



Volume 63 (RNI) ♦ Number 12 ♦ December 2019 ♦ Kolkata

JOURNAL & COMPAN MEDICAL ASSOCIATION Official Publication of the Indian Medical Association

Indexed in



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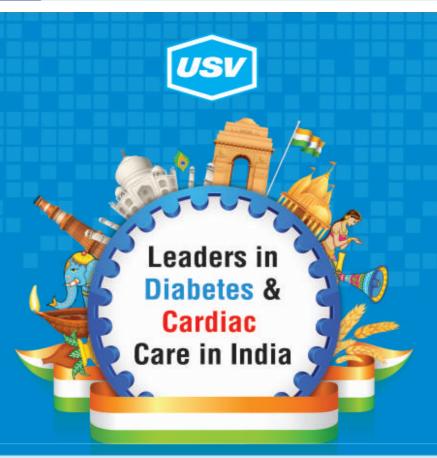
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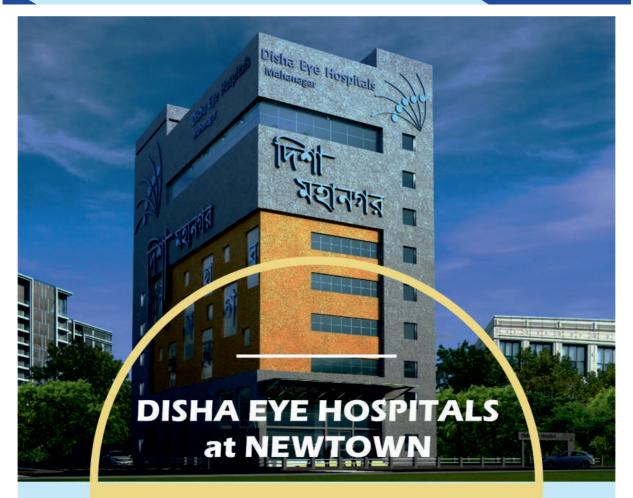
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JOURNAL of the INDIAN MEDICAL ASSOCIATION

Volume 117 (JIMA) • Number 12 • December 2019 • Kolkata

ISSN 0019-5847

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Editorial

Vertigo

Vertigo is a symptom, rather than a condition itself. It is a sensation that a person or the environment around a person is moving or spinning.

This feeling may barely benoticeable or it may be so severe that a person finds it difficult to keep his balance while doingeveryday tasks. The attack of vertigo can develop suddenly and last for few seconds, or they may last much longer. In case of severe vertigo the symptoms may be constant and lasts for several days, making normal life difficult.



Dr Golokbihari Maji MS (Ortho) Hony Editor, Journal of IMA (JIMA)

Other symptoms associated with vertigo may include —

- Loss of balance which can make it difficult to stand and walk.
- Feeling sick or being sick
- Dizziness.

Causes of Vertigo:

Vertigo is commonly caused by a problem with the way balance works in the inner ear, although it can also be caused by problems in certain parts of the brain.

- Benign paroxysmal postural vertigo-where certain head movements trigger vertigo.
- Migraines severe headaches.
- · Labyrinthitis an inner ear infection.
- Vestibular neuromas inflammation of the vestibular nerve, which runs into the inner ear and sends massages to the brain that help to control balance.
 - Meniere's disease here some people have repeatedepisodes for many months or even years.

Symptoms of Vertigo:

Vertigo is often triggered by a change in the position of head. People with vertigo typically describe it as feeling like

- Spinning
- Tilting
- Swaying
- Unbalanced
- · Pulled in one direction

Other Symptoms That May Accompany Vertigo Include:

- Feeling nauseated
- Vomiting
- Abnormal or jerking eye movements (Nystagmus)
- Headache
- Sweating
- Ringing in the ears or hearing loss

Ear Related Causes: -

BPPV ie, Benign Paroxysmal Postural Vertigo:

It occurs when tiny calcium particle (canaliths) clump in the canals of the inner ear. The inner car sends signals to the brain about head and body movements relative to gravity that help to keep one body balance. BPPV can occur for no reason and may be associated with age.

Meniere's Disease:

This is an inner ear disorder thought to be caused by a buildup of fluid and changing pressure in the ear. It can cause episodes of vertigo along with ringing in the ears (tinnitus) and hearing loss.

Vestibular Neuritis or Labyrinthitis:

This is an inner ear problem usually related to infection (usually viral). The infection causes inflammation in the inner ear around nerves that are important for helping the body sense balance.



Other Causes of Vertigo:

Vertigo may arise from the damage to central nervous system (CNS) often from a lesion in the brainstem or cerebellum. Then it is called as central vertigo. These are:—

- · Infraction In The Brain
- Haemorrhage In Brain
- Tumor In The Cerebello-pontine Angle Such As Vestibular Schwannoma
 - Epilepsy
 - · Cervical Spondylosis
 - Migraine Headache
 - Lateral Medullary Syndrome
 - · Chiari Malformation
 - Multiple Sclerosis
 - Parkinsonism.

Central vertigo may not improve or may do so more slowly than vertigo caused by peripheral structure like inner ear problem.

Vertigo in Orthopaedics: -

Cervical spondylosis (advanced neck bone arthritis) may be another potential cause of neck related dizziness. This condition causes the vertebra and disc to wear and tear over time. When this system works improperly, receptors cannot communicate to the brain and causes dizziness and other sensory dysfunction. Poor neck posture neck disorders and/ or trauma to cervical spine cause this condition.

There are several potential causes of cervical vertigo, though this condition is still being researched. Blockage of arteries in the neck from hardening (atherosclerosis) or tearing of these arteries (dissection) may cause vertigo, by disruption of blood flow to the inner ear or to lower brain region called the brainstem. Arthritis, surgery, and trauma to the neck can also block blood flow to these important region, resulting in vertigo.

Cervical spondylosis may be another potential cause of neck related dizziness. In this condition there is degeneration of neck vertebra and discs due to constant wear & tear. The degenerated structures put pressure on the spinal cord and spinal nerves and block flow to the brain and internal ear. A slipped disc alone without any spondylosis can do the same.

The muscles and joints in the neck have receptors that send signals about head movement and orientation to the brain and vestibular apparatus in the inner ear responsible for balance. This system also works with a larger network in the body to maintain balance and muscle coordination. When the system works improperly, receptors can't communicate to the brain, causing dizziness and other sensory dysfunction.

Dizziness from cervical vertigo can last minutes or hours. If neck pain decreases, the dizziness also begin to subside. Symptoms may worsen after exercise, rapid movements and sometimes sneezing.

Treatment for vertigo: -

Treatment for vertigo depends on what's causing it. In many cases vertigo goes away without any treatment. This is because the brain is able to adapt, at least in part, to the inner ear changes, relying on other mechanisms to maintain balance.

For some treatment is needed and may include:

(1) Vestibular Rehabilitation:

This is a type of physical therapy aimed of helping strengthen the vestibular system. The function of vestibular system is to send signals to the brain about the head and body movements relative to gravity. Vestibular rehabilitation is recommended when there is repeated bout of vertigo.

(2) Canalith Repositioning Maneuvers:

Guidelines from the American Academy of Neurology recommend a series of specific head and body movements for BPPV. The movements are done to move the calcium deposits out of the canal in the internal can chamber, so they can be absorbed by the body. A doctor or physical therapist will guide and these movements are effective and safe.

- (3) Medicines: In some cases, medication may be given to relieve symptoms such asnausea and motion sickness associated with vertigo.
- (4) If the vertigo is caused by an infection or inflammation, antibiotics and / or steroids may reduce the swelling and cure infection.
- (5) For Meniere's disease, diuretics may be prescribed to reduce pressure from fluid buildup.
- (6) Surgery: In a very few cases surgery may be needed for vertigo.
- (7) If vertigo in caused by more serious underlying problems, such as tumour, injury to brain or neck, treatment for those problems may alleviate the vertigo.

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— Hony Editor



Prevalence of Tuberculosis and its drug resistant strains in the Eastern region of Bihar

D P Singh¹, S K Ghosh², Pratik Kumar³

One third of the world's population is harboring bacilli causing Tuberculosis (TB). The severity of TB has increased several times with the emergence of anti-TB drug resistance detected for almost all key anti-TB drugs. Effectual patient management requires early diagnosis of TB cases and their screening for drug resistant TB followed by supervised treatment with specific drug regimen. The present study shows the prevalence of Multi Drug Resistant (MDR)/Rifampicin Resistant TB (RR-TB), Pre-extensively Drug Resistant (Pre-XDR) and Extensively Drug Resistance TB (XDR TB) cases in the eastern region of Bihar and its comparison with other regions of the State. The study shows the higher percentage of drug resistance for some of the key anti-TB drugs in Bihar as compared with the data of National Drug Resistant TB survey of India and some recent Global TB reports. The fluoroquinolone resistance in the present study was found to 50.80 % RR-TB cases, while it was found to be only 24.14% in NDR Survey. The higher fluoroquinolones resistance in Bihar may be attributed to the widespread use of quinolones in other infections.

[J Indian Med Assoc 2019; 117(12): 10-2 & 21]

Key words: Tuberculosis (TB), Multi-drug resistant (MDR) TB, Rifampicin resistant (RR) TB, Extensively drug resistant (XDR) TB, Pre-XDR TB.

Tuberculosis (TB) is a disease caused by the infection of a group of mycobacterial species called as *Mycobacterium tuberculosis* Complex (MTBC)¹. The bacilli carry the competency to infect any part of the human body but mostly it is a pulmonary pathogen². TB is the leading cause of death from a single infectious agent³. One third of the world's population is infected with mycobacterium tuberculosis⁴:

Studies revealed that more than 40% of the Indian population is harboring TB bacilli⁵. India carries 30% of the global TB burden⁶ and more than 1400 Indians are dying every day because of TB⁷. The severity of TB has increased several times with the emergence of anti-TB drug resistance. Resistance has developed in almost all key anti-TB drugs. Effectual patient management requires early diagnosis of TB cases and their screening for drug resistant TB followed by supervised treatment with specific drug regimen⁸. The first line anti-TB drugs are Rifampicin, Isoniazid, Pyrazinamide and Ethambutol⁸. The supervised treatment is provided with first line anti-TB drugs for

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MSc, Bio Tech, Microbiologist, C & DST Lab, Department of Microbiology, JLN Medical College, Bhagalpur diagnosed susceptible TB cases under DOTS strategy for at least six months duration. The treatment is divided in two phases- the intensive phase of two months where Rifampicin, Isoniazid, Pyrazinamide and Ethambutol were used followed by the continuation phase of four months with Rifampicin, Isoniazid and Ethambutol⁹. Multi Drug Resistant (MDR) TB is a form where the TB bacilli get resistance with at least Rifampicin and Isoniazid¹⁰. These MDR TB bacilli when get additional resistance with any fluoroquinolones and one of the three second line injectable drugs (Capreomycin, Kanamycin and Amikacin) are called as an extensively drug resistant (XDR) TB¹¹.

