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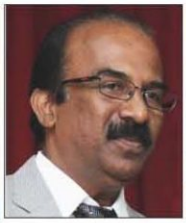
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[1]International Committee of Medical Journal Editors—Uniform Requirements for Manuscripts Submitted to Biomedical Journals. *JAMA* 1997; **277:** 927-34.

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[1]Cogo A, Lensing AWA, Koopman MMW, Piovella F, Sivagusa S, Wells PS, *et al* —Compression ultrasonography for diagnostic management of patients with clinically suspected deep vein throm-bosis: prospective cohort study. *BMJ* 1998; **316:** 17-20.

Reference from Book :

[2]Handin RI — Bleeding and thrombosis. In: Wilson JD, Braunwald E, Isselbacher KJ, Petersdorf RG, Martin JB, Fauci AS, *et al* editors—Harrison's Principles of Internal Medicine. Vol 1. 12th ed. New York: Mc Graw Hill Inc, 1991: 348-53.

Reference from Electronic Media :

[3]National Statistics Online—Trends in suicide by method in England and Wales, 1979-2001. www.statistics.gov.uk/downloads/ theme_health/ HSQ 20.pdf (accessed Jan 24, 2005): 7-18.

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Editorial

Robots in Surgery

— **Sanjoy Banerjee**
Hony Editor, JIMA

The field of Robotics has entwined with the human life in various form since long. Since past 40 years, the robots, which are programmable machines that can perform human actions[1], have also made their place in the surgical field of medical science, helping us provide better healthcare.

The first robot assisted surgery was performed by Kwoh, *et al* for neurosurgical (brain) biopsy in the year 1985 using the **PUMA 200** robotic platform, followed by the use of the platform by Davies, *et al* to perform Transuretheral Resection of Prostrate (TURP), which ultimately led to the development of **PROBOT** while in 1992, **ROBODOC** surgical system was designed for utilization in prosthetic hip placement[2]. The need and the rise of Robotic Surgery (RS) can be mainly attributed to it's advantage of telepresence – this feature can be used by military to operate on the injured in battle fields and remote areas even when the surgeon is physically absent, thereby reducing mortality and morbidity. In 1989, a company named Computer Motion, to fulfill this goal , developed the Automated Endoscopic System for Optimal Positioning (**AESOP**) robotic platform which allowed the surgeons to voice control the placement of laparoscopic cameras. Later modifications resulted in the system being re-launched as the **ZEUS** operating system. At about that time, Intuitive Surgical released the SRI Green Telepresence system, which later underwent many modifications to form the early version of the current da Vinci® system.

There are three types of robotic systems being used in surgery - active , semi active and the master slave system[2]. Active systems work autonomously (while remaining under the control of the surgeon) and undertake pre-programmed tasks like the PROBOT and ROBODOC platforms. Semi-active systems allow for a surgeon-driven element to complement the pre-programmed element of these robot systems. Formal master–slave systems like the da Vinci and ZEUS platforms lack any of the pre-programmed elements and are entirely dependent on surgeon activities which are reproduced intracorporeally by the robot.

The **da Vinci Surgical system** is the robotic platform which is being globally currently was approved by the USFDA in 2000. It is a master-slave platform, with following features - **ENDOWRIST** technology for maneuvering different surgical instruments, having seven degrees of freedom, binocular lens and camera which magnifies the 3D image and transmits it to the console. The **da Vinci Si** is the second generation (2009) of this technology, with enhanced image quality, and another additional surgeon console for training purpose or for a second surgeon to

participate in the surgery. The latest edition is the third generation of the robot namely **daVinci Xi** (2014).

RS has advantages over laparoscopy for its 3 dimensional magnified high definition view, improved ergonomics, improved precision and accuracy of dissection leading to less intra-operative blood loss, avoidance of factors like tremors[3]. Despite these many positive features, it also has certain disadvantages, absence of tactile sensation, increased cost of setup leading to it's limited availability, and requirement of a large sterile field as the robot is large. A lot of work is going on to overcome these disadvantages.

VerroTouch[4] is a haptic sensation system under development by Kuchenbecker et al which is an add-on system that attaches onto the da Vinci robotic system, which analyses high frequency accelerations in the robotic arm movements and processes these accelerations in real time. Vibrotactile feedback is then provided as a combination of both naturalistic high-frequency vibrations at the surgeon's hand controls and/or stereo sound. This system attaches to the arm of the robot, which allows it to be used in consecutive cases without being sterilised[5]. "Augmented vision" is another advanced feature which provides better and more precise images. Tracking systems are being developed to achieve real time overlay onto a surgical field by accounting for the dynamic movement of the target organ, allowing CT or MRI images to be superimposed on the surgical field [5]. **TilePro** is a three imensional navigation model which is used with da Vinci surgical system for radical prostatectomies . It reconstructs a 3D model of the TRUS visible histologically confirmed index cancer, which it superimposes with the actual lesion, and helps in better dissection during radical prostectomies.[6] Another advanced tracking system is the body- 'global positioning system' which predicts the ideal surgical plane before performing the actual surgical manoeuvre. A colour-coded zonal navigation model would then be overlaid on the surgical field to help achieve better oncological and functional outcomes. Using **Firefly** laparoscopic camera system with robots, one can use Indocyanin green and Fluorescein dye to visualize the lymphatic and vascular anatomy[7].

India got its first urologic robotic installation at the All India Institute of Medical Sciences, New Delhi, in 2006. This was followed by an unprecedented growth of robotic surgery in India. There are currently 66 centers and 71 robotic installations as on July, 2019, with more than 500 trained robotic surgeons in our country with more than 12,800 surgeries during this time[8]. Vast range of RS are happening – cholecystectomy, colorectal surgery, hysterectomy, radical prostatectomy, radical cystectomy, coronary artery bypass, hip replacement and even spinal surgery[3,8].

On January 27, 2022 , Science Direct reported that a laparoscopic surgery consisting of end to end anastomosis was performed by a robot on a pig, fully automated, without the guidance of a surgeon and the result was satisfactory. It was designed by John Hoopkins University researchers and named as Smart Tissue Autonomous Robot (STAR)[9] and is a step into the future. As science progresses and artificial intelligence becomes more and more incorporated in our lives, there will be more instances when the surgeon's hands will be replaced by the Endowrist of the robot. At present, RS is mostly present in the private hospitals of India and available for a limited section of the society, but we can all one day the robot shall cater to all the population.

Further Readings

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Original Article

Study of Prevalence of Vitamin B12 Deficiency and Hyperhomocysteinemia in Patients of Deep Vein Thrombosis

Mithun Vinod Barot[1], Jayeshkumar B Bagada[2], Rakesh A. Makwana[3], Gunvant H Rathod[4]

Background : Common condition encountered by surgeons are Pulmonary Embolism (PE) and Deep Venous Thrombosis (DVT). About one-third of individuals with symptomatic Venous thromboembolism have PE, whereas the remaining two-thirds exhibit DVT alone.

Aims and Objective : To assess the Serum homocysteine & serum Vitamin B12 levels in patients with DVT and to examine the influence of various risk factors on serum homocysteine levels and serum Vitamin B12 levels.

Material and Methods : It is a retrospective study conducted in Department of General Surgery, BJ Medical College and Civil Hospital, Ahmedabad from May, 2017 to September, 2018 including 20 Patients. Patients having a DVT diagnosis older than five years were included.

Results : Out of 20 patients, Hyperhomocysteinemia was present in 8(40%) and Vitamin B12 Deficiency in 9 (45%) patients. The mean age was 34.6 years & only one female patient (5%). Immobility was present in 6(30%), Smoking history in 8(40%), Cardiac Co-morbidity in 4(20%) Patients.

Conclusion : Hyperhomocysteinemia & Vitamin B12 Deficiency are potentially modifiable risk factors that must be considered when evaluating patients for DVT.

