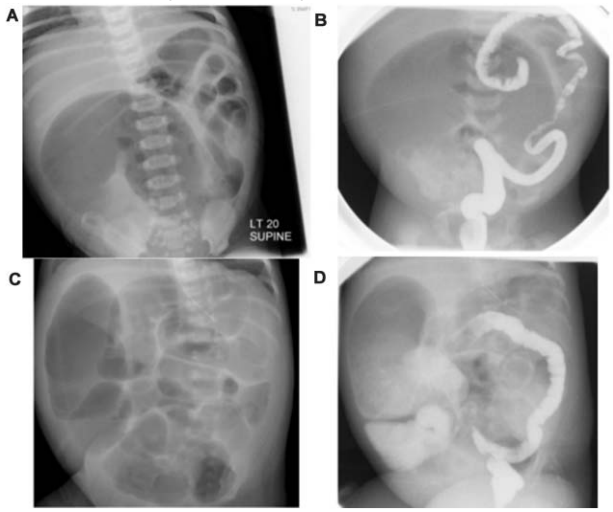


Fig 3 — Pre and post operative Plain abdominal radiograph and contrast enema of case 3

followed by ceco-colic end to end anastomosis was carried out (Fig.4A). The postoperative period was uneventful and the silastic tube was removed after 7 days which closed itself (Fig 4B). He is doing well at 6 years follow up.

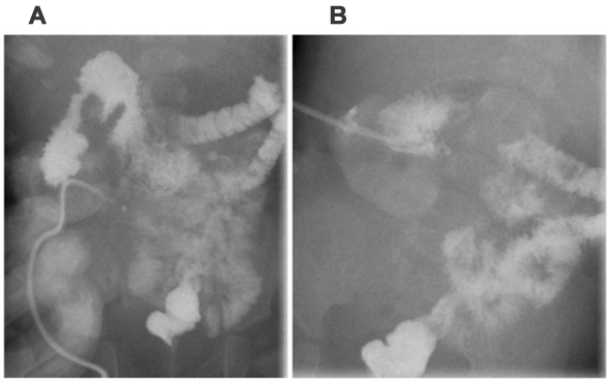


Fig 4 — Follow up postoperative prograde contrast via appendicostomy tube in Case 3

Case 4

Term baby, 38 weeks of gestational age was born with 2578-gram weight to a diabetic mother, who was positive for HIV for 18 years of age, currently with plasma viral levels undetectable.

On the 1st day of life, the baby presented with milky vomiting, has not passed meconium despite glycerin suppository with a normal size and site of the anus and per rectal examination did not reveal any gripping finger or gush of gas or fecal matter suggestive of Hirschsprung's disease. In a couple of hours, clinical deterioration and abdominal distension was noticed and the abdominal radiograph and a decubitus view suggested multiple air fluid levels and step ladder pattern suggestive of low intestinal obstruction (Fig 5 A and B). Repeat radiographs at 6 hours suggested increased distention and no gas in the distal colon or rectum with dilated proximal bowel loops and air fluid levels (Figs 5 C & D).

The baby was quite ill and resuscitated. Once stabilized, the baby was taken to operation theatre and an exploratory laparotomy with the diagnosis of low intestinal obstruction.

At the exploration, stomach, duodenum and jejunum were normal. A segment of terminal ileum starting at about 10 cm of the ileo-cecal valve, was hugely dilated, extending on to the caecum that also was very large and ending in a atretic segment as a blind pouch in the region of transition between caecum and right colon with normal appendix. The rest of the colon was not present except for the rectosigmoid stump in the pelvis supplied by superior rectal vessels (Fig 6, A-D). The middle colic vessels and the inferior mesenteric vessels were missing.

An Ileostomy was performed. The patient started to receive feeds on the 3rd day postoperative, increasing slightly which were all tolerated very nicely while stoma was functioning well. Baby was finally discharged home

after 14 days. The plan is to slow down the motility of proximal functioning gut using loperamide and increase micronutrient absorption and lengthen the bowel, rectal suction biopsy to exclude Hirschsprung's disease or other congenital motility disorders and volume expansion of the distal rectosigmoid stump to lengthen and widen and allow Anastomosis and gain extra colon surface for absorption of water and electrolytes thus reducing diarrhea after restoring the continuity with ileo-colic anastomosis at a later date.

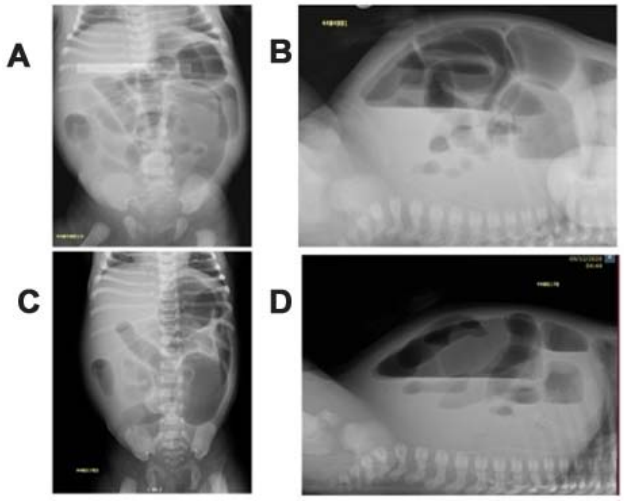


Fig 5 — Plain and decubitus view of abdominal radiographs after birth-Case 4

Case 5

Male term baby was born with 38 weeks of gestational age and had no pre-natal abnormalities on scans and no perinatal problems. Breast feeding was started but on the second day of life was brought to intensive care due to abdominal distension and bilious vomiting, The anus was at normal site and of normal size and no meconium found on the rectal examination. Babygram showed dilated stomach and bowel gas in the abdomen and no gas in the rectum or pelvis (Fig 7A).

The abdominal circumference increased rapidly over the next hours and a contrast enema showed microcolon and cut off sign at rectosigmoid junction with no meconium but small mucoid white plug came out suggestive of Colonic Atresia (Fig 7 B).

At laparotomy Global dilatation of the small intestines as well as the entire colon until the transition between the left colon and the sigmoid, where a type I atresia was present (Fig 7 C-F). A diverting loop stoma was performed proximally to the site of the atresia. Postoperative period was uneventful and a suction rectal biopsy to exclude associated Hirschsprung's disease followed by volume tissue expansion of the distal stump using saline is planned before closure of the stoma.