After the implementation of universal Drug Sensitivity Test (DST) in India, at least Rifampicin DST is done for all notified cases 12. All the Rifampicin resistant TB cases are further evaluated for second line drug resistance and based on the results of second line DST, patients are subjected to appropriate treatment. The estimated global MDR/RR TB burden was 4.1 % for new cases and 19 % for previously treated cases for the year 20163. A new case is defined as patient who had never been treated before with anti-TB drugs or treated with anti-TB drugs for less than one month but if a patient has a history of more than a month of TB treatment, it will be considered as previously treated case 13. WHO estimated that for MDR TB, around 21% cases have strains with additional resistance with fluoroquinolones (including Levofloxacin, Ofloxacin and Moxifloxacin) and 9.5% cases of XDR TB14.

In the present study, the prevalence of MDR/RR-TB, pre-XDR and XDR TB cases has been estimated in the eastern region of Bihar.

METHODS AND MATERIALS

The Tuberculosis Culture and DST laboratory functioning in the premise of Jawaharlal Nehru Medical College and Hospital, Bhagalpur is one of the quality assured TB containment laboratories in Bihar. This TB culture and DST laboratory is certified by Central TB Division, New Delhi for various molecular and culture based drug susceptibility testing methods. The laboratory is receiving samples from ten districts of Bihar, namely -Araria, Banka, Begusarai, Bhagalpur, Jamui, Katihar, Khagaria, Kishanganj, Munger and Purnia. Culture based DST has been done by MGIT (Mycobacterium Growth Indicator Tube) 960 system. CBNAAT (Cartridge Based Nucleic Acid Amplification Test) and LPA (Line Probe Assay) technique has been used for molecular DST. Following laboratory testings were included in this study.

- (1) First line culture based DST of 100 new TB cases were performed.
- (2) CBNAAT was performed on samples from presumptive TB and presumptive DR-TB cases.
- (3) Samples of MDR/RR TB diagnosed patients were subjected to second line LPA.

Culture Based Drug Susceptibility Testing:

Molecular diagnostics promise the rapid and accurate diagnosis of TB but culture is still considered as the gold standard. Liquid media offers three dimensional growth of cells and hence retrieval is faster15. MGIT 960 instrument has been used for the study. 137 samples were processed by NALC-NaOH method and inoculated in the MGIT tube to get 100 pure M.tuberculosis culture. First line drug susceptibility testing kit of BD includes four drugs, ie, Streptomycin, Isoniazid, Rifampicin and Ethambutol, DST was performed for all the 100 culture samples as per the user's instructions.

CBNAA7 :

The Xpert MTB/RIF is the name of machine performing CBNAAT manufactured by Cepheid Inc, Sunnyvale, California, USA. This technology performs nested real time PCR based qualitative detection of Mycobacterium tuberculosis complex (MTBC) and its susceptibility with rifampicin. WHO has conditionally recommended the use of Xpert MTB/Rif as the first-line diagnostic test for presumptive TB cases16. Xpert MTB/Rif has achieved an overall sensitivity of 88% and specificity of 99% 17. This technology can be used in much lower facilities as compared with facilities TB culture technique requires. Also, the machine can provide results within 2 hours from the start of the test. Both these properties promise the effective utilization of CBNAAT for rapid diagnosis of Rifampicin resistant TB.

Both the pulmonary and extra pulmonary samples can be tested by CBNAAT. 2-4 ml of samples are ideally required for testing. Double the volume of sample, reagent was added carefully for most of the sample type. Intermittent shaking with reaction time of 15 minutes is required. The processed samples were then added to the CBNAAT cartridges and tested in the machine as per the protocol18. Sample Processing Control (SPC) was present to ensure adequate processing of target bacilli and monitors the PCR step.

Line Probe Assay (LPA):

LPA is a type of molecular DST that detects the mutation associated with drug resistance. The kits are being manufactures by HAIN life sciences, Gmbh, Hardwiesenstr, Nehren, Germany. LPA for rifampicin and isoniazid has been used from the introduction of Programmatic management of drug resistant TB in India19. The introduction of LPA has reduced the turnaround time of DR-TB diagnosis from months to days. Recently, WHO has recommended the use of second line LPA for detection of resistance in fluoroquinolones and second line injectable drugs²⁰.

Samples were processed by NALC-NaOH method. DNA extraction, PCR and reverse hybridization was carried out as per the manufacturer's instructions²¹.

RESULTS

Culture DS7 (First line):

Out of 100 first-line liquid culture based DST performed, 92 cases were susceptible with all four drugs (SIRE). However, 03 cases were resistant with all four drugs. 02 cases were resistant with both Rifampicin and Isoniazid but susceptible with Streptomycin and Ethambutol. 01 case of Isoniazid mono- resistance and 02 cases of Rifampicin mono-resistance were detected.

Molecular DS7 (First line):

A total of 2974 CBNAAT tests have done during the year 2017 and 2018. Out of these, number of M tuberculosis detected and M. tuberculosis not detected were 599 and 2334 respectively. Out of 599 M tuberculosis cases, Rifampicin resistance was detected in 110 cases and Rifampicin resistance have not detected in 449 cases. 41 tests have given nonconfirmatory results like invalid, error, etc.

Molecular DS7 (Second line):

A total of 472 second line LPA of rifampicin resistant TB cases were done. Out of 472 tests, 183 cases were susceptible to both fluoroquinolones and second line injectables. However, 44 XDR cases were detected. 240 cases of fluoroquinolones resistant and susceptible to

SLID were observed. 05 cases were detected as resistance to SLID and susceptible to fluoroquinolones. Out of these 05 cases, 02 cases were detected as low level kanamycin resistant.

DISCUSSION

World Health Organization has proposed the END TB strategy in order to end the global TB epidemic by 2035²². With the agenda of "detect-treat-prevent-build", India has committed to defeat TB by 2025²³. Along with active

implementation of programme, India needs to focus more on research to achieve the target²⁴.

The present study depicts the prevalence of drug resistant strains of M tuberculosis in the eastern region of Bihar. One hundred diagnosed TB patients with no history of prior anti-TB therapy were selected to study the incidence of first

line anti-TB drug resistance. 5 % MDR TB cases were observed in our study. However, the National anti TB drug resistance survey (NDRS) done at National Tuberculosis Institute, Bangalore in the year 2014 and 2015 reports 2.84% MDR cases amongst new patients²⁵. The incidence of Rifampicin resistance was 7% in our study and NDRS reported 2.84%. Isoniazid resistance was 6% in our study and 11.06% in NDRS. The global TB report 2018 shows 7.1% isoniazid resistance in new patients and 7.9% in previously treated patients. We did not observe any streptomycin mono-resistance cases in the present study.

The target of TB control cannot be achieved without the involvement of private medical practitioners. More than 20% of referrals for CBNAAT testing at JLNMCH Bhagalpur were from private practitioners. A total of 599 (20 % of total sample tested) TB cases have detected from CBNAAT in the year 2017 and 2018. Out of these TB cases, 110 (18.36%) reported as rifampicin resistant. NDRS reported 2.84% rifampicin resistance in new cases and 11.67% in previously treated cases. The global TB report 2018 showed 3.5% in new and 18% in previously treated cases globally. However, prevalence of 2.8% for new cases and 12% in previously treated cases has been observed in India.

In the present study, second line LPA reported 240 (50.8%) fluoroquinolones resistance and second line injectables susceptible cases. The Intermediate Reference Laboratory, Patna is serving other regions of Bihar and they have reported 146 (52.51%) flouroquinolones resistant out of 278 cases tested in the first quarter of 2019. However, the NDRS reported only 21.82 % cases of MDR plus any of the flouroquinolones resistance. 21% flouroquinolones resistance was reported in the Global TB report 2016, 20% in Global TB report 2017 and 22% reported in the Global TB report 2018.

The XDR detected at our lab was 44 (9.32%) and IRL

Patna has reported 30 (10.79%) cases. However, NDRS has reported 1.30% XDR cases. The Global TB report 2016 estimated 9.5% XDR TB cases by the end of 2015. The Global TB report 2017 reports 6.5% and 2018 reports 8.5% XDR TB cases.

The laboratory findings of the current study have been compared with the National and global data and observed a higher resistance percentage for some key anti-TB drugs in this study as depicted in Table 1.

Table	1 — Showin	g compariso	n of drug res	istant TB	in different stud	lies
Percentage of d	lrug resistant	TB reported	l in different	studies		
Type of drug resistant TB cases	Global TB report 2016	Global TB report 2017	Global TB report 2018	TB NDRS (India)	Current Study (Eastern Bihar)	Other regions of Bihar
XDR TB MDR TB with	9.50%	6.50%	8.50%	1.30%	9.32%	10.79%
FQ resistance	21%	20%	22%	21.82%	50.80%	52.51%

Fluoroquinolone is one of the most effective second line drugs for drug-resistant TB²⁶. Patients of MDR may develop resistance to quinolones during treatment and become Pre-XDR or even XDR if they develop resistance to second line injectables. The main target of action of Quinolone in Mucobacterium Tuberculosis is DNA gyrase where lie the quinolone-determining sites gyrA and gyrB. Mutations in these sites lead to fluroquinolone resistance. A meta-analysis has shown that previous exposure of quinolones led to the development of quinolone resistance. Duration of treatment with quinolone is another factor promoting quinolone resistance.