[*J Indian Med Assoc* 2024; **122(1):** 13-6]

Key words **: Deep Vein Thrombosis, Hyperhomocysteinemia, Vitamin B12 Deficiency.**

The development of a semisolid coagulum inside the venous system is known as venous thrombosis, which may affect the superficial system (often referred to as superficial thrombophlebitis) or the Deep Venous Thrombosis (DVT)[1].

According to estimates, the prevalence of DVT in the general population ranges from 80 to 100 per 100,000 yearly in western countries to 4-75 per 100,000 in South Asia[2]. Swelling and pain, particularly in the calf, are the most typical symptoms of a Deep Vein Thrombosis, which often affects one lower limb. Nevertheless, bilateral Deep Vein Thrombosis is frequent, occurring in up to 30% of cases.

The objective of the present research is to assess the Serum Homocysteine & Serum Vitamin B12 levels in patients with DVT and to examine the influence of various risk factors on serum homocysteine levels and serum Vitamin B12 levels (Fig 1).

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Editor's Comment :

- In Indian Scenario, in patients of Deep Vein Thrombosis, folic acid, pyridoxine and cyanocobalamin supplementation has shown significant reduction in incidences of Thrombosis.

Treatment for hyperhomocysteinemia depends on the underlying reason; however, Vitamin supplementation (with Vitamin B12, pyridoxine, and folic acid) is often successful in lowering homocysteine levels.

A ruptured Baker's cyst, arterial ischaemia,a thrombosed popliteal aneurysm,a ruptured plantaris muscle and a calf muscle haematoma are among the potential diagnoses for a DVT (Figs 2&3).

Pathophysiology :

There are a number of acquired risk factors for DVT, like surgery, cancer/cancer treatment or pregnancy, as well as genetic risk factors, like defects in protein C, protein S and antithrombin. Moreover, adaptable risk factors like hyperhomocysteinemia and obesity are notable from a preventative perspective.

There are multiple causes of hyperhomocysteinemia, such as vitamin deficiency (Vitamins B12, B6 and Folate), renal failure and many drugs, such as anticonvulsants and antihyperlipidemics, as well as physiological factors like advancing age or male gender, MTHFR gene polymorphism[3].

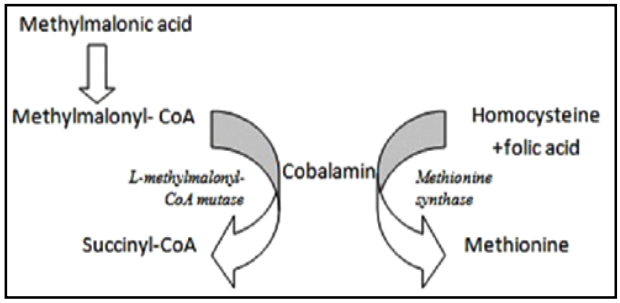

Fig 1 — Conversion of Homocysteine to Methionine

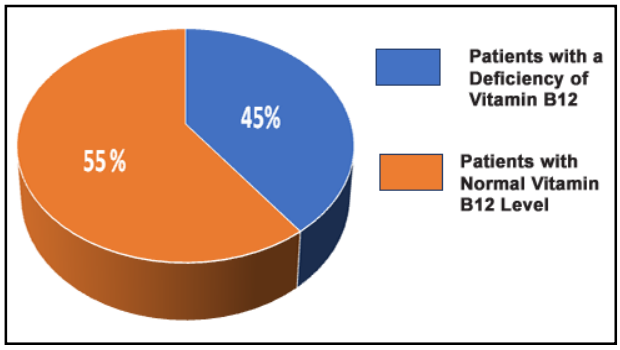

Fig 2 — Percentage of patients with Vitamin B12 Deficiency

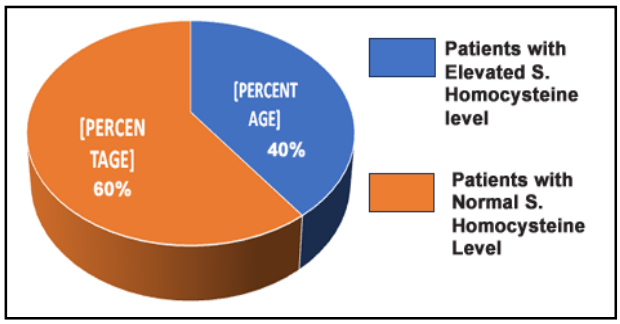

Fig 3 — Percentage of patients with Hyperhomocysteinemia

Vitamin B12 deficiencies are a common problem Worldwide. Chronic gastritis,Atrophic gastritis, Pernicious anaemia, Sjögren's syndrome, Vegetarianism, older people and chronic alcoholism, *Helicobacter pylori*-related gastritis, ileal resection and Post-gastrectomy, chronic pancreatic exocrine insufficiency, Crohn's disease, Small intestinal bacterial overgrowth, achlorhydria and coeliac disease, Oral contraceptive, Transcobalamin II deficiency, Drugs Metformin, hormone replacement therapy and pregnancy,histamine H2-receptor antagonists and proton pump inhibitors[4].

The three elements identified by Virchow more than a century ago continue to have a role in the onset of venous thrombosis. These are :

- blood contact with an abnormal surface (like endothelial damage);
- abnormal flow (such as stasis);
- abnormal blood (like thrombophilia).

Homocysteine is a sulphur-containing "amino acid" that is generated from the necessary amino acid methionine by demethylation.

In the above diagram, there is a requirement of Cobalmin& folic acid for the conversion of Homocysteine into methionine, in deficiency of Vitamin B12 & Folic acid, there is elevated Homocysteine which carries atherogenic propensity as a consequence of endothelial dysfunction and damage caused thrombus formation and platelet activation. Smooth muscle hypertrophy, elastic lamina degradation and Intimal thickening are three of the main processes of homocysteine-induced vascular injury.

The thrombus begins as a platelet cluster. The lumen of the vein wall is eventually blocked by a mesh made of fibrin and red blood cells. The coralline thrombus eventually develops into a loose red fibrin clot with many red blood cells. The clot may break off and travel as a pulmonary embolus to the lung since it is likely to continue up to the next big venous branch[3].

Homocysteine concentrations may be decreased by Folic acid alone or in combination with Vitamins B6 and B12. Normal plasma homocysteine levels return 4 to 6 weeks after starting medication, although they might return as soon as two weeks later[5].

Materials and Methods

This Retrospective Observational study was conducted in Department of General surgery, B J Medical College and Civil Hospital, Ahmedabad from May, 2017 to September, 2018 including 20 Patients.

DVT diagnoses in patients older than five years were included.

Exclusion Criteria :

- Patients with concurrent medication use (such as thiazide diuretics, isoniazide, carbamazepine, penicillamine, niacine, theophylline, L-Dopa, hormone replacement therapy, antiepileptics, Vitamin B12 and B6 antagonists, phenytoin, methotrexate) or conditions that could affect the blood level of homocysteine should be particularly careful.
- many co-morbidities (ie, hypothyroidism)
- inflammatory Bowel diseases and pernicious anaemia diseases
- respiratory insufficiency
- Sepsis was thoroughly eliminated from the research.

Demographic information, signs and results and the background of potential risk factors for Deep Vein

Thrombosis were noted. Deep venous "Doppler Ultrasonography" of the extremities is used to identify DVT.

Blood investigations (CBC, RFT, LFT, APTT, PT-INR), S Lipid Profile, S Vitamin B12, Serum. Homocysteine Electrocardiography, Chest X-ray, Echocardiography and screening of USG Abdomen-Pelvis were done. Kang, *et al* have categorized hyperhomocysteinemia as moderate (homocysteine concentration 15-30 mmol/litre), intermediate (greater than 30 to 100 mmol/litre) and severe (greater than 100 mmol/litre) based on concentrations obtained in fasting[3] (Tables 1&2).

Results

An overall of twenty patients with a mean age of 34.6 years who satisfied the inclusion criteria throughout the course of 16 months was engaged in the research.

Risk factors for the expansion of DVT were assessed. Detected risk factors were examined in 6 participants with DVT, 5 Patients had Surgery, and 1 Patient had Trauma.