Discussion

We strongly believe in ileo-cecal valve, appendix and colonic preservation in atresia where associated short

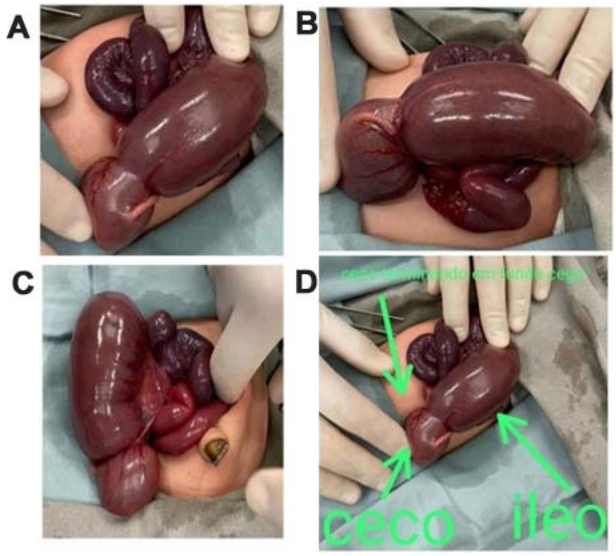


Fig 6 — Operative photographs, note blind ending cecum and dilated terminal ileum with absent colon and colorectal stump-Case 4

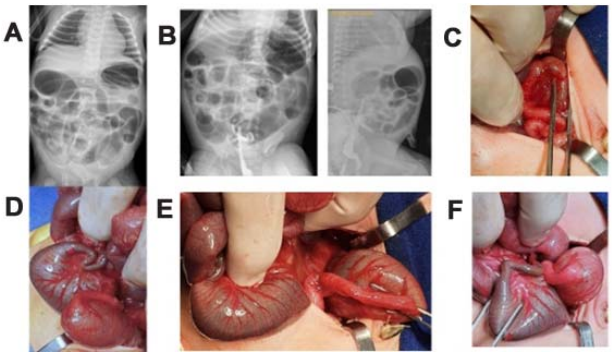


Fig 7 — radiological and operative findings in Case 5

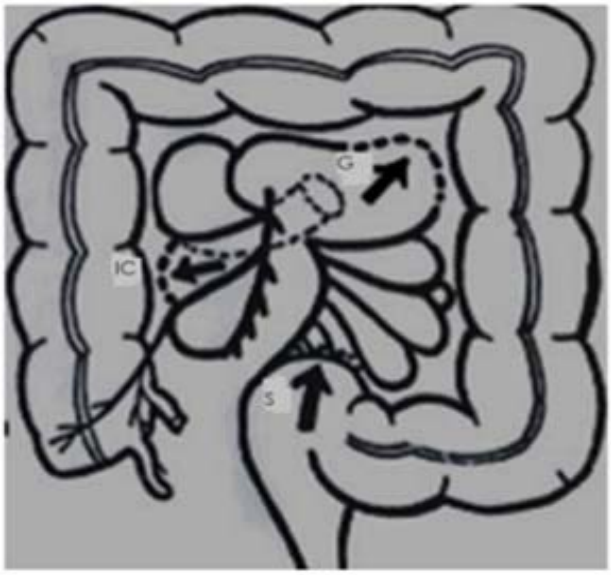


Fig 8 — Colonic blood supply with three weak points in the marginal arterial arcade

bowel and variable length of bowel may have been absorbed and missing, in advanced pediatric intussusceptions and adult population whenever feasible[12-15]. Rupture of intussuscepiens and dual transanal and transperitoneal prolapse of intussusception was first reported in 1982 as an unusual and rare complication[16]. These cases came mainly from north and west of India and an anecdotal case was reported from Europe and a plausible explanation that it is due to the prolonged and constant pressure of the intussusception in the antimesenteric part of the intussuscepiens, which is already stretched in a convex arch did not appear altogether satisfactory[16-19]. However, it was only later when we observed venous thrombosis of the intussuscepiens and marginal arterial arcade defects in a similar case in a West African infant presenting late, the vascular etiology of this phenomenon was very clear[19].

The most likely sites of Colonic Atresia would be where the Anastomosis of the marginal artery is least effective. The marginal artery does not link up certain vessels in a rare congenital anomaly of colonic blood supply as shown in figure 8, thus forming three weak points in the arcade[20]. If the artery supplying the area of the atresia has been affected beyond the neighboring branch at these sites, there is little chance of an effective collateral circulation being established[21-22]. It is very rare to involve multiple points in the marginal arterial arcade which happened in our fourth case as an extreme rarity. Colonic Atresia cannot be diagnosed prenatally, usually not suspected as very rare and pre-operative diagnosis requires contrast enema.

There is an association of Hirschsprung's disease or its variants in the colon distal to the site of atresia due to arrest of migration of craniocaudal migration of ganglion cells[23]. It is therefore, suggested that all cases of Colonic Atresia must be biopsied from distal part of the colon as well as rectum to rule out Hirschsprung's disease or its variants as an associated anomaly. Further detailed studies are required based on histology and immunohistochemistry of intestine to decide the level of resection of the proximal dilated colon and distal colon to achieve early bowel activity and reduce the morbidity[24].

We have previously reported modified classification of intestinal and biliary atresia-cystic malformations[25-27] and now we suggest a modified spectrum of atresia-stenosis-cystic malformation classification of these lesions and we believe that it is a continuation of the spectrum depending on the altered vascular supply of the segment (Table 1). We have made

Table 1 — Atresia-segmental dilatation-cystic malformation spectrum classification

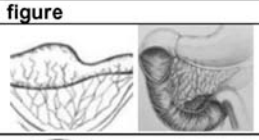
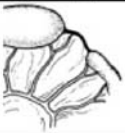
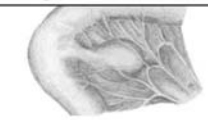
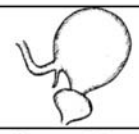
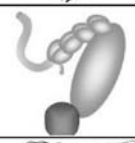
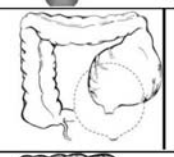
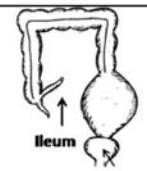
Type	Description	figure
Type 0	Stenosis/Web	
Type I	Atresia with a mucosal defect	
Type II	Fibrous cord connecting the atretic end	
Type IIIa	Atresia with a V-shaped mesenteric gap defect	
Type IIIb	Apple-peel deformity	
Type IV	Multiple atresia	
Diverticulum	Part of the wall protrusion with preservation of embryonic blood supply	
Fusiform dilatation /Segmental dilatation/stenosis	A segment of bowel having stenosis or dilatation as a result of altered blood supply	
Cystic malformation Type!	Normal colon absent, ileum enters the pouch	
Type II	Subtotal (except Caecum and part of ascending colon) colonic cystic dilatation	
Type III	Left colonic cystic dilatation	
Type IV	Localised Rectosigmoid colonic cyst	
Type V	Multiple Cystic dilatations with normal segment of colon interposed	

Table 2 — *Prognostic subclassification of atresia-segmental dilatation-cystic malformation spectrum*

Type	Lesion	Prognosis
A	Isolated	excellent
B	Multiple single system	good
C	Multisystem anomalies	poor
D	Syndromic/Genetic	worst

easy subclassification of these lesions based on prognosis of these lesions into subdivisions ranging from A to D (Table 2).