The study has depicted the status of anti-TB drug resistance in the Eastern Bihar. However, further studies with bigger sample size for all the districts of Bihar would be more beneficial for the effective TB control programme assessment

Summary:

The incidence of MDR TB is rapidly increasing. The present study shows that prevalence of fluoroquinolone resistance is more in TB patients of eastern Bihar. The widespread use of quinolones in infections other than TB may be the cause of this increased Quinolone resistance. It seems prudent to suggest that the use of respiratory quinolones needs to be reserved for the specific indications in order to preserve their effectiveness²⁷.

ACKNOWLEDGEMENTS

We are thankful to Dr HK Sinha, Principal, JLNMC Bhagalpur for his valuable guidance. We are thankful to Dr RC Mandal, Medical superintendent, JLNMCH, Bhagalpur for his motivation and support. Also, we would like to thank the team of TB Culture & DST laboratory, Bhagalpur and Intermediate Reference Laboratory, Patna for their support in the study.



Outcomes of Tunnelled venous catheters for maintenance hemodialysis: an experience from Eastern India

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Hemodialysis (HD) is most common form of renal replacement therapy (RRT) available to end stage renal disease (ESRD) in India. Vascular access (VA) is an essential component of HD. We planned this study to analyse incidence and risk factors of tunnelled venous dialysis catheter (TVC) related infectious and non-infectious complications. A prospective observational study conducted in a tertiary care hospital in Eastern India from May 2014 to May 2017. Consecutive ESRD patients of any etiology on maintenance HD via TVC were included. Data regarding etiology of ESRD, demographic profile, investigations, complications related to TVC insertion and those during follow up were noted and analysed. 120 patients were screened. 107 participants satisfied eligibility criteria and were included. Average follow up was 146.87±55.19 days. Cumulative incidences of infective and non-infective complications at the end of study period were 2.7 and 3.5 events per 1000 patient-days. 43(40.18%) patients developed catheter related infection, 42(39.25%) had catheter dysfunction and 13(12.15%) features of central venous stenosis (CVS). 29(27.10%), 14(13.18%) and 8(7.47%) patients needed catheter removal due to infection, catheter dysfunction and stenosis respectively. 21 (19.62%) and 2(1.86%) patients underwent TVC removal after arteriovenous fistula (AVF) maturation and renal transplantation respectively. 6(5.61%) patients died with a functioning TVC due to causes unrelated to TVC and 1(0.93%) died due to infection despite removal of TVC. We found a significant association of catheter related infection with economic class, place of living, previous internal jugular vein non tunnelled venous catheter (IJV NTVC) insertion, diabetes, prophylactic antibiotic catheter lock, haemoglobin and serum albumin levels.

Despite catheter related infection and catheter dysfunction, TVCs are an efficient form of VA in patients requiring unplanned dialysis initiation or for those without functioning AVF and complications are significantly lower than with non-tunneled venous catheters.

[J Indian Med Assoc 2019; 117(12): 13-7]

Key words: ESRD, Tunneled Venous Catheter, AV fistula.

Hemodialysis (HD) is the commonest form of renal replacement therapy (RRT) in India¹ and therefore vascular access (VA) for HD and access related complications are immensely important issues. Arteriovenous fistula (AVF) is associated with least incidence of complications and is recommended as VA of choice for ESRD patients².

However, most chronic kidney disease (CKD) patients

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in India are referred late to nephrologists which precludes systematic planning for AVF prior to initiation of HD3. Therefore majority of patients started dialysis with uncuffed non-tunneled venous catheter (NTVC) followed by AVF and very few used grafts or tunneled catheters4. As compared to AV grafts, tunneled venous catheters (TVCs) are more readily available, relatively more economical and can be inserted by trained nephrologists. TVCs are preferable over NTVC owing to lesser risk of infectious complications5.

Despite the risk of infection in some patients, potential advantages of TVC include no need of any maturation time ie, they can be used immediately, repeated skin puncture not required for HD, no short-term hemodynamic consequences, eg, changes in cardiac output or myocardial load which may occur after creation of AVF, they can provide access for a period of months to years unlike NTVC, permitting fistula maturation in patients who require immediate HD6.

TVCs are therefore an under-utilised form of VA.

The data regarding the use of TVCs and TVC related complications from eastern part of India are scarce. Hence we planned this observational study with the aim of observing the complications of TVCs including the current sensitivity patterns for the catheter related blood stream infections (CRBSI) and to analyse the factors associated with these complications.

MATERIALS AND METHODS

This is a prospective observational study conducted in a tertiary care hospital in Eastern India from May 2014 to May 2017. Consecutive ESRD patients of any etiology who presented to our institution requiring dialysis initiation and continuation of maintenance hemodialysis twice or thrice a week via TVC aged 12 years or more were included. Patients were followed up till end of study period or until removal of TVC whichever was earlier. Written informed consent was taken from all patients. As a protocol TVC is inserted electively in ESRD patients both indoor and as a day care procedure for outdoor ESRD patients, in those who did not have a mature AV fistula at the time of HD initiation or those awaiting renal transplant, after stabilisation and two or more heparin free dialysis sessions via a NTVC in femoral or left internal jugular vein (IJV) to minimise the risk of uremic bleeding and to prevent complications during TVC insertion. If patients were referred to our institute with non-tunnelled dialysis catheter inserted in right IJV, inserted within prior 2 weeks and had no evidence of active infection they are considered for right IJC TVC insertion over the guide wire if the site was optimal else a new site was used.

All patients undergo a screening ultrasonography (USG) with doppler imaging of right internal jugular vein to assess its patency and relation to internal carotid artery. The TVC used is Mahurkar Staggered tip catheter without sidehole, 14.5 Fr Insertion is done with all aseptic precautions with cardiac and vitals monitoring under local anaesthesia with USG guidance in an operative room. Skin is disinfected with 10% providone iodine solution and left for air drying before starting the procedure. After insertion povidone ointment 10% is applied to the exit site and dressing is done. Postprocedure the patency and flow in each of the catheter lumens is checked. Heparin lock is given in each of the lumen according to the volume indicated on the catheter. An X-ray PA view is obtained on the same day to confirm appropriate placement of catheter. Prophylactic systemic antibiotics at the time of catheter insertion and antibiotic locks are not routinely used and the decision regarding its use is left to the discretion of the treating nephrologist. Following successful placement of the catheter the temporary venous access is removed and dialysis is continued via TVC.

The data regarding the etiology of ESRD, demographic

profile, complications related to TVC insertion and those during follow up were noted. In case of TVC removal, the reasons were noted. Blood investigations including hemoglobin and serum albumin were recorded. Blood cultures using samples from the catheter and from peripheral vein were done whenever the patient was febrile and did not have any other likely source of infection. Definitions of catheter related infections and catheter dysfunction used were as per KDOQI (Kidney Disease Outcomes Quality Initiative) guidelines7.

Exit site infection, tunnel infection and definite, probable as well as possible catheter related bacteraemia were all considered together as infectious complications. All patients with catheter related bacteremia were treated with systemic antibiotics for at least 2 weeks if they clinically responded. If patients presented with severe sepsis and/ or did not respond within 48 hours of initiation of empiric broad spectrum antibiotics, TVC was removed and further dialysis was continued via NTVC. For catheter dysfunction not due to catheter malposition conservative management with raw heparin lock, 2500U/ml of urokinase, 2ml in each limb of permeath was tried and repeated once. If it did not result in improvement of catheter dysfunction then TVC was removed. In all patients were counselled for AVF creation at the earliest. TVC was removed after fistula maturation or successful renal transplantation. Data was analysed using SPSS software version 21. Factors associated with various complications of TVC were studied.

RESULTS

120 patients with ESRD without any ready VA requiring dialysis initiation were screened. Of these, only 41 patients (34.16%) had been counselled for AVF before referral to our institute and 8 (7.47%) of these patients had AVF failure. In 13 of 120 patients had evidence of clot or narrowing of right IJV lumen and were not considered for Rt. IJV TVC insertion. A total of 107 ESRD patients underwent Rt. IJV TVC insertion during the study period. In one patient TVC could not be inserted in Rt. IJV despite absence of occlusion on screening ultrasonography and doppler. TVC was inserted in femoral vein. This patient has been excluded from analysis. The demographic profile of these patients has been shown in Table 1. The range of age of patients was 12 to 70 years. Of these 36(33.6%) had diabetic kidney disease. The other etiologies of CKD were glomerulonephritis, urinary tract obstruction.

Details of previous VA and dialysis duration have been shown in Table 1.

The range of blood flows used immediately postprocedure was in 280-320 ml/min with an average flow of 288 ml/min. Complications associated with TVC insertion have been shown in Fig 1. Other complications include one episode each of seizures and flash pulmonary edema. Two patients had accelerated hypertension.

Table 1 - Patient Characteristics (n=107)

Age		40.7 ±21.42
(average ± standard deviation)	<18	18 (16.82%)
	18-44	44 (41.12%)
	45-59	16 (14.95%)
	≥60	29 (27.1%)
Sex	MALE	62 (57.9%)
	FEMALE	45 (42.1%)
Socio economic condition	LOWER MIDDLE (III)	40 (37.4%)
	UPPER LOWER (IV)	53 (49.5%)
	LOWER (V)	14 (13.1%)
Living place	RURAL	56 (52.3%)
	URBAN	51 (47.7%)
Number of previous venous access	0	19 (17.8%)
	1	28 (26.2%)
	2	38 (35.5%)
	3	20 (18.7%)
	4	2 (1.9%)
Previous right internal jugular NTVC*	YES	48 (44.9%)
	NO	59 (55.1%)
Diabetic kidney disease	YES	36 (33.6%)
	NO	71(66.4%)
Number of HD** sessions per week	2	54 (50.5%)
	3	53 (49.5%)
Hemodialysis duration (month)		12.1±5.55
Hemoglobin(gm/dl)		8.79±1.02
Albumin (gm/dl)	I	3.2±0.62
Prophylactic antibiotic catheter lock	YES	54 (50.5%)
	NO	53 (49.5%)
*NTVC: non-tunnelled venous catheter.		