Patients were treated with Standard treatment protocol Injection Unfractionated heparin 5000 IU/8 hourly for days and overlapped Tablet warfarin 5 mg once a day on the 4th day, continued for 6 months.

Regular Prothrombin Time-International Normalized Ratio was done.

Moderate Hyperhomocysteinemia in 4 Patients and intermediate Hyperhomocysteinemia in 4 patients was diagnosed. Nobody of the patients had a severe case of homocysteinemia.

A deficiency of Vitamin B12 was found in 9 (45%) patients.

Table 1 — *Comparative Studies*

	Present Study	Kamat, *et al*[7]	Kokturk, *et al*[8]
Males	95%	75%	39%
Females	5%	25%	61%
Immobility	30%	5.71%	29%
Diabetes Mellitus	10%	41.43%	17%
Hypertension	5%	37.14%	29%
Hyperhomocysteinemia	40%	31.42%	63%

Table 2 — *Various Parameters*

Parameters	Patient (n=20)
Age (Mean)	34.6 years
Sex (Female), n (%)	1 (5 %)
Symptoms at admission :	
Pain, n (%)	16 (80%)
Swelling, n (%)	4 (20%)
Pain and Swelling both, n (%)	16 (80%)
Fever, n (%)	2 (10%)
Immobility	6 (30%)
Smoking History, n (%)	8 (40%)
Systemic hypertension, n (%)	1 (5%)
Diabetes mellitus, n (%)	2 (10%)
Cardiac comorbidity, n (%)	4 (20%)
Serum urea, n (%)	1 (5%)
Total cholesterol, mg/dL n (%)	4 (20%)
Echocardiography, n (%)	4 (20%)
USG Abdomen-Pelvis, n (%)	1 (5%)
Upper-Limb Involvement, n (%)	2 (10%)
Elevated Serum Homocysteine, n (%)	8 (40%)
Vitamin B12 Deficiency, n (%)	9 (45%)

Discussion

In our study, there is a 40% prevalence of Hyperhomocysteinemia & 45% Prevalence of Vitamin B12 Deficiency out of 20 patients with DVT.

The mean serum Homocysteine level was 19.67 micromol/L and the average serum Vitamin B12 level was 345.35 pg/ml.

The baseline demographical characteristics, risk factors, clinical signs and laboratory results of the patients with DVT were similar when compared based on the prevalence of Hyperhomocysteinemia with the exception of total cholesterol levels, which were considerably greater and Vitamin B12 levels, which were substantially lower in patients with "Hyperhomocysteinemia".

Evidence for elastic lamina injury, intimal thickening and smooth muscle hypertrophy as one of the main processes of Homocysteine-induced vascular injury is rapidly emerging.

A further meta-analysis of twenty prospective trials observed that a 5-mmol per L rise in overall plasma homocysteine was linked to a 32% rise in the likelihood of developing ischemic heart illness and a 59% rise in the likelihood of suffering a stroke[3].

Although the exact processes behind this impact of homocysteine are yet unknown, the greatest evidence points to the involvement of oxidative stress and impaired nitric oxide.

Hyperhomocysteinemia and Vitamin B12 Deficiency are two clinically significant risk factors for venous thromboembolism that are considered to be modifiable. Normal levels vary greatly between different groups owing to the unique lifestyle variables that impact levels of plasma homocysteine, like nutrition, coffee use and smoking history.

According to Venous thromboembolism is independently correlated with Hyperhomocysteinemia and low Vitamin B levels: findings from the study of EDITH: Low serum folic acid and low Vitamin B12 levels have been found to be independently related with

venous thromboembolism in a hospital-based case-control analysis. However, the connection between low Vitamin B12 or low serum folic acid levels and venous thromboembolism is not entirely mediated by increased serum homocysteine[6].

Another previously mentioned risk factor for Hyperhomocysteinemia is growing older. Additionally, a number of lifestyle variables, including exercise, coffee use, protein intake and alcohol use which were not specifically examined in the research, could contribute to elevated Homocysteine levels.

Conclusion

The standard therapy for "Hyperhomocysteinemia" is folate supplementation, often with vitamin B12/B6. Hyperhomocysteinemia & Vitamin B12 deficiency is potentially modifiable risk factors that must be considered when evaluating patients for DVT. A large sample size is needed to study the prevalence of Vitamin B12 deficiency and Hyperhomocysteinemia.

Conflict of Interest : None

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Original Article

A Comparative Study on the Efficacy of Pregabalin Over Gabapentin in Controlling Neuropathic Pain due to Spinal Cord Disc Diseases in Bankura Sammilani Medical College and Hospital

Upasana Choudhury[1], Chirantan Banerjee[2], Riya Sural[3]

Background : Neuropathic Pain (NP) due to Spinal Cord Disc Diseases (SDD) have been treated extensively with medical therapy before surgery. Gabapentin (GBP) and Pregabalin (PGB) are anti-convulsants which have proved effective in controlling NP due to SDD.

Aims and Objectives : (1) To determine the efficacy of GBP and PGB individually in controlling NP due to SDD. (2) To compare their efficacy in doing so.

Materials and Method : This study was conducted among the patients with SDD in the Neurosurgery OPD of Bankura Sammilani Medical College & Hospital between April, 2023 to September, 2023 with 50 patients receiving GBP (600mg/day) tablets and another 50 patients receiving PGB (150mg/day) tablets, along with Amitriptyline (25mg/day) tablets and Multivitamin tablets (given to all).The pain scores were recorded according to the visual analog scale before the drug usage followed by at the end of 1st, 2nd and 3rd month after consumption of the drugs, along with their opinion on the action of the drug according to the Odom's criteria. The data were compared using paired 't' test in MS Excel and values <0.05 were considered significant.

Results : Among the patients receiving GBP, the mean pain score initially was 6.66±1.52 while after the administration of the drug, it decreased to 4.84±1.80, 4.14±1.64 and 3.52±1.42 at the end of 1st, 2nd and 3rd month respectively. Among the patients receiving PGB, the mean pain score initially was 6.78±1.33 while after drug usage, it decreased to 4.64±1.71, 3.74±1.58 and 3.16±1.58 at the end of 1st, 2nd and 3rd month respectively.

Conclusion : Both GBP and PGB are equally effective in controlling NP. PGB is more effective than GBP possibly owing to it's better pharmacokinetic profile.

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Key words **: Gabapentin, Pregabalin, Neuropathic Pain.**

Spinal Cord Disc Diseases (SDD) include degeneration of intervertebral discs which leads to pain in the back and the neck with radiating pain to the legs and arms respectively[1]. These SDD leads to central canal stenosis and/or foraminal stenosis, which causes entrapment of the nerve roots, leading to pain, numbess and tingling sensations to their respective areas as well as neurological deficits[2]. SDD is estimated to affect about 5 percent of the population in developed countries each year[1]. The annual incidence of an episode of Lumbosacral Disc Disease (sciatica) ranges from 1 to 5%[3]. These diseases incur a huge financial and social cost for the country as well as causes emotional sufferings.

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Editor's Comment :

- Both GBP and PGB are effective in producing significant relief of neuropathic pain. However, due to certain pharmacological advances, PGB is more effective than GBP.

Initially all SDD are managed by medical and physical therapy. Medical therapy includes the usage of NSAIDS, analgesics like tramadol, morphine, epidural inoculation of corticosteroids and transforaminal periradicular injections of corticosteroids[4], use of stimulated form of methylcobalamine (Vitamin B_{12})[5] along with physical therapy, behavioral therapy and multidisciplinary treatment have shown promising results. However, for patients for whom medical therapy has failed and have presented with neurofocal deficits, surgery in the form of discectomy and laminectomy is attempted.

Gabapentin (GBP), an analog of the c amino butyric acid (neurotransmitter) and Pregabalin (PGB) a lipophilic GABA analog are anticonvulsants which binds with the $\alpha 2\delta$ subunit of the voltage gated calcium channels have proved to be efficacious in the management of the Neuropathic Pain (NP). They

decrease the release of neurotransmitter associated with central sensitization[6].