Conclusion

Left Transverse Colostomy in rectosigmoid atresia at Sudeck point is more convenient than the Right Transverse Colostomy as it reduces colostomy associated diarrhea and morbidity and mortality as compared to right sided Transverse Colostomy. Hydrodistension of the distal rectosigmoid stump is a very good tissue expansion technique which allows the distal colon to be of good caliber reducing disparity between proximal and distal segments and coco-colostomy at a later date will be easier[28]. Although our experience with coloplasty from dilated colon in pouch colon syndrome suggest that the tube coloplasty may not be long lasting but certainly it provides a temporary conduit and allows initial growth and development and it allowed preservation of appendix and ileocecal valve in our third case. In conclusion, we believe that even if prenatal diagnosis is not possible in Colonic Atresia, high index of suspicion and immediate plain radiograph and contrast enema allows prompt diagnosis by differentiating with other distal intestinal obstruction such as Hirschsprung's disease, meconium ileus, left colon syndrome, etc and appropriate management provides excellent prognosis.

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Case Report

Cervico-vaginal Aplasia : A Rare Anomaly with Review of Literature

Priya Sanjeev Potdukhe[1], Avinash Parshuram Dhok[2]

Cervico-vaginal anomalies are thought to be a rare condition in general Obstetrics and Gynaecology practice. Cervico-vaginal aplasia is notoriously difficult to diagnose. The ability to make an accurate diagnosis prior to surgery offer significant benefits to the patient. The utmost significant of that is proper pre-operative planning and preparation. The use of Magnetic Resonance Imaging (MRI) to diagnose Cervico-vaginal atresia is a novel modality in the medical literature and it provides the advantage of diagnosis non invasively prior to surgical intervention. Here, we are reporting a rare case of Cervico-vaginal atresia who clinically presented with primary amenorrhoea and cyclical lower abdominal pain.

[*J Indian Med Assoc* 2024; **122(2):** 61-2]

Key words **: Cervico-vaginal Aplasia, MRI.**

Uterovaginal anomalies are linked to a lower rate of fertility and a variety of obstetric complications. Cervico-vaginal agenesis is a common type of such anomaly. Cervico-vaginal agenesis is an exceptionally rare congenital anomaly occurring in about 1 in 80,000-100,000 births. It can be in isolated form or combined with partial or complete vaginal agenesis[1]. Only about 200 cases have been reported since 1900, according to a review of the literature[2]. Patients with cervical agenesis mainly present with complaints of primary amenorrhea and menstrual blood retention, which initiates the symptom of cyclic low abdominal pain without menstrual flow, prompting the patient to seek gynecological evaluation and care[3] MRI can be analysed in a systematic way to allow for prompt and appropriate treatment. Associated pelvic lesions or urogenital anomalies should also be reported if noted. MRI makes it possible to diagnose obstructive causes of uterovaginal anomalies in which determining the site of obstruction is important for planning the proper surgical approach[4]. Here we present a case of Cervico-vaginal aplasia . Our case was diagnosed using transabdominal ultrasound and confirmed on MRI.

Editor's Comment :

- Cervico-Vaginal aplasia is an exceptionally rare congenital anomaly with only 200 cases reported since 1900. It is linked to a high rate of infertility and obstetric complications. Magnetic Resonance Imaging is novel, non invasive, gold standard modality for diagnosis and pre-operative planning.

Case Report

A female aged 16-year-old presented with cyclical lower abdominal pain with primary amenorrhea. Her secondary sexual characters were normally developed. She had no associated genitourinary or digestive complaints and she did not give a history of any familial or hormonal disorder. On physical examination, labia majora and minora were well developed but no separate vaginal opening was noted, only vaginal dimpling was found. On per rectal examination, uterus was palpated and appeared normal in size. An ill defined cystic mass was palpated in the left adnexa however, the right adnexa was free. Her other lab investigations were normal.

Transabdominal ultrasound showed a small conical structure in the region of cervix, however no vaginal lumen was noted. Uterus showed presence of thick dense collection with multiple moving echoes in the endometrial cavity causing thinning of the myometrium in the lower uterine segment. Both the ovaries were normal in size with the left ovary showing presence of a hemorrhagic follicle within. Adnexa showed presence of cystically dilated fallopian tubes on left side with collection containing multiple moving echoes showing layering within. Moderate loculated fluid collection was noted in the adnexa. Both the kidneys were scanned and no renal anomalies were found.

MRI was done which showed a thin fibrous cord like structure in the region of cervix and vagina with no lumen within it. A collection, which was hyperintense on T1WI and hypointense on T2WI, showing levelling within was noted in the endometrium and in the fallopian tubes on left side suggestive of hematometra and hematosalpinx. However, right fallopian tube was normal. Moderate free fluid was present in both adnexa.

Hysterectomy was performed which confirmed the diagnosis of cervicovaginal aplasia with hematometra. Hematosalpinx was demonstrated on left side, however the right Fallopian tube was normal (Figs 1&2).

Discussion

Primary amenorrhea is caused by obstructive uterine

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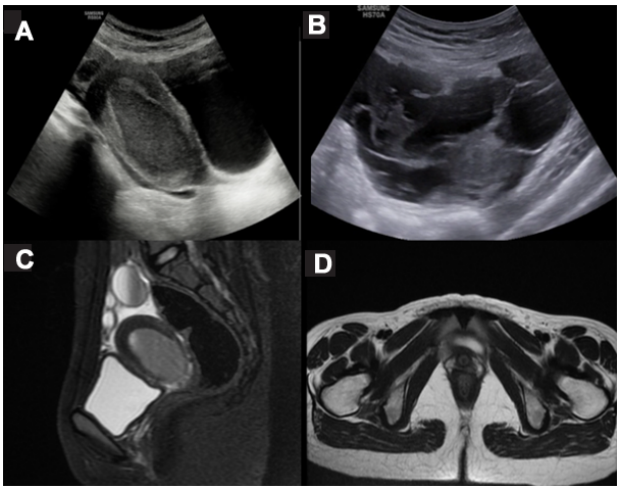

Fig 1 — Transabdominal Ultrasound (A, B) and MRI Pelvis (C, D) demonstrating Cervico-vaginal aplasia with hematocolpos

anomalies that obstruct normal menstrual flow. Any pain in the abdomen or pelvic region in a adolescent girl should raise the possibility of an obstructive cause of genital anomaly. Clinically, it can cause obstructive symptoms such as Hematometra, Hematocolpos and Cyclical lower abdominal pain[5].