NTVC: non tunnelled venous catheter

**HD: Hemodialysis

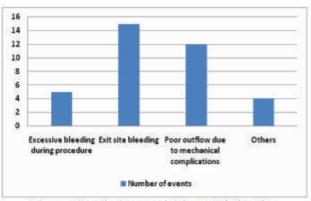


Fig 1 - Complications associated with TVC insertion

The average follow up was 146.87±55.19 days. The cumulative incidences of infective and non-infective complications at the end of the study period were 2.7 and 3.5 events per 1000 catheter-days. In 43 (40.18%) patients developed catheter related infection during the study. 42(39.25%) patients had catheter dysfunction and 13 (12.15%) patients had features of central venous stenosis (CVS). Total 81 (61.68%) required TVC removal during the study period. 13 (12.15%) patients at 3 months and 70 (65.42%) patients at 6 months underwent TVC removal. 29(27.10%); 14(13.18%) and 8 (7.47%) needed catheter removal due to infection, catheter dysfunction and stenosis respectively. 21 (19.62%) and 2(1.86%) patients underwent TVC removal after AVF maturation and renal transplantation respectively. 6 (5.61%) patients died with a functioning TVC due to causes unrelated to TVC and 1 (0.93%) died due to infection despite removal of TVC. Four patients had exit site infection, all were treated conservatively initially. Three of these responded to therapy while one patient developed tunnel infection and required removal of dialysis catheter. Two patients had tunnel infection as well as bacteraemia and the TVC was removed in both these cases. Thirty seven patients had catheter related bacteraemia and 26 of these required TVC removal. Positive blood cultures (sent prior to initiation of antibiotics) were available for 10 patients. 5 of these were positive for methicillin resistant staphylococcus aureus, two coagulase negative staphylococci, one each for drug resistant enterococcus. klebsiella pneumoniae and acinetobacter. The factors that were associated with catheter related infection, catheter dysfunction, central venous stenosis and the corresponding

Odds ratios have been shown in Table 2. Rural living place, number of previous venous accesses, haemoglobin, serum albumin and use of catheter lock were significantly associated with catheter related infection. Number of previous venous accesses and duration of HD were significantly associated with central venous stenosis.

DISCUSSION

VA is the cornerstone of HD and the best form of VA is AVF. AVF should ideally be placed 6 months prior to anticipated dialysis initiation6 to facilitate planned dialysis initiation when indicated. However, most CKD patients in our country are referred late to nephrologists which results in unplanned, often emergency dialysis initiation4. The delay in planning and creation of AVF was reflected in our study as well, as only about 30% patients of the screened patients had been counselled for AVF prior to anticipated dialysis initiation. However, of these only 23.52% patients actually had AVF done. This is in sharp contrast from developed countries where majority of patients had failed or immature AV access as the indication for TVC placement8. Almost 50% patients had >2 NTVC insertions prior to TVC insertion. Late referral, lack of motivation of patients and primary health care providers for timely VA creation, inadequate availability of technical expertise for TVC insertion at peripheral health care centers may have been

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Table 2 — Factors associated with catheter related infection, catheter dysfunction and central venous stenosis

	Catheter related infection			Catheter dysfunction			Central vein stenosis		
Variable	OR	95% CI	p value	OR	95% CI	p value	OR	95% CI	P value
Age	1.016	0.997- 1.035	.099	1.001	0.983- 1.019	0.925	0.999	0.972- 1.026	0.921
Sex (f)	1.867	0.851- 4.100	0.119	2.041	0.930- 4.481	0.075	2,465	0.749- 8.114	0.132
Socio economic condition(upper lower)	0.244	0.061- 0.974	0.046	0.455	0.138- 1.502	0.455	1.067	0.2- 5.696	0.94
Living place (rural)	2.839	1.265- 6.369	0.002	0.534	0.245- 1.164	0.115	0.754	0.236- 2.414	0.635
No of previous venous access	2.970	1.804- 4.888	<0.00	1.047	0.722- 1.516	0.810	18.29	3.987- 83.925	<0.00
Previous right internal jugular NTVC*	0,342	0.154- 0.762	0.009	0.821	0.379- 1.781	0.618	0.052	0.006- 0.415	0.005
Diabetic kidney disease	3.1182	1.357- 7.164	0.007	1.458	0.648- 3.281	0.362	1.828	0.565- 5.912	0.313
Number of HD** sessions per week	1 115	0.515- 2.416	0.782	1.205	0.557- 2.605	0.636	0.857	0.268- 2.742	0.795
Hemodialysis duration (month)	1.017	0.949- 1.091	0.628	0.953	0.888-	0.184	1.142	1.014- 1.288	0.029
Hemoglobin	0.609	0.406- 0.914	0.017	0.886	0.606- 1.294	0.530	0.668	0.374- 1.195	0.174
Albumin	0.064	0.022-	<0.00	0.626	0.329- 1.190	0.153	0.515	0.190- 1.393	0.191
Prophylactic antibiotic catheter lock	5.957	2.518- 14.092	<0.00	1 926	0.882- 4.206	0.1	2.557	0.736- 8.884	0.14

the factors responsible for multiple previous NTVC insertions resulting in occlusion of Rt.IJV lumen. As early as 2 weeks of NTVC insertion was found to occlude Right IJV lumen.

Only about 1/3rd of the patients were diabetics. Though diabetes is the most common cause of ESRD in our country the representation of diabetic kidney disease was low. This is possibly due to relatively earlier detection of CKD in diabetic patients, better and continued follow up of diabetic CKD patients allowing timely VA creation and also probably due to proportionately higher referral of non-diabetic CKD than diabetic kidney disease to our institute.

As shown in Fig 1, the most common complication associated with TVC insertion was exit site bleeding. Catheter related infection and catheter dysfunction were both equally common complications of TVC insertion. However, catheter dysfunction more often resulted in TVC removal. 67.44% of patients with catheter related infection required catheter removal; in rest of the patients catheter could be salvaged with antibiotic therapy. Change of the TVC for catheter related infection over guide wire was not a part of the study protocol. Hence, we cannot estimate whether this manoeuvre would have resulted in higher catheter salvage. The incidence of infective complications

reported in published studies has been variable and ranged between 2.5 and 5.5 cases/1000 catheterdays⁹.

A recent cohort study by Lisa M et al reported an overall incidence of confirmed or possible CRBSI as 0.19/ 1000 catheter days which was much lower than our study. Another study from United States reported 4.6 episodes / 1,000 catheter days. Multiple factors can be associated with catheter related bacteremia. Studies from other parts of the country reported 0.4 bacteremia episodes per 1000 catheter days10. A possible reason for low incidence could be routine use of prophylactic antibiotic lock solution in all participants in that study. However, such a strategy may be associated with increased risk of antibiotic resistance. The pattern of drug sensitivity and resistance was not specified in that study. We found infections due to

resistant organisms more commonly in patients in whom prophylactic antibiotic locks were used but the statistical significance could not be evaluated because of small number of culture positive reports. The use of antibiotic locks however cannot replace the immensely important role of universal precautions and strict adherence to hand hygiene but is complementary to these measures.

We found a significant association of catheter related infection with economic class, place of living, previous Right IJV NTVC insertion, diabetes, prophylactic antibiotic catheter lock, haemoglobin and serum albumin levels. Early detection of CKD, prompt follow up and timely referral to nephrologists may prevent development of significant anemia and hypoalbuminemia due to malnutrition and this in turn may reduce the risk of catheter related infections. Additionally the presence of anemia and hypoalbuminemia may be related to economic status. It has been suggested that the target for catheter-related bloodstream infection (CRBSI) incidence must be less than 1 per 1000 catheter days¹¹.

TVC are more preferable to NTVC as these are associated with lower incidence of complications. The reported incidence of CRBSI with NTVC was as high as 8.70 per 1000 catheter days in a study from India¹². These are significantly higher than those reported with TVC. Hence, TVC must be given a consideration in patients requiring dialysis for prolonged duration especially in case of ESRD patients in clinical setting when mature AVF is not likely to be available for use within few weeks.

All cases of early catheter dysfunction were due to malposition or kink of catheter and all were corrected. In those with late catheter dysfunction TVC removal was done in 33.33% of cases. CVS required TVC removal in 7.47% of all cases. In other patients with CVS dialysis was continued via TVC as these patients had no other feasible VA options or other forms of RRT. Catheter dysfunction can be because of multiple causes like intraluminal, catheter tip or extrinsic thrombus, uncommonly intra-atrial thrombus, fibrin sheath and central venous stenosis. The reported incidence of these varies from 13 to 57%13 and may be symptomatic or asymptomatic. Contrast venography with fluoroscopy is helpful in definitive diagnosis in most cases but is not accessible widely. As per protocol conservative treatment was tried in cases of catheter dysfunction not due to malposition and if it was unsuccessful TVC was removed. As venography was not used the relative incidence of each of the causes of TVC dysfunction could not be determined. More than 50% of patients with catheter dysfunction also had catheter related infection. Catheter dysfunction particularly due to fibrin sheath can cause both dysfunction and infection. No clinical variable was significantly associated with catheter dysfunction. Overall however number of previous NTVC particularly Right IJV TVC was associated with features of central venous stenosis. This is largely if not entirely preventable cause of CVS.

The causes of TVC drop out (TVC removal for any cause) in our study were quite different from that reported in other part of our country14. Disparate rates of TVC complications mentioned above are likely reasons for the different causes of TVC drop-out and drop-outs do not necessarily indicate technique failure. An important contributing factor may be counselling and continuous evaluation and planning for AVF in our study. AVF was considered at each follow up even when patients had a functioning TVC in situ. As a result AVF maturation was reason for TVC drop-out in significant number of cases.

Limitations of our study include relatively less number of patients, only Right LJV TVC was studied and incidences of exact causes of catheter dysfunction could not be estimated. The strengths of our study include prospective design and technique of TVC insertion with use of only ultrasonography guidance which is widely available. This study also demonstrates that Right IJV TVC insertion can be relatively safely done under ultrasonography guidance when fluoroscopy is not available.