Despite being similar in action, they have some differences in their pharmacokinetics and pharmacodynamics. There have been many individual studies exploring the effects of only GBP or only PGB on their efficacy in controlling NP. However, there are only a few studies comparing the effectiveness of GBP and PGB on NP. Also, PGB is newer drug in this field of pain relief, through this study we shall explore the effectiveness of the drug.

Aims and Objectives

(1) To assess the efficacy of PGB and GBP individually in contolling NP due to Spinal Cord Diseases.

(2) To compare the efficacy of PGB with GBP in contolling NP due to Spinal Cord Diseases.

Materials and Method

This is an institution based prospective study carried out among patients in the Out Patients Department (OPD) of Neurosurgery of Bankura Sammilani Medical College and Hospital between April, 2023 to September, 2023 with final sample size of 100 patients, 50 each in 2 groups.

Inclusion Criteria : All patients between the ages 18 and 70 suffering from SDD with the complaint of NP.

Exclusion Criteria for Patient Selection : (1) Having already received either PGB or GBP for treatment of SDD in the past.

(2) Receiving GBP or PGB as part of treatment of other diseases like epilepsy, anxiety.

(3) Motor deficits like drop foot, claw hands etc.

(4) Have underwent surgery for Spinal Cord Diseases or are planning to undergo surgery for the same.

Data Collection : The patient on being diagnosed (through clinical and radiolological methods) with NP due to SDD, had their pain assessed after informed consent. The patients were put into two groups by simple random sampling. One group was started on GBP, at a dose of 300 mg twice a day; while the other group was put on PGB, at a dose of 75 mg twice a day. Both groups were given Amitriptyline 25 mg/day and multivitamin.

Assessment of Pain : The pain was assessed on the very first visit of the patient, followed by after consumption of PGB or GBP at the end of each for 3 months by using Visual Analogue Scale (Table 1)[7] and Odom's Criteria (Table 2)[8].

Data analysis was done using means, median and standard deviation. The pre-treatment and post-treatment scores were compared by paired 't' test. Any p value <0.05 was considered significant. The data was represented via tables and charts. For determining which drug is more effective, head to head comparison method was used. All the calculations have been done in MS Excel version 2007.

Results

The age distribution of the patients receiving GBP and PGB is represented in the Table 3 (below). The mean age of the patients receiving GBP is 45.56 ± 13.44 years while the mean age of the patients receiving PGB is 44.24±11.18 years.

The number of male and female patients receiving GBP were 25 each.

The number of male patients receiving PGB were 27 while the number of female patients receiving PGB were 23.

Among the patients receiving GBP, the mean score for pain before its administration was 6.66±1.52 while after the administration of the drug , the mean scores for pain were 4.84±1.80, 4.14±1.64 and 3.52±1.42 at the end of 1st, 2nd and 3rd month respectively. When compared with paired t test , all the reduction in pain was found to be significant as shown in Table 4. There were 5 patients who had no reduction in pain despite using the drug for 3 months, while 2 patients had nearly complete (pain score <2) remission of pain at the end of 3 month. The number of patients who considered the drug to be good or excellent (Odom's criteria 1 and 2) at the end of 1st month was 21 which increased to 28 and 36 at the end of 2nd and 3rd month respectively. Table 5 shows the trend of working of the drug according to Odom's Criteria.

Among the patients receiving PGB, the mean score for pain before the administration was 6.78±1.33 while after the administration of the drug , the mean scores for pain were 4.64±1.71, 3.74±1.58 and 3.16±1.58 at the end of 1st, 2nd and 3rd month respectively. When compared with paired 't' test, all the reduction in pain was found to be significant as shown in Table 2. There were 1 patients who had no reduction in pain despite

Table 1 — *The Visual Analog Scale for Assessment of Pain*

0	1	2	3	4	5	6	7	8	9	10
No pain		Mild Pain (Annoying)		Moderate Pain (Uncomfortable)		Severe Pain (Dreadful)		Very Severe Pain (Horrible)		Worst Pain (Agonizing)

Table 2 — *The Odom's Criteria*

Rating	Description	Criteria
1	Excellent	Completely relieved of symptoms and daily lives and occupation not impaired
2	Good	Intermittent discomfort but no interference in occupational activities
3	Fair	Subjective improvement but physical activities still significantly limited
4	Poor	No improvement or symptoms had deteriorated

Table 3 — *The Distribution of Patients in the Different Age Groups*

Age Groups (in years)	Number of Patients Receiving GBP	Number of Patients Receiving PGB
18 - 30	8	5
31 - 40	10	13
41 - 50	13	12
51 - 60	12	17
>60	7	3

using the drug, while 6 patients had nearly complete (pain score <2) remission of pain at the end of 3 month. The number of patients who considered the drug to be good or excellent (Odom's criteria 1 and 2) at the end of 1st month was 31 which increased to 42 and 43 at the end of 2nd and 3rd month respectively.

Discussion

Antiepileptic drugs like GBP and PGB were reported to produce significant pain relief as compared to placebo and achieved significant improvements in Quality of Life in patients with postherpetic neuralgia, painful diabetic neuropathy and postsurgical pain.[9] Analgesic action of GBP is owed to its indirect interaction with the glycine binding sites of the NMDA receptors while PGB decreases the release of excitatory neurotransmitter Glutamate by decreasing the calcium influx after binding to the voltage gated calcium channels leading to decreased AMPA receptor activation[9]. Randomized Clinical Trials (RCTs) that administered GBP for chronic pain reported that with a daily dosages of up to 3600 mg, there was significant pain reduction compared with a placebo in patients with mixed NP syndromes while those trials where

Table 5 — *The Ratings of the Patients According to Odom's Criteria Regarding the Working of the Drugs*

Drugs	Median Rating at the end of 1st Month	Median Rating at the end of 2nd Month	Median Rating at the end of 3rd Month
GBP	3 (fair)	2 (good)	2 (good)
PGB	2 (good)	2 (good)	1.5 (good to excellent)

PGB was administered showed effective pain control at a daily dose ranging from 50 to 300 mg[10].

GR Grice and MK Mertens, in 2008[11] reported of two cases where GBP had shown to reduce NP due to sciatica within a couple of days of starting the drug when hydrocodone-acetaminophene had failed. It also mentions an open labeled trial where the pain relieving efficacy of GBP was evaluated in controlling centrally mediated pain and peripherally mediated pain and tremors[12], where it proved to reduce the latter significantly.

According to an article review by Noor M Gajraj in 2007,[13] certain advances in the pharmacology of PGB may have led to the increased efficacy of PGB over GBP in this study. PGB binds to the $\alpha_2\delta$ subunit of voltage gated calcium channels just like GBP. However, it's binding affinity and potency for the above mentioned receptor is six times more than GBP. Unlike GBP, PGB has a linear pharmacokinetic profile as absorption of PGB is not saturable. It's peak concentration reaches within 1 hour with a bioavailability of 90%; while the peak concentration of GBP reaches between 2-3 hours and has a bioavailability of 27-60%. PGB does not bind to any plasma protein. Time to reach the effective dose is 1 day for PGB, while it is 9 days for GBP. According to L Gianesello[14], patients who have been treated with PGB in the pre-operative period require less opioids and have improved Quality of Life 3 months after spinal surgery.