The presenting symptom is usually primary amenorrhea which can be seen in a wide range of congenital uterine anomalies, including hypoplastic uterus and imperforate hymen. Ultrasonography is the preferred modality for defining internal genital anatomy and classifying the degree of obstruction or aplasia[6,7]. Despite its rarity, ultrasonography can easily detect the first signs of cervical aplasia or dysgenesis[8].

American Society of Reproductive Medicine, classified cervical aplasia as type Ib Mullerian anomaly[9]. Cervico-vaginal aplasia has been further been classified into various types which are as follows : (i) The cervical body is intact with obstruction at the level of the os of the cervix (ii) The cervical body is atrophic and replaced by a thin fibrous band (iii) Cervical Fragmentation (iv) The midportion of the cervix is hypoplastic with a bulbous tip[10]. Correlation of clinical findings with ultrasound and MRI has been helpful in proper diagnosis and management. So far, MRI has been considered as a gold standard for evaluating the vaginal and cervical anatomy[1].

There are different treatment possibilities available but patients with aplasia are typically unsuitable for canalization and total hysterectomy is the preferred management[11]. Consent of the patient was gained prior to the study and patient identity was not disclosed.

Conclusion

Congenital absence of Cervix and Vagina pose a diagnostic challenge. It is a intricate surgical obstacle that requires a thorough evaluation. Ultrasound evaluation with MRI as the gold standard modality, can diagnose this anomaly and provide pertinent details on cervical and vaginal anatomy. In primary amenorrhea, proper

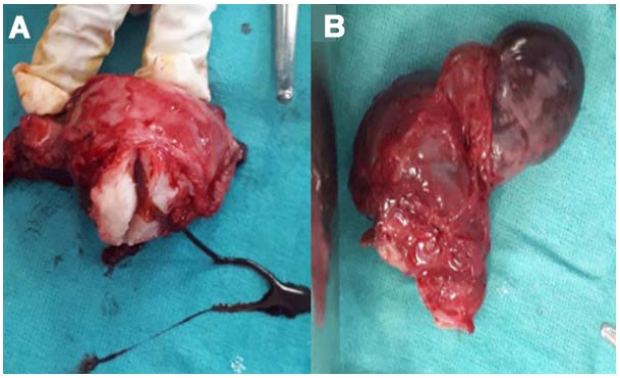

Fig 2 (A and B) — Postoperative image confirming our findings of cervicovaginal aplasia with hematosal

Cervico-vaginal examination is required and the likelihood of Cervical and Vaginal aplasia should always be thought about.

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Drug Corner

A Real-World Evidence Study on Effectiveness and Tolerability of Topical Lincomycin in the Treatment of Surgical Site Infection (SSI) and Skin & Soft Tissue Infection (SSTI)

Milind Ruke[1], Anish Desai[2], Sunaina Anand[3], Sreeni Nair[4]

Aim : The study evaluated the effectiveness and tolerability of topical lincomycin gel 2% in the treatment of Surgical Site Infection (SSI) and Skin & Soft Tissue Infection (SSTI)

Methodology : Patients above 18 years of age undergoing surgery with clinical diagnoses of impetigo, folliculitis, or SSTI were included in the study. Patients received topical lincomycin gel (2%) every 12 hours until the end of treatment. Primary endpoints were to assess signs and symptoms associated with SSI and SSTI, including reduction in severity, signs of infection at the surgical site, wound healing and post-operative pain. Secondary outcomes measured included incidence of adverse events such as allergic contact dermatitis, antibiotic resistance and anaphylaxis.

Result : The study included 165 patients, with 69 females and 96 males, having a mean age of 41 years. The findings of the study demonstrated significant reductions in the mean scores for all outcomes, indicating the efficacy of topical lincomyc in treatment in reducing the severity, signs of infection at surgical sites, wound healing, post-operative pain, erythema, purulence, crusting, oedema, redness, swelling, warmth, and pain.

Conclusion : Topical gel formulation (2%) of lincomycin was found to be effective in the treatment of both SSI and SSTI, with better tolerability.

[*J Indian Med Assoc* 2024; **122(2):** 63-6]

***Key words* : Surgical Site Infection, Skin & Soft Tissue Infection, Topical Lincomycin, Surgery, Emergency Department**

Surgical Site Infection (SSI) is one of the most common hospitals acquired infections and according to recent studies its incidence is estimated to be 2-11% for all surgical interventions. SSIs are associated with increased treatment costs; prolonged hospital stay and increased mortality. SSI leads to scar formation that can reduce the quality of life in patients, commonly in young women. SSIs can be divided in three categories : Superficial which develop within 30 days since surgery and involve skin and subcutaneous tissue; deep which develop after 30 days or within one year if a foreign body was implanted and involve fascia and muscles and organ or body cavity infection near the surgical site which develop within 30 days or one year if a foreign body was implanted[1].

SSIs account for around 20% of all Healthcare-Associated Infections (HAIs) and at least 5% of patients following a surgical treatment acquire a surgical site infection. The frequency of SSIs in patients following inpatient surgery is 2-5%; however, the number of SSIs is likely to be under estimated because around 50% of SSIs become apparent after discharge. Most common micro-organisms are responsible for surgical site infections are S aureus, coagulase negative staphylococci, Enterococcus species and *E coli*. Current pharmacological therapies include drugs like Vancomycin, Daptomycin, Fosfomycin, Linezolid, etc. The prevention of SSIs is becoming increasingly crucial as the number of surgical procedures increases[2].

SSTIs encompass a wide clinical spectrum of common infectious diseases that often require acute treatment and inpatient hospital admission. SSTI affects the epidermis, dermis, superficial fascia, subcutaneous tissues and muscle in an increasing order of severity. Complicated SSTIs (cSSTIs) are the most severe, involving deeper soft tissues and include infective cellulitis, ulcer or wound site infections, surgical site infections, major abscesses, infected burns, skin ulcers and diabetic foot ulcers. The US FDA in 2013 grouped all SSTIs under a unified term, Acute Bacterial Skin and Skin Structure Infection (ABSSSI), which includes cellulitis/erysipelas, wound infection and major cutaneous abscesses. It is defined as a bacterial infection of the skin with a lesion size

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area of at least 75 cm^2 (lesion size measured by the area of redness, oedema, or induration)[3].

Staphylococcus aureus, an aerobic Gram-positive coccus, is the most dominant causative pathogen and has prime epidemiological significance in cSSTI. Pseudomonas aeruginosa, Escherichia coli, and Enterococcus spp have also been identified as causes of cSSTI; however, these are not the pre-dominant causative pathogens[4].The usual oral antimicrobial choices for treatment of SSTI include either penicillin, cephalosporins, clindamycin, trimethoprim-sulfamethoxazole, doxycycline, or linezolid. The parenteral treatments include vancomycin, daptomycin, telavancin[3].