Conclusion:

TVCs are an efficient form of VA in patients requiring dialysis initiation which was not pre-planned or for those in whom AVF creation is not feasible or has failed. It is associated with complications like catheter related infection and catheter dysfunction. Conservative treatment may salvage TVC despite these complications in some cases. Despite these complications TVC has superior outcomes as compared to NTVC. Early diagnosis and continued follow up of CKD with planning of vascular access well ahead of anticipated dialysis requirement may prevent the complications associated with vascular access.

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Evaluation of Maternal and Perinatal Outcome in Hepatitis E during Pregnancy

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Hepatitis E is a single stranded Ribonucleic Acid (RNA) virus transmitted through feco-oral route. The infection usually occurs in young adults and is a mild and self limiting disease. It is of severe degree during pregnancy causing hepatic encephalopathy and even maternal mortality. There is increased obstetric and fetal complications in Hepatitis E Virus (HEV) infection during pregnancy. The present study was conducted to know the maternal and perinatal outcome in hepatitis E infection during pregnancy. A total of 60 patients of hepatitis E who delivered in the tertiary referral centre of Delhi, AllMS, India were included in this retrospective study. The blood was taken for viral markers, liver function tests, bleeding and coagulation factors. Obstetric and fetal outcomes were observed. The mean age was 27.65±4.81 years. There were 30 primigravida and 30 multigravida patients. Preterm delivery rate, intrapartum fetal distress, meconium stained liquor and postpartum complications was 26.66%,13.33%, 20% and 21.66% respectively. Caesarean section rate was 63.33% in study group. There were 2 maternal deaths in hepatitis E patients. Derangement of liver function, coagulopathy and encephalopathy was seen in significant number of cases. Mean fetal birth weight was 2134.22±625.47gm. Fetal respiratory distress rate was 10%. Hepatitis E in pregnancy is associated with adverse maternal and perinatal outcome.

[J Indian Med Assoc 2019; 117(12): 18-21]

Key words: Hepatitis E, Pregnancy, Maternal mortality, Liver function tests.

Tepatitis E is a single stranded RNA virus which causes both sporadic as well as epidemic cases of acute viral hepatitis especially in developing countries¹. It is mainly transmitted through feco-oral route with mean incubation period of 40 days (range 3 to 8 weeks)^{2,3}. The infection usually occurs in young adults and is a mild and self limiting disease⁴. However it is of severe degree during pregnancy usually second and third trimester of pregnancy, causing hepatic encephalopathy and even maternal mortality^{5,6}. Incidence varies in different countries and even different parts of the same country. The incidence is much higher in North India where it can cause case fatality rate of 1-2% and even upto 10-20% in pregnant women⁷. Hepatitis E virus has 5 genotypes with genotype 1 and 2 being more virulent in humans. There is increased obstetric complications in HEV infection during pregnancy such as spontaneous abortion, premature rupture of membrane, intrauterine growth restriction, intrauterine fetal death and postpartum hemorrhage⁸. There is increased incidence of fetal complications like prematurity and low birth weight babies and fetal mortality.

The present study was conducted to know the maternal

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and perinatal outcome in hepatitis E infection during pregnancy.

MATERIALS AND METHODS

A total of 60 patients of hepatitis E who delivered in a tertiary referral centre over last 10 years were enrolled in this retrospective study. The maternal and perinatal factors were assessed in all cases. Serum was tested for IgM Anti HEV by rapid immunochromatographic assay and only Anti HEV IgM positive cases during pregnancy were included in the study. Patients of jaundice due to other causes (Hepatitis A, B, C, HELLP syndrome, drug induced hepatitis etc) were excluded from the study. No patient had chronic liver disease. The antenatal history, need of medication (ursodeoxycholic acid, N-acetyl cysteine, tenofovir) were noted in all cases. Any antenatal, intrapartum or postpartum obstetric events were noted in all cases. Particular attention was made to preterm delivery, intrapartum fetal distress, maternal mortality. Mode of delivery and need and indication of caesarean section was noted in all the cases.

The fetal outcome was noted in all cases and controls especially mean birth weight, small for gestation age fetus, still birth rate, APGAR<8 and respiratory distress syndrome. Perinatal mortaliy rate was calculated in all cases. Fulminant hepatic failure was defined as occurrence of hepatic encephalopathy (altered sensorium) with grossly deranged Liver Function Tests (LFT) with jaundice. Coagulopathy



was defined as deranged prothrombin time (prolonged to >15 seconds).

STATISTICAL ANALYSIS

Data analysis was carried out using statistical software STATA version 12.0. Continuous variables were tested for normality assumptions using appropriate statistical tests. For the variables that were approximately to normal distribution descriptive statistics such as mean, standard deviation and the range values were calculated. Categorical variables were expressed in terms of frequency and percent values.

RESULTS

A total of 60 cases of Hepatitits E (Group 1) with pregnancy over last 10 years in a tertiary referral centre were enrolled in this retrospective study. Maternal and perinatal

outcome was compared in the two groups. Table 1 shows baseline characteristics in the study group. The mean age was 27.85±4.81 years. There were 30 primigravida and 30 multigravida patients. Associated medical problems are shown in Table 1. Table 2 shows obstetric complications and mode of delivery in the study group. Incidence of anemia, preeclampsia, oligoamnios, gestational Diabetes mellitus, premature rupture of membrane, fetal growth restriction and pretern delivery rate was 21.66%, 21.66%, 3.33%, 20%, 13.33%, 13.33% and 26.66% respectively.

Similarly intrapartum fetal distress was seen in significantly higher number of cases of Hepatitis E patients 8(13.3%). Meconium stained liquor was seen in 20% of cases. Postpartum complications were seen in 21.6% (13/60) cases. There were 2(3.33%) maternal deaths in study group. The mode of delivery is shown in Table 2. Vaginal delivery could be achieved in 22(36.67%) cases in study. Cesarean section rate was significantly higher in study cases(63.33%). Emergency cesarean rate was significantly higher (43.33%) in study group.

Table 3 shows abnormalities of liver function tests (LFTs) and use PIH : Pregnancy Induced Hypertension of antiviral drugs. As expected LFTs were severely deranged in hepatitis E in pregnancy. Thus

mean aspartate amino transferase (SGOT) and Alanine amino transferase (SGPT) levels were 120.13 ±192.99U/L and 129.29 ±208.42U/L respectively. Total serum bilirubin was 2.49±4.64 mg/dl. Coagulopathy defined as prothrombin time of more than 15 seconds was seen in [8(13.33%)] cases. Hepatic encephalopathy was also seen in [5(8.33%)] cases. Use of medications like ursodeoxycholic acid, N acetyl cysteine and tenofovir was also seen in 60%, 4% and 10% cases respectively.

Most fetal parameters were poorer in hepatitis E patients. Mean birth weight was 2134±625.47 gm in study group. Small for date was seen in 12(20%) cases. Apgar <8/10 at one minute was also seen [12(20%)] cases in study group. Still birth was seen in 4(6.67%) cases. Respiratory distress

was seen in 6(10%) cases (Table 4).

DISCUSSION

Hepatitis E is an acute viral infection caused by single stranded non enveloped RNA virus 1,8. The first outbreak of hepatitis E in India came in 1953-56 and was described retrospectively8.9. The main source of infection of HEV is through contaminated drinking water. Usually the infection has

Outcome	HEV during
	Pregnancy N=60 (%)
Mean Age	27.65±4.81
18-35	57(95)
>35	3(5)
Obstetric History:	
Primigravida	30(50)
Multigravida	30(50)
Previous Abortions	30(50)
Associated Medical Prob	olems :
Anemia	8(13.33)
Hypothyroidism	8(13.33)
Chronic Kidney Disea	ase 2(3.33)
Rheumatic Heart Disc	ease 2(3.33)

Table 2 - Obstetric Complications and Mode of Delivery in Two Groups

Outcome	HEV during
Fre	gnancy N=60 (%
Obstetric events:	
Anemia	13(21.66)
PIH	13(21.66)
Oligoamnios	2(3.33)
GDM	12(20)
PROM	8(13.33)
FGR	8(13.33)
Preterm Delivery	16(26.66)
Intrapartum Fetal Distre	ss 8(13.33)
MSL at delivery	12(20)
Postpartum complicatio	n 13(21.66)
Maternal mortality	2(3.33)
Mode of Delivery:	
Vaginal	22(36.67)
Spontaneous	10(16.66)
Induced	12(20)
LSCS	38(63.33)
Elective	12(20)
Emergency	26(43.33)

GDM: Gestational Diabetes Mellitus, PROM: Premature Rupture of Membrane FGR: Fetal Growth Restriction

Outcome	HEV during Pregnancy N=60 (9
LFT Abnormality:	
Mean SGOT (in IU/l)	120.13±192.99
Mean SGPT (in IU/l)	129.27±208.42
Mean ALP (in IU/l)	365.23±203.16
Mean T. Bilirubin (in mg	(%) 2.49±4.64
Coagulopathy	8(13.33)
Hepatic Encephalopathy	5(8.33)
Use of Medications:	
Ursodeoxycholic acid	36(60)
NAC	4(6.67)
TENOFOVIR	6(10)
LFT: Liver Function Test SGOT: Serum Glutamin Transaminase SGPT: Serum Glutamate F ALP: Alkaline Phosphatas NAC: N Acetyl Cysteine	yurvate Transamina

Outcome	UEV doring
Outcome	HEV during Pregnancy N=60 (%)
Fetal Outcome :	
Mean Birth Weight	2134.22±625.47
(in gram)	
Small For Dates	12(20)
Large For Dates	4(6.67)
APGAR<8	12(20)
Still Birth	4(6.67)
Congenital Anomaly	3(5)
Respiratory Distress	6(10)

an incubation period of 3-8 weeks with a mild and self limiting illness resolving within 6 weeks with no chronic segulae8. Fulminant hepatitis and case fatality is rare in men and in non pregnant women8. However HEV infection during pregnancy causes a serious illness with risk increasing with progress of pregnancy and there is risk of fulminant hepatic failure and death which may be seen in upto 30-100% patients10. Infact one of the most distinctive features of the epidemic and endemic hepatitis E is higher occurrence and mortality of diseased patients in pregnancy11,12. The obstetric complications like miscarriages, premature rupture of membrane, intra uterine growth restriction and death occurs with greater frequency in women with HEV infection during pregnancy. Infact in a study 58% of death in pregnant women with acute liver disease in hepatitis were due to HEV infection¹³.