K Robertson[15] and co in their article review explored the efficacy of PGB and GBP in controlling NP by considering various RCTs that had been conducted with these drugs. One specific review from their article was the NICE UK[16] guidelines which stated PGB better than GBP in controlling NP because of its lower NNT

Table 4 — *The Mean Scores for Pain Before and After the Usage of the Respective Drugs*

Drugs	Mean Score for pain before usage of the drug	Mean Score for pain after usage of the drug at the end of 1st month	P value	Mean Score for pain after usage of the drug at the end of 2nd month	P value	Mean Score for pain after usage of the drug at the end of 3rd month	P value
GBP	6.66±1.52	4.84±1.80(18.2%)	<0.05	4.14±1.64(25.2%)	<0.05	3.52±1.42(31.4%)	<0.05
PGB	6.78±1.33	4.64±1.71(21.4%)	<0.05	3.74±1.58(30.4%)	<0.05	3.16±1.58(36.2%)	<0.05

The mean scores at the end of each month were compared with the mean score before the usage of the drug using paired 't' test. All the p values which are in bold are significant.
The numbers in the simple brackets show the percentage of pain reduction at the end of each month with respect to before the beginning of the trial

values from meta-analysis, simpler dosing schedule and titration regimen and its cost effectiveness. Another trial which has been mention in this review, is by Pinto, *et al*[17] which showed positive results in reducing NP significantly by GBP but didn't comment on the efficacy of PGB.

According to Saxena, *et al*[18], the treatment approach to neuropathic pain in Indian set up has oral Gabapentinoids (GBP and PGB) as first line of therapy[19]. It was recommended that PGB to be initiated at 50 mg/day and titrated up to 75 mg/day to a maximum of 450 mg/day in two divided doses, while for GBP, the initiating dose was 100 mg/day thrice daily to a maximum of 1800 mg/day in divided doses. A double blinded placebo controlled RCT in New Delhi compared PGB, GBP, amitriptyline and placebo only to find PGB to stand out in controlling NP[20].

However, this study has limitations. The sample size is small and is only limited to patients attending the place of study presenting with chronic NP with no restrictions in motor functions. Secondly, the doses of GBP and PGB have been fixed to 600 mg/day and 150 mg/day – since both the drugs cause significant pain reduction, it can be speculated, that GBP may be better than PGB in higher doses; but such evaluations have not been done. Thirdly, the adverse effects of either of the drugs have not been recorded. Fourthly, this being a study in a government hospital all the drugs that were given to the patients were free of cost. For a drug to be considered better than the other drug, both the adverse effects of the drug and the cost effectiveness of the drug according to it's dosing schedule should also be considered.

Conclusion

In our study, PGB appears to be marginally better than GBP, but further studies with larger subjects is needed to prove or disprove this. As of now, we can say both drugs reduces NP significantly.

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Original Article

Nasal Carriage of Methicillin-resistant *Staphylococcus aureus* (MRSA) among Health Care Workers Working in Intensive and Critical Care Units at a Teaching Hospital in North India

Mousumi Kilikdar[1], Nirmalya Saha[2], Mohan Kumar R[3], Zainab Rehman[4]

Background : Methicillin-resistant *Staphylococcus aureus* (MRSA) is a form of the bacterium that is one of the most common causes of nosocomial infections because it travels quickly from one hospitalized patient to another through the hands, clothes and equipment of medical personnel. Methicillin-resistant *Staphylococcus aureus* (MRSA) may be prevented from spreading by identifying and isolating healthcare personnel who have been colonized.

Objective : We conducted this study to assess the incidence of MRSA among Health Care Workers (HCWs) working in the Intensive and Critical Care Units (ICCU) at our hospital.

Material and Methods : During the research period of 6 months, from 150 healthcare personnel working in the ICCU at RMRI, Bareilly, nasal swabs were collected.

Standard methodology was used to identify *S aureus*. Modified Kirby-Bauer disc diffusion technique was used to test the bacteria for antibiotic resistance. A Cefoxitin 30 mcg disc was used to identify MRSA and the data were analyzed in accordance with CLSI recommendations.

Results : MRSA carriage rate was 14% among the healthcare professionals, with the highest rate among nursing staffs (57.1%). MRSA isolates were 100% resistant to Cefoxitin and Amoxyclav, 53.9% to Cotrimoxazole, 61.5% to Erythromycin and 42.3% to Clindamycin.

Conclusion : The most effective methods of reducing the prevalence of MRSA among HCWs may be screening and decolonization. To reduce the prevalence of either carriage or transmission, medical institutions should implement strict infection control procedures.

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***Key words* : MRSA, Nasal Carriage, Health Care Workers.**

Antimicrobial resistance is a worldwide issue, but it is particularly worrying among nosocomial infections. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a type of *S aureus* that is resistant to a wide variety of antibiotics, including Penicillin, Cephalosporins and Carbapenems[1]. One major link between hospitals and the population that might lead to nosocomial infections is the presence of colonized healthcare personnel[2]. Patients may get MRSA from one another or from healthcare personnel via direct contact or contaminated surfaces in hospitals[3].

MRSA nasal carriage prevalence estimates vary from 0.8 to 3.0 percent in the general population and 6 to 17.8 percent among Healthcare Workers[4].

Infection with MRSA is linked to higher rates of morbidity and death as well as to the need for antibiotic treatment that must be continued for a longer period of time, higher healthcare expenses and longer stays in the hospital[5].

Editor's Comment :

- Health Care Workers (HCWs) can be a potential source of spreading Methicillin-resistant *Staphylococcus aureus* (MRSA) infection to patients. Hence, regular MRSA screening among HCWS should be done and implemented in hospital infection control programme.

The Methicillin-resistant Staphylococcal strains are resistant to many antibiotic classes, including beta-lactams as well as Aminoglycosides, Macrolides, Lincosamides and Tetracyclines but still sensitive to Vancomycin, Teicoplanin, Linezolid, Rifampin and Quinolones. Patients with severe MRSA infections often start with Vancomycin as their mainstay of treatment. As a consequence of the increased usage of this antibiotic *S aureus* strains with reduced susceptibility to Vancomycin has emerged[6].

Hence, the study was done in our hospital to investigate the prevalence of MRSA in the staff working in Intensive and Critical Care Unit (ICCU).

Material and Methods

Place of the study : Department of Microbiology,

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Rajshree Medical Research Institute and Hospital, Bareilly.

Study design : Cross-sectional, descriptive, hospital based study.

Study period : Six months from 01/March/2022 to 30/Sep/2022.

Sample size :

$N=Z^2 P (1-P)/ E^2$

Z=Standard normal variate, P=Prevalence rate, E=Absolute error, N=Required sample

Prevalence of MRSA among HCWs in India was 11.43% from Rongpharpi, *et al*[7].

Here, Z=1.96 at 95% confidence interval, P=11.43%, E=5%

N= (1.96 x 1.96) x 0.1143 x (1-0.1143)/ (0.05x 0.05)

N = 155 with 95% confidence level and 5% absolute precision.

Therefore, calculated sample size is approx. 150 patients.

Study population :

Inclusion criteria : Health Care Workers (Doctors, Residents, Nursing Staffs, Nursing Students, Technicians and Housekeeping staffs) working in the management of patients in the ICCU were included in this study.

Exclusion criteria : Healthcare workers with upper respiratory tract infection, on any antibiotic therapy or unwilling to participate were not eligible for this study.

Enrollment of HCWs :

Healthcare professionals were enlisted after receiving their signed informed permission. Particulars of the HCWs ie, their sex, age, occupation, hospital working time at ICU were collected with standardized proforma. The research was allowed to proceed after approval from the institution's ethical review board.

Nasal Swab Collection :

Both anterior nares were scrubbed with sterile swab using the conventional rotating method to obtain sample. The swabs were first wet with sterile physiological saline. Patients were told to insert the swab's tip into one nostril and spin it three times against the nasal mucosa. The second nostril was cleaned with the same cotton swab and it was kept inside a sealed plastic container. The plastic tube was transported to the microbiology lab for bacteriological investigation after being appropriately labelled.

Culture and Identification :

Less than two hours were needed to process a sample. After swab samples were inoculated into mannitol salt agar (MSA) and blood agar plates, it required 18 to 24 hours of incubation at 37ºC.

Standard techniques were used to determine the growth of *S aureus* by analyzing the colony morphology, appearance of the bacteria in gram stained smears under the microscope, the results of a catalase test, slide and tube coagulase test.