Lincomycin, a naturally sourced lincosamide antibiotic obtained from the actinomycete species, Streptomyces lincolnensis, is used to treat penicillin-allergic patients and drug-resistant bacterial infections of multiple[5]. Significant concentrations of antibiotic are attained in most tissues including bone and, though lincomycin hardly penetrates the normal blood brain barrier, there is some evidence that in the presence of meningeal infection, therapeutic levels can be achieved in CSF. Clinically, lincomycin has been shown to be effective in several bacterial infections including staphylococcal osteitis, septicaemia, respiratory infections, and infective. While some of these reports have included cases of penicillinresistant infections, experience in conditions specifically due to penicillinase-producing strains of Staphylococcus pyogenes is limited, as are reports of the use of lincomycin in young children[6]. Although approved for use in medicine, lincomycin is rarely used nowadays. Lincomycin has an in-vitro activity like that of erythromycin. It has the additional advantage that, unlike erythromycin, bacterial resistance to it develops slowly[7].

The aim of the current study was to assess the effectiveness and tolerability of topical lincomycin gel 2% for the treatment of SSI & SSTI.

Materials and Methods

Setting and Participants :

Patients above 18 years of age who were undergoing surgery and with the clinical diagnosis of impetigo, folliculitis, or minor soft tissue infection including secondarily infected eczema presumed to be caused by Staphylococcus aureus were included in the study. Pregnant and breast-feeding patients were excluded along with patients who were unable to understand the protocol. All patients were administered topical lincomycin gel 2% (manufactured by Wallace Pharmaceuticals), every 12 hours interval till the end of treatment.

Outcomes and Follow-up :

Primary endpoints included evaluation of signs and symptoms associated with SSI: reduction in severity, signs of infection at surgical site, wound healing, post-operative pain and with SSTI: erythema, purulence, crusting, oedema, redness, swelling, warmth and pain after application of Lincomycin topical gel 2%. They were assessed at the time of suture removal or 6 to 8 days after treatment. Incision and drainage after the end of planned course was also included as a primary endpoint. Secondary outcome measures included incidence of adverse events such as allergic contact dermatitis, antibiotic resistance and anaphylaxis (assessed during the antibacterial treatment), wound size at baseline & follow up and length of hospital stay.

Statistical Analysis :

A sample size of 165 was included in the study. The data was presented in mean and percentage form using descriptive statistics. To test for significance, the paired t-test and the Wilcoxon Sign Ranked Test were performed.

Results

The present study comprised of 165 patients, out of which 58.18% were males and 41.82% were females. Most of the patients (32.58%) received topical lincomycin2%for 4 days (Fig 1).

Effectiveness in Surgical Site Infections (SSI) :

The data showed that there was a complete reduction in mean scores of severities of surgical sites infection from 2.24. ($P<0.05$). Reduction in signs of infection at the surgical sites was also observed (2.11 to 0.04, $P<0.05$). Other parameters like wound healing and post-operative pain also decreased from 3.00and 2.15 to 0.38 and 0.04, respectively ($P<0.05$)(Fig 2).

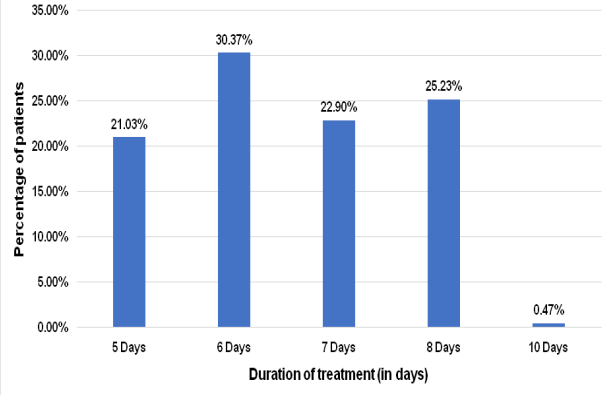

Fig 1 — Duration of treatment

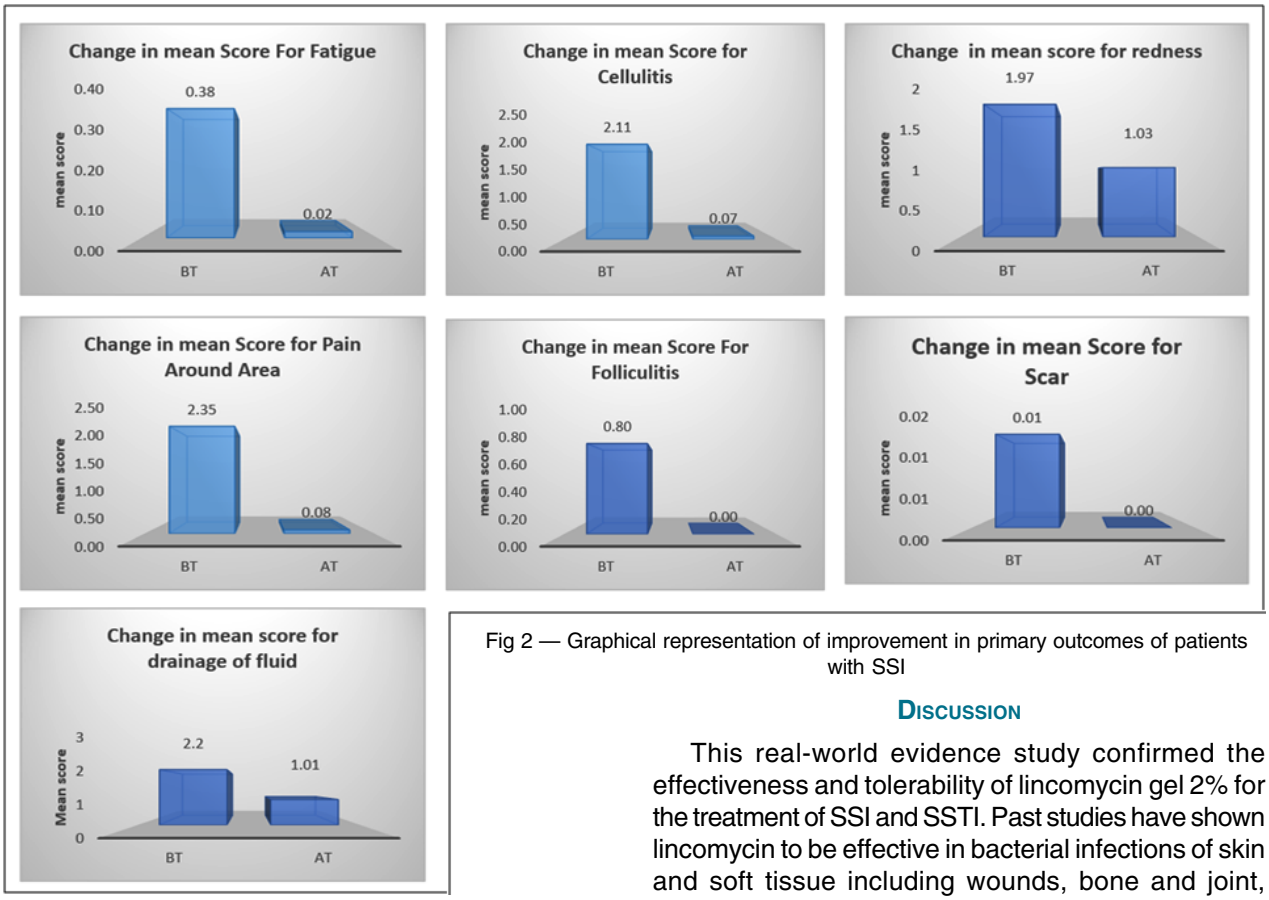

Fig 2 — Graphical representation of improvement in primary outcomes of patients with SSI