In the present study, we observed increased obstetric complication like preterm delivery (26.6%), intrapartum fetal distress (13.33%), meconium stained liquor (20%) in pregnant patients infected with HEV infection. We observed 2 maternal deaths (3.33%) in 60 cases of HEV which corresponds to maternal mortality rate (MMR) of 3333 per lac live births which is 33 times higher than our hospitals average MMR of 110 per lac births during this period (hospital statistics, unpublished data). Shinde et al8 also observed a very high maternal mortality of 32% in their study on acute HEV infection in pregnancy. We also observed a higher fetal complications like lower mean birth weight, small for dates fetuses, increased chances of low APGAR babies, still births and respiratory distress rate in our study. Results are similar to Prasad et al4 who observed 80% risk of prematurity in their study. Shinde et al8 observed 23.5% preterm delivery, 48.15% poor fetal outcome in their study. Beniwal et al14 also observed adverse maternal and fetal outcome with high mortality rate, increased frequency of abortion, preterm delivery, still birth and neonatal death in their study. Other authors have also observed increased preterm delivery rate, increased fetal and maternal death in their studies on HEV infection during pregnancy 15,16,17. Hepatitis E infection during pregnancy was also most important medical condition presenting in obstetric critical care18. In a chinese study Xu et al19 also observed adverse maternal and perinatal outcome with HEV infection during pregnancy. Hepatitis E can also cause vertical transmission causing fetal and neonatal morbidity and mortality20,21,22.

Prevention and control of hepatitis E in developing countries is a daunting task and mainly rests on provision of supply of clean portable drinking water, adequate sanitation, proper hygiene, proper sewage disposal21. Clean India campaign, a Government of India campaign 2014 is a 10 billion US dollar project meant to clean environment, construct toilets in most homes and schools and a plan to have 1.2 billion Indians to have access to public latrines in next 5 years23. It will go long way in reducing incidence of various water borne disease in india including hepatitis E. Hepatitis E vaccine-239, marketed in China has shown high efficacy with sustained protection for over four years but is still not available and used in India.

Conclusion:

Hepatitis E infection in second and third trimester and during labor is a serious disease causing higher incidence of obstetric complications, maternal morbidity and maternal mortality, increased chances of caesarean section, hepatic encephalopathy, coagulopathy, poor perinatal outcome (low mean birth weight babies, still birth and respiratory distress rate). Hence all pregnant women with HEV infection should be treated on tertiary referral centres with facilities for intensive care unit. As HEV is transmitted by feco-oral route, sanitation, adequate disposal of excreta and provision for safe drinking water can go long way in preventing this menace.

ACKNOWLEDGEMENT

Author is thankful to all residents of Department of Obstetrics and Gynaecology, AIIMS, Delhi for their support.

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Diaphyseal Aclasis — A case report

Soumik Das1, Debalina Sarkar2, Avishek Bhadra3

Diaphyseal aclasis is a rare genetic skeletal condition due to developmental abnormalities of the growth plate causing multiple cartilage covered exostoses to form on the surface of the metaphysis or the adjacent diaphysis region of long bones. A diagnosis of diaphyseal aclasis can be made when radiologically at least two osteochondromas of the juxta-epiphyseal region of long bones are observed. Radiological examination of the case revealed multiple exostoses involving the metaphysis of proximal end of both humeri, medial border of left scapula, distal end of both radii and both ulnae, distal end of both femora, proximal end of both tibiae and both fibulae, and distal end of right tibia and right fibula associated with shortening of the 4th and 5th metacarpals of left hand. A diagnosis of diaphyseal aclasis was made. No treatment was recommended at that time and the relatives of the patient were counselled regarding the future potential complications and what actions may be taken.

[J Indian Med Assoc 2019; 117(12): 22-3]

Key words: Diaphyseal aclasis, exostosis, osteochondroma.

Diaphyseal aclasis, also known as hereditary multiple exostoses or osteochondromatosis is a rare autosomal dominant condition, characterized by the development of multiple osteochondromas. Here we present a classical case of diaphyseal aclasis in a 14-year-old boy who presented with swelling of the wrist and knee, which had appeared at the age of 2 years, and since then had slowly increased in size, associated with asymmetry in the length of the upper limbs. The diagnosis was confirmed on radiological examination.

CASE REPORT

A 14-year-old boy presented with swelling of the wrist and knee, which had appeared at the age of 2 years, and had slowly increased in size, associated with asymmetry in the length of the upper limbs. The patient did not complain of any pain or paraesthesia distally. There was no history of fracture or pulsatile mass in the popliteal fossa.

Family history — A similar condition was present in his mother but these swellings had not shown any increase in size since she stopped growing.

Examinations — Examination of the patient revealed a normally developed child with short stature (height – 141 cm. which is below the 3rd percentile line representing height-for-age of boys between 5 to 19 years as per WHO growth chart 2007) and multiple, nontender and non-mobile bony swellings over both knee, both wrists, and proximal end of both humeri. There was no evidence of any neuro-vascular deficit distal to the swellings.

Radiological examination revealed multiple exostoses involving the metaphysis of proximal end of both humeri, medial border of left scapula, distal end of both radii and both ulnae, distal end of both femora, proximal end of both tibiae and both fibulae, and distal end of right tibia and right fibula associated with shortening of the 4th and 5th metacarpals of left hand.

A diagnosis of diaphyseal aclasis was made. No treatment was recommended at that time and the relatives of the patient were counselled regarding the future potential complications and what actions may be taken.

DISCUSSION

Hereditary Multiple Exostoses (HME), alternatively called diaphyseal aclasis or osteochondromatosis, is a highly penetrant, autosomal dominant trait characterized by slightly stunted growth of long bones and multiple osteochondromas¹.

Osteochondroma (osteocartilaginous exostosis), according to the 2002 WHO definition, is a cartilage capped benign bony neoplasm on the outer surface of bones containing a marrow cavity that is continuous with that of the underlying bone². A diagnosis of diaphyseal aclasis can be made when radiologically at least two osteochondromas of the juxta-epiphyseal region of long bones are observed.

The prevalence of diaphyseal aclasis is estimated at 1:50,000 persons within the general population and seems to be higher in males (male-to-female ratio 1.5:1). Approximately 62% of the patients with multiple osteochondromas have a positive family history¹.

Two genes, EXT1 and EXT2 located respectively at 8q24 and 11p11-p12, have been isolated to cause diaphyseal aclasis. In osteochondromas in which EXT expression is decreased due to mutation or deletion, the heparan sulphate proteoglycans seem to accumulate in the cytoplasm of the cell, instead of being transported to be expressed at the cell surface, resulting in abnormal proliferation of growth plate cartilage.

The chief complaint is the discovery of single or multiple hard, painless masses near joints. Osteochondromas develop and increase in size in the first decade of life, ceasing to grow when the growth plates close at puberty but may recur during pregnancy. The

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MBBS, MS (Obstet & Gynaecol), RMO-cum-Clinical Tutor, Department of Obstetrics and Gynaecology, Calcutta National Medical College, Kolkata 700014 distribution is usually bilateral and may be symmetrical.

In diaphyseal aclasis patients variety of orthopaedic deformities can be found like deformities of the forearm (shortening of the ulna with secondary bowing of radius) giving the characteristic "bayonet hand" deformity, inequality in limb length, varus or valgus angulation of the knee, deformity of the ankle and disproportionate short stature. Complications include osseous and cosmetic deformities, bursa formation. arthritis impingement on adjacent tendons, nerves, vessels or spinal cord.

Malignant degeneration occurs in 5%-25% of cases into chondrosarcoma5.4. The most common sites are the pelvis and shoulder girdle5.

Vascular complications of the popliteal vessel occur due to ossification of the previously protective cartilage cap, around the 2nd decade and relative immobility of the artery in the popliteal fossa between exiting Hunter's canal and the trifurcation6. The artery undergoes chronic abrasion on the sharp exostosis forming a defect in the adventitia resulting in pseudoaneurysm formation7.

Osteochondromas are only removed when they cause pain, when they give functional complaints for instance due to compression on nerves or vessels, or for cosmetic reasons. If the diagnosis of multiple osteochondromas is established and all tumours are identified, patients should be well instructed to seek earlier medical attention if their condition changes, for instance if there is pain or growth of a known lesion. In case of malignancy, en-blocresection of the lesion and its pseudocapsule with tumour-free margins, preferably in a bone tumour referral centre, should be performed, resulting in excellent long term clinical and local results.

Osteochondromas are benign lesions and do not affect life expectancy.

Dysplasia Epiphysealis Hemimelica (DEH, Trevor's disease, tarso-epiphysial aclasis) and metachondromatosis (MC) are considered in the differential diagnosis of solitary and hereditary osteochondromas.

Moreover, diaphyseal aclasis should be distinguished from enchondromatosis (Ollier disease and Maffucci syndrome), in which multiple cartilage tumours are found in the medulla of bone, with a predilection for the short tubular bones and a unilateral predominance.

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Fig 1 - Showing multiple exostoses involving the metaphysis of proximal end of both humeri, medial border of left scapula, distal end of both radii and both ulnae, distal end of both femora, proximal end of both tibiae and both fibulae, and distal end of right tibia and right fibula associated with shortening of the 4th and 5th metacarpals of left hand

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Case Report

Spontaneous Expulsive Choroidal Hemorrhage

Rajesh S Joshi¹

An 80 year-old lady presented with sudden onset bleeding from her right eye. A through history did not reveal any trauma or previous ocular surgery. Other eye had central leucoma grade corneal opacity. She was blind by both eyes since last 20 years and was not under follow up with any ophthalmologist. On surgical exploration, it was found that contents were extruded out from the superior limbus in the form of iris, choroids and vitreous. There was no lens. Patient was taken to the operation theater and an evisceration was done. Eviscerated contents sent for histopathological study did not show any inflammatory signs or any malignant changes. A trivial trauma to the eye like rubbing can lead to the spontaneous expulsion of the contents of the globe in presence of old corneal disease.