Antimicrobial Susceptibility Testing:

After isolating *S. aureus* strains, we used the modified Kirby-Bauer technique to test them for Methicillin susceptibility which included inoculating discs of Cefoxitin (30 µg) onto Mueller-Hinton agar (MHA) at 35°C overnight with an inoculum density equal to McFarland's 0.5 standard (1.5×10^8 CFU/ml) of the isolates. Isolates were identified as MRSA strains if their inhibitory zone diameters were less than 21 millimetres[8].

All *S aureus* isolates were tested for antibiotic susceptibility by modified Kirby-Bauer technique using Amoxicillin/Clavulanic acid (20/10 µg), Ciprofloxacin (5 µg), Ceftriaxone (30 µg), Cotrimoxazole (23.75/1.25 µg), Erythromycin (15 µg), Gentamicin (10 µg), Linezolid (30 µg), Penicillin (10 units), Teicoplanin (30 µg) and Clindamycin (2 µg). Sensitivity to Vancomycin was tested by E strip. While performing antibiotic susceptibility testing, *S aureus* ATCC 25923, MRSA ATCC 29213 and MSSA ATCC 33591 were employed as controls alongside the test strains[9]. According to latest CLSI recommendations, antibiotic sensitivity tests were carried out and the results were evaluated[10].

Results

Overall, 150 Healthcare Workers were screened for the study; 7 (4.6%) were specialists, 30 (20%) were Trainee/ resident doctors, 40 (26.6%) were staff nurses, 42 (28%) were nursing students, 5 (3.3%) were technicians, and 26 (17.3%) were housekeeping staff. The majority (108) of these people were female while the rest were male. Most of them were young adults (48%) between the ages of 25 and 35 (Table 1).

This study revealed that 14% (21/150) had MRSA in their noses, whereas 37.3% (56/150) carried *S aureus* (Table 2). The prevalence of MRSA among doctors was 28.5% (6/21) followed by nursing staff and students 66.6% (14/21) and housekeeping staff 4.7% (1/21) (Fig 1)(Table 2).

In area wise prevalence of MRSA isolates ICCU tops the list (23.8%), followed by CCU, MICU, SICU, NICU and PICU (Table 3).

Males had a carriage rate of 42.8% (9/21) whereas females had a rate of 57.1% (12/21). With respect to age, the largest frequency (47.6%, 10/21) was seen in those between the ages of 25 and 35. The highest rate of MRSA infection, 47.6% (10/21) was found in

Table 1 — *Characteristics of study participants*

Parameters		Number of Healthcare Workers No (%) N=150
Profession	Specialists	7 (4.6)
	Trainee doctors	30 (20)
	Staff Nurses	40 (26.6)
	Nursing students	42 (28)
	Technicians	5 (3.3)
	House keeping staff	26 (17.3)
Sex	Male	42 (28)
	Female	108 (72)
Age (in years)	<25	36 (24)
	25-35	72 (48)
	36-45	29 (19.3)
	46-55	8 (5.3)
	56-65	3 (2)
	66-75	1 (0.6)
	>75	1 (0.6)

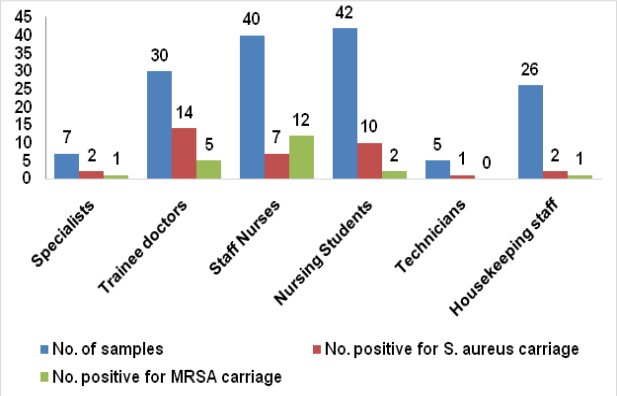

Fig 1 — Profession/cadre related distribution of *S. aureus* and MRSA carriage

Table 2 — *MRSA carriage status*

No of Healthcare Workers sampled	No positive for *S aureus*	No positive for MRSA
150	56	21

Healthcare Workers with 1-5 years of working experience in the hospital (Table 4).

Penicillin was efficient against 88.5%(31/35) of Methicillin susceptible *S aureus* isolates. Cefoxitin sensitivity was 82.8%(29/35). The sensitivity to Erythromycin, Co-trimoxazole, Ciprofloxacin, Amoxyclav, Gentamicin, Ceftriaxone, Clindamycin were 52.6%(18/35), 85.9%(30/35), 73%(26/35), 70.5%(25/35), 60.2%(21/35), 88.4%(31/35), 77%(27/35) respectively. All the *S aureus* strains were 100% sensitive to Vancomycin, Teicoplanin and Linezolid (Fig 3).

Among the MRSA isolates tested, 96.2% (20/21) were resistant to Penicillin. In this case, Cefoxitin resistance was at a staggering 100% (21/21). The resistance to Erythromycin, Co-trimoxazole, Ciprofloxacin, Amoxiclav, Gentamicin, Ceftriaxone, Clindamycin were 61.5%(13/21), 53.9%(11/21), 69.3%(15/21), 100%(21/21), 61.5%(13/21), 73%(15/21), 42.3%(9/21) respectively. The isolates were 100% sensitive to Vancomycin, Teicoplanin and Linezolid (Fig 4).

Table 3 — *Distribution of S aureus and MRSA among health care workers of different ICUs and critical care areas*

Areas	Total sample Number=150	MRSA Number=21	*S aureus* Number=56
ICCU	14	5 (23.8%)	18 (32.1%)
CCU	17	4 (19%)	9 (16%)
MICU	35	4 (19%)	4 (7%)
SICU	30	3 (14.2%)	2 (3.5%)
NICU	33	3 (14.2%)	2 (3.5%)
PICU	21	2 (9.5%)	1 (1.7%)

Table 4 — *Characteristics of MRSA carriers*

Parameters	No of Healthcare Workers sampled (N=150)	No positive for MRSA (%) (N=21)
Sex :		
Male	42 (28)	9 (42.8)
Female	108 (72)	12 (57.1)
Age :		
<25	36 (24)	5 (23.8)
25-35	72 (48)	10 (47.6)
36-45	29 (19.3)	4 (19)
46-55	8 (5.3)	2 (9.5)
56-65	3 (2)	0
66-75	1 (0.6)	0
>75	1 (0.6)	0
No of years of working in the hospital :		
<1 year	29 (19.3)	3 (14.2)
1-5 years	74 (49.3)	10 (47.6)
6-10 years	29 (19.3)	6 (28.5)
>10 years	18 (12)	2 (9.5)

Discussion

It is very difficult to detect MRSA carriage among healthy HCWs working in critical care areas. These apparently healthy MRSA carriers are one of the most important reasons for patient's extended hospital stay. Regular screening of Healthcare Workers and subsequent treatment until they test negative for MRSA will help to combat this situation. While *S aureus* colonization is most common in the anterior nares, it can also occur in other sites, including the Axilla,