Effectiveness in Skin and Soft Tissue Infections (SSTI) :

Topical treatment with lincomycin reduced the mean symptom scores of erythema, purulence and crusting from 2.51, 2.95 and 2.95 to 0.09, 0.13and 0.09, respectively (P<0.05). Edema, redness, swelling and warmth at infection sites also showed reduction in mean scores from 1.98, 2.27, 2.04and 2.00to 0.05,0.82,0.07 and 0.14, respectively (P<0.05). Complete reduction in mean score of incision and drainage was also observed at the end of treatment. (P<0.05).

Thus, there was asignificant reduction in the mean scores of all outcomes such as severity, signs of infection at surgical site, wound healing, post-operative pain, erythema, purulence, crusting, oedema, redness, swelling, warmth and pain, indicating topical lincomycin's effectiveness (Fig 3).

Tolerability :

Topical Lincomycin treatment was well tolerated by the patients. Patients did not report any adverse reactions like allergic contact dermatitis and anaphylactic reactions. No other major adverse reactions were reported.

Discussion

This real-world evidence study confirmed the effectiveness and tolerability of lincomycin gel 2% for the treatment of SSI and SSTI. Past studies have shown lincomycin to be effective in bacterial infections of skin and soft tissue including wounds, bone and joint, respiratory system, dental infections and against penicillinase producing and erythromycin resistant strains.It acts by inhibiting protein synthesis in susceptible bacteria by binding to the 50 S subunits of bacterial ribosomes and preventing formation of the peptide bond during transcription[8].

Topically applied lincomycin has strong tissue penetration and exhibits potent activity against P. acnes with a Minimum Inhibitory Concentration (MIC) ranging from <0.1 to 1.6 mcg/ml. Its mechanism of action involves eliminating the production of free fatty acids and other local irritating enzymes produced by P acnes bacteria. Additionally, lincomycin may possess immunomodulating properties, which contribute to reducing inflammation[9].

Topical lincomycin is indicated in bacterial skin infections as a 2% gel formulation. This is the first real world evidence study for lincomycin gel in the treatment of SSI and SSTI. In the past, a multicentric, randomized, double-blind, placebo-controlled clinical trial was conducted in 200 patients with grade II and grade III acne vulgaris[9]. The patients were treated with either lincomycin hydrochloride 2% gel or a placebo for 4 weeks. Good to excellent response was seen in 70% of the patients compared to 23% in placebo group.

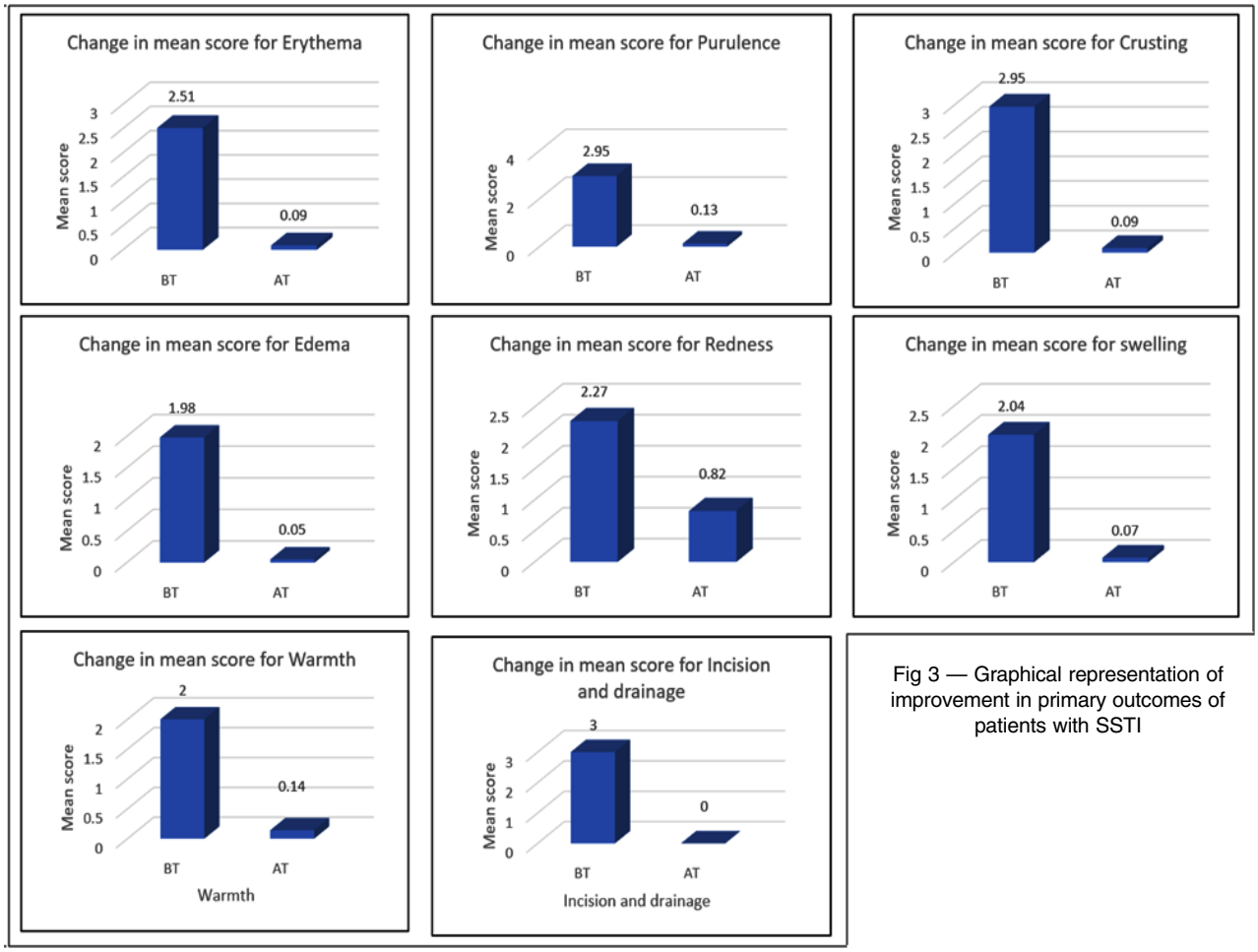

Fig 3 — Graphical representation of improvement in primary outcomes of patients with SSTI

Conclusion

The substantial decrease in the mean scores of erythema, purulence, crusting, edema, redness, swelling, warmth and pain shows the notable efficacy of topical lincomycin. This real-world study establishes that the application of a 2% lincomycin gel formulation is highly effective in management of both SSI and SSTI, while also demonstrated enhanced tolerability.