[J Indian Med Assoc 2019; 117(12): 24-5]

Key words: Expulsive choroidal hemorrhage.

expulsive choroidal hemorrhage (ECH) is the most feared Ecomplication of ocular surgery. Reported incidence is 0.05-0.08% intra-operatively12. It's rarely seen in absence of surgical procedure or trauma. It is seen due to sudden lowering of intraocular pressure during intra-ocular surgery. Reports have indicated that, it is related to cataract and glaucoma surgery, vitreous surgery, perforating and blunt injury to the globe. The

incidence of non-surgical ECH is not known.

We report a case of sudden onset expulsive choroidal hemorrhage in a patient having no systemic problems but an old corneal opacity of unknown origin, suggesting that patient having compromised eye need to be followed carefully.

CASE REPORT

An 80-year-old lady presented with sudden onset bleeding from her right eye since last 8 hours. It was associated with severe pain in that eye. She did not have any history of trauma or any surgical procedure in that eye. She was diagnosed having corneal opacity in both the eyes since last 20 years. Records of previous ocular examination were not available with the patient. Patient's general condition was normal. She was non-diabetic and nonhypertensive. She was not using any drugs locally as well as systemically. There were no sings and symptoms of hemorrhage in any other parts of the body. Blood pressure was 110/70 mm of Hg. Haematological investigations were normal.

Examinations — On examination, both eyes had no perception of light. Right eye had active bleeding with ocular contents extruded out (Fig 1). Left eye had leucoma grade corneal opacity measuring 9x9 mm with thinning of peripheral cornea. No scleral thinning was seen. Intra-ocular pressure by air-puff tonometer was normal in left eye. On exploration of right eye, a perforation was seen in the superior part of the comea with uveal tissue prolapse. Scleral thinning was seen in the superior and inferior part of the sclera (Fig 2). A decision was taken to eviscerate the contents. A large hemorrhagic mass with intra-ocular tissues were removed through the corneal defect. Cultures for bacteria and fungi from the dissected tissue were negative. Histopathological examination did not show any inflammatory signs and malignant changes.



Fig 1 - Extruded contents of the globe with scleral thinning (arrow)

DISCUSSION

Ophir et al Classified supra choroidal hemorrhage (SCH) in two forms (a) the surgical type, which occur during or shortly after ocular surgical intervention and (b) the spontaneous type, which is extremely rare, associated with perforation of the comea or the limbus3. Surgical type occurs in patients who are at risk during surgical intervention. The risk could be in the form of systemic conditions which are not under control like diabetes, hypertension, thrombocytopenic4.

Local conditions causing surgical expulsion choroidal hemorrhage

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are atherosclerosis, vascular diseases, glaucoma, corneal ulcer, stepylomatous globe, intra-ocular malignancy5. Our patients had old corneal opacity and the scleral staphyloma near the limbus on the superior and inferior side. There is still a debate on an initial event of the spontaneous expulsive choroidal hemorrhage. Some believe that hemorrhage in the ocular cavity as an initial event and some, sudden decompression of the globe in both surgical and non -surgical cases as an initial event6. The mechanism leading to expulsion choroidal hemorrhage in our case is unclear. The defect on the superior side of the cornea was 8-10 mm. We presume perforation of the comea as an initial event followed by bleeding. The perforation could be because of trivial trauma to the eye like rubbing of the eye, which patient denies. This is likely to be, as bleeding from the eye started at

night. There were no active inflammatory corneal signs. This is also supported by histopathology of eviscerated contents which did not show active inflammatory signs.

In reviewing the literature, glaucoma was proposed to be an initial event producing spontaneous expulsive choroidal hemorrhage67. The mechanism of expulsive hemorrhage in these cases were thought to be a sudden decompression of the globe leading to anterior displacement of the retina and choroid then rupture of the posterior ciliary arteries. Chronic glaucoma causes bullous keratopathy that may become infected secondarily leading to corneal perforation. In our case patient had an old corneal opacity in both the eyes but it was not clear from the history and examination whether patient had an old glaucoma or corneal ulceration. Other eye had normal intra-ocular pressure on non-contact tonometer. One day prior to the bleeding patient did not have any complaints pertaining to the development of the corneal ulcer. Thus we think trivial trauma to the eye during the sleep initiated the event of the bleeding.

Case of spontaneous expulsive choroidal hemorrhage without an ocular surgery is rare. Expulsive choroidal hemorrhage occurring during the ocular surgical procedure is related to systemic factor like uncontrolled hypertension, diabetes and bleeding disorders. Best thing to prevent expulsive choroidal hemorrhage in these cases is to control them preoperatively. But spontaneous expulsive choroidal hemorrhage occurring in cases having comeal inflammatory diseases, chronic glaucoma is unpredictable. This case is presented to highlight the need to follow such cases carefully.

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Fig 2 - Showing scleral thinning (arrow)

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Case Report

A rare case presentation of foreign body in Esophagus (large mango seed)

Dipayan Biswas¹, Aloke Bose Majumdar², Shib Shankar Paul³, Souradeep Ray⁴

Fish bones, meat bones, coins are common foreign bodies in the throat encountered by Otolaryngologist in their day to day practice, but a large mango seed as a foreign body in the pharynx is rarest of the rare. We report a case where a whole large mango seed accidentally entered the throat of a 70-year-old male, where it became lodged causing throat pain, dysphagia and respiratory distress due to pressure effect over the trachea. The mango seed was removed as an emergency procedure.

[J Indian Med Assoc 2019; 117(12): 26-7 & 29]

Key words: Foreign body, mango seed, esophagus, esophagoscope.

Foreign body impaction in upper aero digestive tract frequently encountered in Otolaryngological practice. Various kinds of foreign body impactions have been reported of which coins, buttons, batteries and metal artifacts are commonly encountered foreign bodies in the pediatric age group, while dentures and bones are more common in adults. Accidental impaction of a large mango seed is a very rare foreign body to be encountered by the Otolaryngologist. We report one such rare case of accidental large mango seed impaction in the pharynx with its presentation and complications. From the review of literature we have come across two similar case reports and we report this as most unusual case of foreign body in an adult.

CASE REPORT

A 70 year old man presented to the casualty department of MGM Medical College & LSK Hospital, Kishanganj on 12-06-2013 with history of accidental ingestion of a large mango seed 4 hrs back followed by severe pain, complete inability to swallow food or water and increasing respiratory distress.

Examinations — A hard foreign body could be palpated in the left side of neck. The mango seed was transversely impacted. On indirect laryngoscopy- there was pooling of saliva in left pyriform fossa. Patient was immediately taken to emergency operation theatre and general anesthesia was administered. On introducing the rigid esophagoscope a foreign body could be located in the left pyriform sinus lying transversely. The foreign body was firmly impacted. With conventional foreign body forceps, the foreign body could not be taken out. The anesthetist was asked to increase the dose of muscle relaxant which helped to rotate the foreign body manually by putting pressure on left side of the neck externally. The foreign body was realigned along the long axis of pharynx. Then from below upwards it was pushed manually from outside. With the gradual manipulation, this large foreign body could be disimpacted in the hypo pharynx. Esophagoscope was withdrawn & the foreign body

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could be taken out with the help of anesthetic laryngoscope & Magill's forceps. On removal, this foreign body was found to be a large mango seed measuring - 7cm x 4cm. Thorough suction of the pharynx was done to remove any residual debris. Minor abrasions was noted over the pharyngeal mucosa. The endotracheal tube was withdrawn after reversal of anaesthesia. The patient was immediately placed in left lateral position and ventilated with 100% oxygen with mask for five minutes. Patient was further observed for ten minutes for any stridor and then shifted to the ward. A post extraction X-ray soft tissue neck lateral view showed normal pharyngeal contour without any parapharyngeal gas shadow (Fig 1). Patient was free of symptoms and was then given oral liquids which he could swallow with slight discomfort, oral analgesics and a prophylactic antibiotic course was given and patient was discharged the following day.

The case was a challenging one because it was an unusual presentation of an unusual foreign body (Fig 2). So in this kind of situation innovation and resourcefulness of surgeon & anesthetist are of paramount importance. A thorough search of the medical literature was done by us and we came across two reported articles of mango seed impaction and such an unusual foreign body is thus being reported



Fig 1 — X-ray soft tissue neck lateral view showing a shadow in front of c4-c6 vertebra



Fig 2 - Intra-op picture of the patient following induction of general anesthesia for removal of the foreign body

for its rarity with advice on preventive measures (Fig 3).

Prior to submitting this paper for publication, approval of the ethical committee was duly obtained from the institution authority. DISCUSSION

Foreign body impaction is a commonly encountered ailment in otolaryngological practice. Historically foreign impaction have been reported in mummies. In ancient India around 6th century BC among the various practices of pursuit of death by the Ajivika monks to achieve salvation one such practice was voluntary choking oneself by ingesting mango seed (Barua).

Accidental foreign body ingestion is a common occurrence in the pediatric age group but is also seen in the edentulous elderly subjects who report with various kinds of foreign bodies like denture impaction, meat balls, meat bones and large food bolus. Masood and Irshad in their series of 186 cases reported an incidence of 16.67% of foreign body impaction in the elderly age group. Foreign bodies are most frequently encountered in the pediatric age group in whom coins are most common objects ingested accidentally. Seeds are more frequently reported as tracheobronchial foreign bodies in pediatric age group (Endican S). Mango seed impaction in the pharynx was reported by Masood et al Sajid et al in their study of 50 pharyngoesophageal foreign bodies reported another case of mango seed impaction.

Metallic foreign bodies like coins, metal artifacts and toys are most common types of foreign bodies that are seen in the pediatric age group worldwide. Multiple foreign bodies (coins) have been reported by Isser and unusual metallic foreign bodies like wrist watch dial, toy key and metallic end of ball point pen were reported by Jagade. Sarkar et al reported maximum incidence of foreign bodies in throat of which coins, ear rings, chains, were reported fish bones being commonest from a report of foreign bodies from a teaching hospital in Eastern India. Koempel and Hollinger reported an incidence of 84% incidence of foreign bodies in children under 5 years of age the cause being attributed to the curiosity of child to explore the surrounding world with their mouth and also to poorly developed swallowing muscles and posterior dentition. History of foreign body impaction was present in all cases and most patients presented early for symptoms to the hospital with few exceptions



Fig 3 — Mango seed being removed from esophagus

of asymptomatic cases who after few choking and coughing bouts remained largely asymptomatic hence did not seek immediate medical advice. Incidence of foreign body impaction was more in males from rural population. The most common site of impaction was at cricopharyngeal junction, dysphagia being the most common symptom (Masood et al), followed by chocking and cough bouts, neck pain and tenderness. Koempel et al reported that despite advances in prevention, first aid techniques and advanced anesthesia incidence of foreign body impaction still remain a diagnostic and therapeutic challenge especially in the pediatric age group and the early suspicion and prompt diagnosis remains the key to successful management of these cases. Sumanta K dutta reported a case of growth retardation due to long retained foreign body in the oesophagus in an 8 years old child which was removed by thoracotomy.