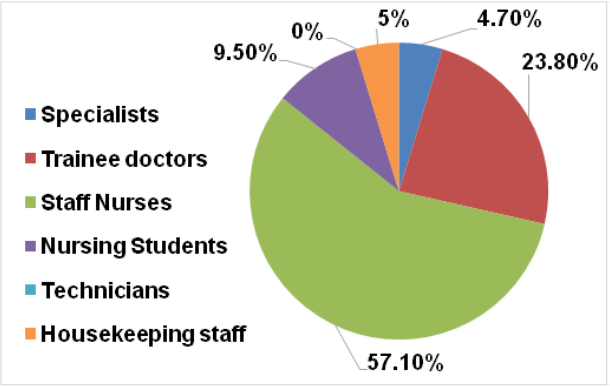

Fig 2 — Distribution of MRSA carriers

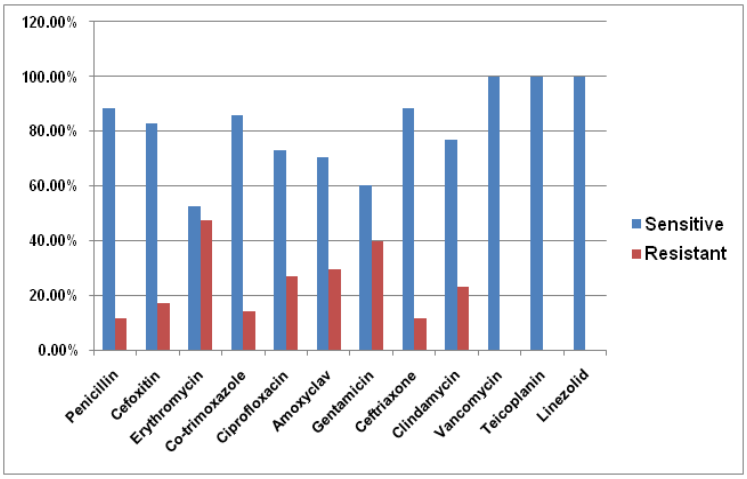

Fig 3 — Antibiotic susceptibility profile of *S. aureus* isolates

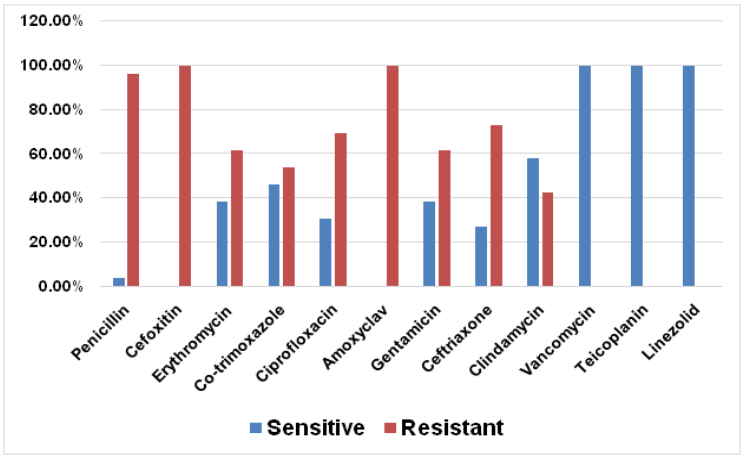

Fig 4 — Antibiotic susceptibility profile of MRSA isolates

Perineum, Throat and Gastrointestinal system[11].

Our research indicates that 14% of HCWs have the MRSA carriage. It's in line with the 5.8-17.2% range of MRSA transmission among hospital staff described by Shakya B, *et al*[12]. Although our findings are in concordance with those of previous research, they differ from those of 2006 study by Albrich, *et al*[13], which found that 4.6% of Healthcare Workers were infected or colonized with MRSA.

Our research found that the highest percentage of MRSA carriage was among nursing staffs (57.1%). The results of Shinde RV, *et al*[14] from Karad India, revealed that the nurses were the most prevalent carriers of MRSA transmission (34.61%). In contrast, Radhakrishna M, *et al*[15] found a negligible carriage incidence among nurses in Mangalore (2.7%).

In our research, females accounted for 57.1% of those infected with MRSA. Wesolowska, *et al*[16] found that the frequency was greatest among females (17.7%) in southern Poland. In contrast, the greatest frequency of MRSA (55.9%) was seen in men in a research done by Garoy, *et al*[17] in Asmara.

Caretakers with up to five years of experience had the greatest prevalence of MRSA carriage (47.6%). In a Saudi Arabian study, Al Humaidan, *et al*[18] found that Healthcare Workers with 4-6 years of experience had the greatest proportion of MRSA carriage (26%), while those with 7 years or more of experience had the lowest rate.

The antibiogram for each S aureus isolate in our study revealed susceptibility to Vancomycin, Teicoplanin and Linezolid, which is consistent with earlier studies from St Louis (Morelli, *et al*[19]) and and Radhakrishna, *et al*[15] in South India. All of the MRSA isolates showed complete receptivity to the antibiotics Vancomycin, Teicoplanin and Linezolid.

By Radhakrishna, *et al*[15] in South India, Jindamwar, *et al*[20] in West Bengal, Bhowmik, *et al*[21] in the northeastern part of India and Askarian, *et al* [22] in Iran, no isolates were found to be resistant to Vancomycin, Teicoplanin or Linezolid. In contrast, El Aila, *et al*[23] in Gaza found that 84.3% of the bacteria they tested were sensitive to Vancomycin.

The antibiogram of the MRSA isolates supported the results of a research by Rutvi, *et al*[24] carried out in Gujarat, India, which discovered that 100% of the isolates showed resistance to Amoxiclav and that 61.5% of them showed resistance to Erythromycin and 61.5 % to Gentamicin.

All of the MRSA strains tested showed sensitivity to the antibiotic Vancomycin. Therefore, the individuals with active MRSA infections can be treated with this drug.

Limitation and Strength of the Study :

This study being conducted in a teaching hospital where data on antimicrobial resistance is limited, we have to admit some limitations. Here the actual source of infection is unknown. The isolates were not subjected to molecular testing to know the molecular features and associated virulence factors. Also differentiation between Hospital acquired and community acquired MRSA was not done. However, in this study the burden of MRSA in critical care areas was highlighted along with antimicrobial resistance pattern. Hence, this knowledge will help in building strong infection control practices in hospitals.

Conclusion

In this research, Nursing staffs were the most prevalent carriers of MRSA (57.1 %). As compared to 14% overall among healthcare professionals. Since nurses have a larger role in patient care, they should be the ones to get education and training on this topic. Most importantly in the fight against nosocomial infections, adherence of Healthcare Workers to prescribed hygiene and antimicrobial practices should be strictly advocated. Education of HCWs about MRSA control policy is an important step toward this goal". The use of sterile aprons, gloves, masks, and other protective clothing, nasal decolonization with mupirocin ointment and using Chlorhexidine soap as well as the isolation of patients who are colonized or infected, have all been found to significantly prevent the transmission of infection. Regular screenings and warnings for the presence of antibiotic resistant bacteria are necessary for the Healthcare Professionals who harbour MRSA in their nasal passages.

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Original Article

Presence of Malaria Parasite in Vivax Malaria Patients after Completion of Anti-malaria Therapy in a Tertiary Care Hospital of Kolkata : A Real World Observational Study

Koushik Mukherjee[1], Udas Chandra Ghosh[2], Arunansu Talukdar[3], Aneek Ghosh[4], Shambo Samrat Samajdar[5]

Background : Malaria is one of the most prevalent protozoal diseases in the world caused by the genus Plasmodium. The disease is transmitted to humans through the bites of infected Anopheles mosquitoes and is widespread in tropical and subtropical regions around the Equator. Despite efforts to eradicate the disease, global malaria cases are on the rise again and delayed parasite clearance and relapse are major hindrances to malaria elimination. The only drug that can prevent these and provide radical cure are the 8-aminoquinolines, but they are underused due to the risk of oxidant hemolysis in patients with G6PD deficiency.

Materials and Methods : The study was conducted to assess the persistence of parasites in peripheral blood smear, the level of G6PD in blood and the markers of severity of Plasmodium vivax infection in patients diagnosed with vivax malaria attending MOPD, Medical College and Hospital, Kolkata, India. The study was a prospective observational study, including proper history taking, collection of blood samples, and monitoring of peripheral blood smears after day 3, 2 weeks (day 14) and 6 weeks (day 42) from the initiation of antimalarial therapy.

Results : The results showed that out of 110 patients, 9.1% had parasites in the peripheral blood smear. The mean G6PD level was significantly lower in patients with a positive parasite smear than in those with a negative smear. Additionally, markers of severity of Plasmodium vivax infection were also assessed and the results suggest that thrombocytopenia is a strong marker of severe vivax malaria.