Declaration : Article is not published / submitted in any other journal.

Acknowledgments : The authors thank all the study investigators, study coordinators and other study personnel who participated in the study, for their contributions.

Conflict of Interest : No

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Letters to the Editor

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

Uncontrolled and Resistant Hypertension : A major challenges for Clinicians

Sir, — I am writing to express my appreciation for the recent publication of the Resistance Hypertension Study in your esteemed journal, JIMA cited as Bhuvaneswari K, Jegatheeswari Murugesan, Mohamed Musthafa S, Aathira S. Drug Utilization in Resistant Hypertension. *J Indian Med Assoc* 2023; **121(12):** 21-3[1]. This is good efforts not only contributed to our understanding of resistant hypertension but also holds potential implications for public health.

Resistant hypertension is a common clinical problem faced by both primary care clinicians and specialists. The exact prevalence of resistant hypertension is unknown. In various studies its prevalence has been reported to be 20% to 30% of study participants. The diagnosis of Resistant Hypertension (RHT) requires use of good blood pressure measurement technique to confirm persistently elevated blood pressure levels. Patients with RHT typically have higher prevalence of target organ damage and worse cardiovascular prognosis than those with non RHT.

Study conducted by us and published in JAPI revel that approximately 19.51% HT patients were on ≥3 anti-hypertensive medications and received ARB + CCB + Diuretics. Diabetes and dyslipidaemia were the major comorbidities reported in patients with uncontrolled and resistant hypertension[2].

The prevalence mentioned by author in this is quite low ie, 3.45%. the reason could be study was conducted at one particular location[1]. The combination used predominantly was ACE inhibitor with a Diuretic and Beta blocker. Co-morbidity observed were coronary artery disease (64%), Diabetes (57%), Dyslipidemia (22%), CKD (23%), Hypothyroidism (10%)[1].

I our study finding are similar, but most of resistant hypertensive patients were on ≥3 antihypertensive medications and received ARB + CCB + Diuretics as the most preferred anti-hypertensive combination therapy. Diabetes and dyslipidaemia were the major comorbidities reported in patients with uncontrolled and resistant hypertension[2].

As per WHO, 1.28 billion adults aged 30-79 years worldwide have hypertension, two-thirds living in low- and middle-income countries. 46% of adults with hypertension are unaware that they have hypertension. Less than half of adults with hypertension are diagnosed and treated**. Approximately 1 in 5 adults (21%) with hypertension have it under control.** Hypertension is a major cause of premature death worldwide. One of the global targets for noncommunicable diseases is to reduce the prevalence of hypertension by 33% between 2010 and 2030[3].

Various guidelines like NICE, ESC, WHO, ESH, JNC, JSG Indian guidelines are available, wanted to highlight WHO 2021 guidelines which are simpler and easy to follow.

The 2021 WHO hypertension guideline provided the most current and relevant evidence-based global public health guidance on the initiation of treatment for hypertension in adults[4].

The guideline makes eight recommendations[4] :

BP threshold for starting drug treatment	Those with diagnosis of HTN and BP of ≥140/≥90 mmHg Those with CVD and SBP ≥130 139 mmHg	Recommendation: strong Evidence: moderate–high certainty
	Those without CVD but with high CVD risk, diabetes, CKD and SBP ≥130 139 mmHg	Recommendation: conditional Evidence: moderate–high certainty
Whether screening and assessment are needed before treatment is started	Obtain tests to screen for comorbidities and conduct CV risk assessment but only if it doesn't t delay treatment	Recommendation: conditional Evidence: low certainty
Which drug(s) to prescribe	Any of these drug classes diuretics/ACEi /ARB/CCBs	Recommendation: strong Evidence: high certainty
Combination therapy	To improve adherence and persistence combination therapy recommended. preferably in a single pill	Recommendation: conditional Evidence: moderate certainty
BP target for control of HTN	140/90 mmHg in those without comorbidities SBP 130 mmHg in those with CVD	Recommendation: strong Evidence: moderate certainty
	SBP 130 mmHg in those with high CVD risk, diabetes and CKD	Recommendation: conditional Evidence: moderate certainty
Follow up intervals	Monthly follow up until patient reaches target BP.	Recommendation: conditional Evidence: low certainty

Causes of resistant hypertension specially in Indian patients are poor adherence to antihypertensive therapy, irregular patient follow-up, lack of patient counselling, suboptimal antihypertensive therapy including inappropriate selection of anti-hypertensive combinations as well as clinician inertia, a failure to change or increase dose regimens in order to obtain adequate treatment of poorly controlled hypertension despite awareness of the condition, Poor adherence to lifestyle and dietary approaches such as a reduced sodium intake, long term consumption of certain medications such as steroids, NSAIDs etc.

Role of Ambulatory Blood Pressure Monitoring (ABPM) in Resistance hypertension.

Ambulatory Blood Pressure Monitoring (ABPM) can be used in certain cases as ABPM provides a more comprehensive and accurate assessment of blood pressure throughout the day and night, capturing variations that may be missed during clinic measurements. This helps in obtaining a more reliable picture of blood pressure control. It also helps to differentiate between true resistant hypertension and "white coat hypertension". ABPM allows healthcare providers to assess the effectiveness of prescribed medications and make adjustments as needed. This is

particularly important in resistant hypertension cases where finding the right combination of drugs can be challenging. Resistant hypertension often involves elevated blood pressure during the night. ABPM helps identify nocturnal hypertension, which is associated with an increased risk of cardiovascular events. In summary, Ambulatory Blood Pressure Monitoring is a valuable tool in the management of resistant hypertension. It assists healthcare providers in making accurate diagnoses, tailoring treatments and monitoring the effectiveness of interventions, ultimately improving patient outcomes.

How to achieve better BP goals in difficult to treat hypertension.