Radiographs of the neck and chest often show radio opaque foreign bodies like metallic objects and meat bones, meat balls often show on the skiagram as vague opacities with surrounding air shadow. Negative radiological evidence is not a reliable diagnostic aid and positive history of foreign body along with persistent symptoms are strong indicators for suspicion and endoscopy must be done in these patients to conform the diagnosis.

Rigid endoscopy can lead to iatrogenic trauma in patients while foreign body extraction especially in old retained foreign bodies with surrounding luminal wall inflammation. Proper anesthesia and muscular relaxation and use of appropriate grasping forceps is of paramount importance in successful atraumatic removal of foreign bodies.

Sajid et al reported one case of mango seed impaction in post cricoids area in an edentulous elderly male with dysphagia and respiratory distress which could be removed successfully.

In our case the patient was an elderly edentulous male patient coming from rural area who had accidental impaction of mango seed in the pyriform sinus with chocking episodes and dysphagia and progressive respiratory distress. The case was managed successfully due to early presentation and prompt surgical intervention in the emergency operation theatre without any loss of time for radiological investigations. Preventive measures in these type of cases need to discourage the rampant common rural practice of joyfully sucking ripe mangoes during summer (a season for mangoes in this part of continent) frequently churning out the juice by gobbling the whole fruit in the mouth which hazards such accidental ingestion of mango seed.

ACKNOWLEDGEMENT

The authors are grateful to the Director (Dr Dilip Jaiswal); the Academic Director (Dr PK Mukherjee) and HOD of the Department of ENT and Head & Neck Surgery (Dr BK Bhattacharjee) for kindly

Case Report

Kaposiform Hemangioendothelioma in an adult — A case report

Surbhi Rajauria¹, Ramesh C Purohit²

Kaposiform Hemangioendothelioma is a rare vascular neoplasm that previously has been described in infancy and early childhood. It has rarely been observed in head and neck region. We report a case of nineteen year-old female who developed a lesion in superficial soft tissue of lateral aspect of neck. Tumor size was 1.8x1.8x1.5cm. Clinically, diagnosis of accessory thyroid was given. Histologically, it was involving the lymph node. Immunohistochemistry was positive for CD31 and negative for CD34. A diagnosis of Kaposiform Hemangioendothelioma was given.

[J Indian Med Assoc 2019; 117(12): 28-9]

Key words: Adult, Hemangioendothelioma, Kaposiform.

The term Hemangioendothelioma was introduced by Mallory in 1908 to include all tumor arising from blood vessels endothelium¹. Zuckerberg et al described it as an intermediate/borderline vascular neoplasm between a hemangioma and angiosarcoma². It is a locally aggressive rarely metastatic neoplasm, does not have tendency for spontaneous regression and has characteristic histopathological features, including tumor cell architectural pattern resembling a Kaposi Sarcoma³.

It is usually identified in infancy and first decade of life at sites like extremities and retroperitoneum and uncommonly in head and neck region. It is known for its association with lymphatic component namely lymphangioma/lymphangiomatosis and Kasabach Merritt phenomenon (KMP). At times, Kaposiform Hemangioendothelioma (KHE) can occur without KMP². It has not been documented primarily in the lymph node.

Herein, we present an extremely uncommon case of KHE in a lymph node unassociated with KMP and lymphangioma, in a nineteen year-old female.

CASE REPORT

A nineteen year-old female presented with swelling neck (?) Lymph node (?) Accessory thyroid clinically diagnosed as accessory thyroid on lateral aspect of neck.

Pathological findings — On gross, a grey brown nodular soft tissue piece was measuring 1.8x1.8x1.5cm. External surface was smooth to rough. Cut surface grey brown tan with central cystic space 1 cm in diameter filled with (?) blood.

Histologically sections from different areas of the specimens were studied. Sections predominantly revealed partial effacement of lymph node with a few remnant follicles. There was vascular proliferation along with nodules showing proliferation of endothelial cells and malignant cells having vesicular nuclei and showing spindling at many places (Fig 1). Tumor cells exhibited the vasoformative slit like lumen. Extravasated blood, hemosiderin pigment lying free and in macrophages was seen (Fig 2). This picture was suggestive of Kaposi Sarcoma.

Department of Pathology, Dr S N Medical College, Jodhpur 342001 ¹DNB (Pathology), Senior Resident and Corresponding Author ²MD (Path & Bact), FICP, R P Diagnostic Centre, Jodhpur 342001 Patient's HIV status was negative. PAS stain was negative. Immunohistochemical staining of spindle cells revealed CD31+ve and CD34-ve. A diagnosis of Kaposiform Hemangioendothelioma was given.

DISCUSSION

Kaposiform Hemangioendothelioma (KHE) is a locally aggressive, immature vascular neoplasm, characterized by predominantly Kaposi sarcoma like fascicular spindle cell growth pattern.

Synonyms are Kaposi- like infantile hemangioendothelioma⁴, hemangioma with Kaposi sarcoma like features.

The tumor most commonly occurs in the retroperitoneum^{2,4} and the skin^{3,5} but it can also occur in the head and neck region⁶, deeper soft tissue of extremities of the trunk and extremities^{2,7}. No case of KHE primarily in lymph node has been reported except for a case of KHE in tonsil of child associated with cervical lymphangioma⁶.

KHE typically occurs in infancy and first decade of life, but adult cases are also recognized^{1,6,8}. Lymphangioma and consumption coagulopathy (Kasabach-Merritt Syndrome) may complicate the

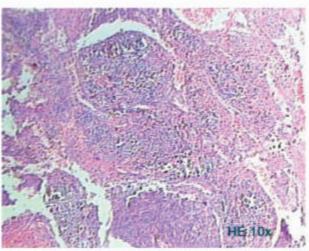


Fig 1 — Kaposiform Hemangioendothelioma (H & E Section): low power view (10x) showing nodular growth pattern of tumor cells.

larger tumor. Sometimes it may not be associated with Kasabach Merritt syndrome⁸. Soft tissue tumors are greyish to reddish multinodular and may coalesce and encase surrounding structures.

Microscopically, the tumor grow in the form infiltrative vague lobules separated by fibrous septa. It consist of criss-crossing spindle cell fascicles interspersed with slit like sieve like blood vessel^{4,6}, Nuclear atypia and mitotic activity are inconspicuous^{4,6}. Fibrin thrombi, in the capillaries and areas of haemorrhage and hemosiderin deposit were seen⁶. No known association with HIV infection or HHV-8 was seen.

In adults the differential diagnosis of KHE comprises especially Kaposi sarcoma and spindle cell hemangioendothelioma, further differential diagnosis include tufted hemangioma and cellular capillary hemangioma which occurs rarely in adults⁶.

Immunohistochemical staining in spindle cells were positive for CD31 and negative for CD34. In our case, patient's HIV status was negative though Immunohistochemistry for HHV-8 was not done.

To conclude, KHE is an uncommon tumor with a distinct clinicopathologic features, including IHC profile and differs from a Kaposi Sacroma and other

histological mimics. Careful attention towards its histopathological features coupled with IHC, is helpful in its identification, especially at rare sites like lymph node.

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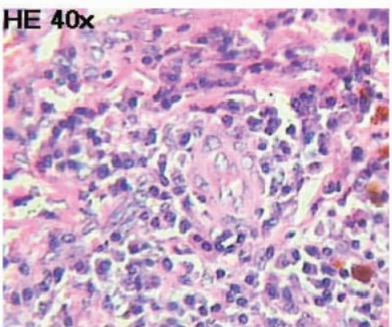


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permitting us to use hospital records for publication of this case report.

Conflict of Interest: The authors declare that there is no conflict of interests regarding the publication of this paper

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ABBREVIATIONS USED

(C) Correspondence; (CR) Case Report; (DTR) Drug Trial Report; (Ed) Editorial; (GEd) Guest Editorial; (OA) Original Article; (OS) Observational Study; (PCME) Pictorial CME; (RA) Review Article

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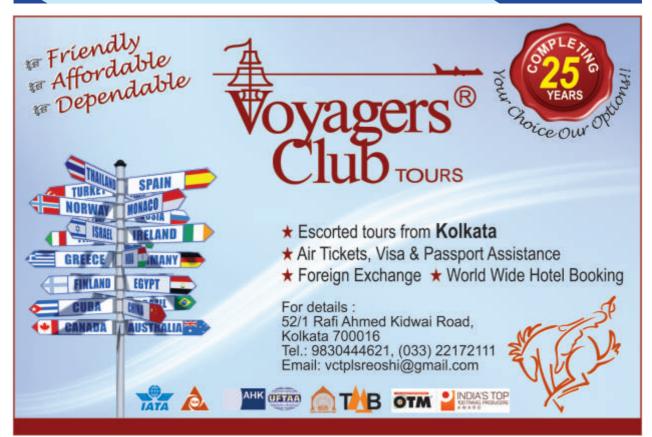


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Date of Publication: 15th December, 2019

Registration No. KOL RMS / 476 / 2017-19

RNI Regd. No. 2557/1957 VOL. 63, NO. 12, December 2019, Kolkata

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Printed and Published by Dr Sanjoy Banerjee on behalf of Indian Medical Association and printed at Prabaha, 45, Raja Rammohan Sarani, Kolkata 700009, and Published from Sir Nilratan Sircar IMA House, 53 Sir Nilratan Sarkar Sarani (Creek Row), Kolkata 700014. Editor: Dr Golokbihari Maji