Resistant hypertension is always multifactorial in etiology. Lifestyle changes, including weight loss; regular exercise; ingestion of a high-fiber, low-fat, low-salt diet should be encouraged. weight loss should be promoted in any patient with resistant hypertension who is either obese oroverweight. The advantage of dietary salt reduction is well demonstrated in hypertensive patients with approximate reductions in systolic and diastolic blood pressure of 5 to 10 and 2 to 6 mm Hg, respectively. Ingestion of a diet rich in green leafy vegetables fruits and; low-fat dairy products, potassium, magnesium, and calcium; and low saturated fats reduced systolic and diastolic blood pressure by approximately 11.4 and 5.5 mm Hg[5].

Initiate with Combination therapy: Initiation with FDC of preferred anti-hypertensive medications, this will help to achieve BP goal faster, overcome therapeutic inertia, reduces pill burden, also to great extend reduces BP variability. Right selection of anti-hypertensive medications from different class can be considered. Adding mineralocorticoid receptor antagonists provide significant antihypertensive benefit to existing multidrug anti-hypertensive treatment regimens.

The protective measures to be taken to control hypertension includes reduction of physician's inertia, diet and physical activity, regular patient follow-up with BP measurements and counselling, and the improvement in patient adherence.

Efforts to address resistant hypertension in India should focus on comprehensive lifestyle interventions, improved healthcare infrastructure, and increased awareness about the importance of blood pressure control.

It is crucial to emphasize the societal impact of such research, considering the increasing prevalence of hypertension globally. The Resistance Hypertension Study has the potential to guide medical practitioners in optimizing treatment strategies and improving patient outcomes. Additionally, it lays a foundation for future investigations and advancements in the management of hypertension.

I believe that featuring this study in your journal contributes significantly to the dissemination of knowledge in the medical community. The clarity of presentation and the thorough discussion of results make the study accessible to a wide readership, including healthcare professionals, educators, and policymakers.

In Conclusion, I would like to express my gratitude for the valuable contribution of the Resistance Hypertension Study to the scientific literature. By highlighting its importance, I hope to further encourage the exploration of innovative approaches to address the challenges posed by resistance hypertension.

Thank you for your commitment to advancing medical knowledge, and I look forward to reading more scientific studies in your esteemed journal.

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Simplifying Day-to-Day Practice with AI

Sir, — Artificial Intelligence (AI) has emerged as a transformative force in healthcare and medical education. In healthcare, integration of rule-based expert systems and machine learning through AI enhances clinical decision-making, minimising errors and optimising safety[1]. Open Evidence and Google MedPaLm are generative AI specialised in aligning Large Language Models (LLMs) with the medical domain. LLMs are trained on extensive data, including books, articles, and codes, enabling them to comprehend and generate human-like text. Open Evidence scored 90% on the US Medical Licensing Exam, showcasing its exceptional expertise[2]. The impact of AI extends to patient and clinician interaction through resources like the ADA Health app, a telemedicine chatbotthat helps patients identify symptoms to make informed decisions about seeking the right medical care. Increasing integration of big data and AI in professional practice seeks a reboot of medical education and curriculum shift[3]. Immersive learning tools like Virtual Reality and Augmented Reality, exemplified by simX in anatomy dissection halls, contribute significantly to this educational transformation, providing students with interactive experiences beyond conventional methods. AI has emerged as a boon to simplify the administrative aspects of healthcare. Automation tools such as Calendly, Time-tap, and 10-8 can be used to streamline out patient

tasks, thereby allowing practitioners to focus more on patient care.

Advanced AI in healthcare and medical education leads to holistic progress in the field. These cutting-edge developments improve medical outcomes and equip future medical professionals with the skills to navigate modern healthcare.

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Rifampicin induced Thrombocytopenia : a rare complication

Sir, — Thrombocytopenia is a condition of decreased platelet count less than 1,50,000/mm^3. It can be due to decreased platelet production from bone marrow, sequestration and increased platelet destruction. The decrease in platelet numbers can lead to variety of conditions and risks ranging from mild epistaxis to life threatening bleeding like hematuria and bleeding per rectum. Drug induced Thrombocytopenia is a life-threatening, under-recognised condition, and is often a diagnostic challenge.[1] Rifampicin induced thrombocytopenia was first reported in 1970[2]. The drug classes that are most often associated with drug-induced immune thrombocytopenia are cinchona alkaloid derivatives (quinine, quinidine), sulphonamides, NSAIDs, anticonvulsants, disease modifying antirheumatic drugs and diuretics[3].

We report a case of a 72-year-old female who presented to another hospital with an on & off history of fever for 15-20 days, headache & vomiting for 3 days. On clinical examination, neck rigidity was present and Kernig's sign was positive. CSF examination was done and it showed 200 cells (90% lymphocytes & 10% neutrophils). The glucose was 21 mg/dl, protein was 147 mg/dl. ADA was positive. Serum electrolytes showed hyponatremia (Na^+ :120 meq/L). At that time the platelet count was 2,53,000/mm^3. Other electrolyte values, RFT, LFT were found within normal limits. The diagnosis of Tubercular meningitis was made and the patient was started on anti-tubercular therapy category 1. After around 3 weeks of ATT, the patient developed Hematuria and generalized body purpura. Followed by which patient presented to our hospital.

The patient was admitted, urgent complete blood count was sent, and it showed platelet counts of 5000/mm^3. Urgent 4 units of random donor platelets were arranged and transfused. On repeat complete blood counts the platelet count was found 71000/mm^3. But next day the platelet count dropped to 4000/mm^3. Again 4 units of RDPs were transfused, platelet count reached to 56000/mm^3. Again, the next day it dropped to 7000/mm^3. Then ATT induced thrombocytopenia was suspected. ATT was stopped, 1unit of SDP was transfused, within 3 days the platelet count of the patient increased to 278000/mm^3. ATT was stopped for 7 days and reintroduced again one by one. First ethambutol 800 mg/day was added for 5 days, CBC was done after 5 days it showed platelet count 441000/mm^3, the ethambutol was continued. Then pyrazinamide 1250 mg/day was added, and after 5 days CBC was repeated, it showed platelet count of 478000/mm^3. There was no decrease in platelet counts after adding two drugs, so they were continued. Third drug isoniazid 300 mg/day was added after 10 days and again after 5 days CBC was repeated and it showed platelet count of 453000/mm^3. All the three drugs were continued. Rifampicin was added after 15 days, for 3 days, CBC was repeated and it showed platelet count of 80000/mm^3 (thrombocytopenia). Rifampicin was stopped immediately. It was removed from the regimen and the patient was treated with ethambutol, isoniazid, pyrazinamide, streptomycin and steroids. Platelet count became normal during the follow up. No further clinical or laboratory abnormalities were found during the follow up.

Conclusion : Our case highlights this rare occurrence of rifampicin induced acute thrombocytopenia. Rifampicin is an essential component of the anti-tubercular regimens generally well tolerated. But on rare occasions it can cause such life-threatening adverse reactions like thrombocytopenia. Therefore, the possibility of such adverse reactions should be kept in mind during anti tubercular therapy.

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