Discussion & Conclusion : Overall, the study highlights the importance of monitoring parasite clearance and relapse in vivax malaria patients and the need for careful consideration of G6PD deficiency status before administering primaquine. It also emphasizes the importance of monitoring the markers of severity of Plasmodium vivax infection to identify patients at risk of developing severe malaria.

[*J Indian Med Assoc* 2024; **122(1):** 26-8]

Key words **: Plasmodium vivax, Radical Cure, Primaquine, G6PD Deficiency.**

Malaria, caused by the genus Plasmodium, is one of the most prevalent protozoal disease in the world. It is one of the few diseases in which morbidity is measured in hundreds of millions of cases per year[1]. The disease is widespread in the tropical and subtropical regions that exist in a broad band around equator. Malaria is transmitted to humans through the bites of infected Anopheles mosquitoes. Five parasite species namely P vivax, P falciparum, P malariae, P ovale and P Knowlesi cause malaria in humans. Among them, two of these species-P falciparum and P vivax-pose the greatest threat and account for more than 90% of the total malaria cases worldwide. Based on recent trends and outcomes, global malaria cases are on the rise again with increasing mortality from the severe manifestations of malaria, raising concerns of a resurgence of this too often deadly disease[2].

Efforts to eradicate malaria have clearly been unsuccessful in many regions of the world and current

Editor's Comment :

- Persistence of Malaria Parasites Post-Therapy : A significant finding was that 9.1% of patients still had malaria parasites in their blood after completing antimalarial therapy, indicating the need for effective post-treatment monitoring.
- Importance of G6PD Level Testing : The study emphasizes the importance of G6PD deficiency testing, as lower G6PD levels were significantly associated with the presence of parasites post-treatment. This has implications for safe and effective primaquine use.
- Significance of Severe Malaria Indicators : The research highlighted thrombocytopenia as a strong marker for severe vivax malaria, underscoring the need for careful monitoring of severe malaria indicators in patients.

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efforts to control the disease focus on reducing attributable morbidity and mortality. Delayed parasite clearence and relapse are major hindrance to malaria elimination, because the only drug that can prevent them and thereby provide radical cure are the 8-aminoquinolines and they are underused. In patients with G6PD deficiency, this drug causes oxidant hemolysis which is very common in tropical areas. Testing of G6PD is often unavailable, so prescribers are commonly reluctant to risk hemolysis in order to prevent relapse. The clearence of malaria parasites from blood and reduction in the probablity of relapse depends on the dose, the quality and bioavailability of the drug 8 aminoquinoline (primaquine) and the number of activable hypnozoites in liver.

Clinical efficacy is defined by the clearence and recurrence of parasitemia. In most patients these occur at relatively low level of patency and thus expert microscopy is crucial in the assessment of blood films. Parasitemia clearing within 4 days and not reappearing in 35 days may be defined as chloroquine sensitive malaria. There is no evidence of resistance to therapeutic doses of Primaquine by hypnozoites of P vivax. A loss of function cyt P 450 2D6 genotype resulting in inadequate metabolism of Primaquine is an important cause of therapeutic failure. Other possible causes of therapeutic failure must be ruled out including insufficient Primaquine quality, reinfection after therapy.

Materials and Methods

Definition of study population : Patients diagnosed with vivax malaria attending MOPD, Medical College and Hospital, Kolkata including age more than 12 years during the study period.

Inclusion criteria : Cases diagnosed with vivax malaria by thick/thin smear or rapid diagnostic kit encompassing ages more than 12 years.

Exclusion criteria :

(1) Patients with malaria infection other than vivax and Mixed infection (vivax plus falciparum)

(2) Malaria with other bacterial or viral coinfecion

(3) Pregnant patients

Sample size calculation : Assuming 1.5% of the patients attending our OPD are suffering from P vivax. 5% presision and 5% alpha error, the required sample size was 118(~120). We have collected data from 110 patients. Due to COVID-19 pandemic, study population inclusion was restricted.

Study Design : Prospective Observational Study

Study procedure : Our study was a prospective observational study. It included proper history taking, collection of blood samples and monitoring of peripheral blood smears after day 3, 2 weeks (day 14) and 6 weeks (day 42) from the initiation of antimalarial therapy. We intended to look for the presence of malarla parasite in peripheral blood smear of those patients, the level of G6PD in blood and also assess the markers of severity of Plasmodium vivax infection.

Results

In our study, 45 (40.9%) patients were female and 65 (59.1%) patients were male and 15 (13.6%) patients were from Rural area and 95 (86.4%) patients were from Urban area (Table 1).

Table 1 — *Distribution of Parasite of Peripheral Blood Smear on follow up*

Parasite of Peripheral Blood Smear	Frequency	Percent
Absent	100	90.9%
Present	10	9.1%
Total	110	100.0%

In our study, 10 (9.1%) patients had Parasite of Peripheral Blood Smear. Table 1 had depicted the presence or absence of parasites in peripheral smear.

Table 2 had shown G6PD deficient status and persistence of parasites in peripheral smear. In patients not having parasites in peripheral blood smear, the mean G6PD Level (Mean±SD) of patients was 14.8570± 3.2146 and patients with parasites in peripheral blood smear, the mean G6PD Level (Mean±SD) of patients was 8.1900±4.4859. Distribution of mean G6PD Level with parasite positive peripheral blood smear was statistically significant (p<0.0001). Fig 1 had shown the distribution of mean G6PD Level with presence or absent of parasites in peripheral blood smear.

Discussion

Our study was done to look for the rate of parasite clearence for peripheral blood smear of Plasmodium vivax malaria. In case of Plasmodium vivax malaria, following reasons are there for which malaria parasite may presenet in peripheral blood smear after completion of anti-malarial therapy. First of them is,drug resistance malaria. Kiran K Dayananda, *et al*[4] have discussed about drug resistance malaria. Nicoholas J, *et al*[5] study shows anti malarial drug effect on parasite dynamics in vivax malaria. Second

Table 2 — *Distribution of mean G6PD Level: Parasite of Peripheral Blood Smear*

		Number	Mean	SD	Minimum	Maximum	Median	pvalue
G6PD Level	Absent	100	14.8570	3.2146	8.3000	20.1000	15.1000	<0.000
	Present	10	8.1900	4.4859	4.3000	17.1000	6.2000	1

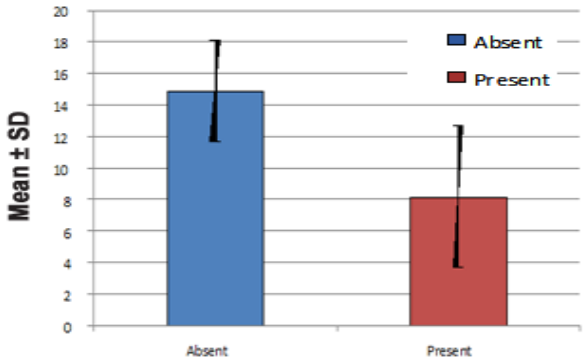

Fig 1 — Distribution of mean G6PD Level with presence or absent of parasites in peripheral blood smear

important reason for delayed parasite clearance is severe vivax malaria. Rishikesh Kumar, *et al*[6] shows how severity of malaria affect the parasite clearence. T Angel Miraclin, *et al*[7] study found slow parasite clearance. Now in case of recrudesence or relapse, which is not very uncommon in case of vivax malaria, we may found malaria parasite in peripheral blood smear after completion of therapy. Brian Greenwood, *et al*[8] study shows vivax malaria recurrence in Brazil.

In our study, a total of 110 patients were studied over a period of one and a half years. Among them 10 patients have malaria parasite in peripheral blood smear after completion of anti-malarial therapy. Male population was higher than the female population and we found that, most of the patients were 31-40 years old. 9.1% patients had Parasite in Peripheral Blood Smear and mostly observed in patients from urban population which was not statistically significant. It was shown that malarial parasites were found significantly in the blood smear of the patients who are receiving chloroquine alone than the group of patients who was receiving both chloroquine and primaquine. G6PD Level was significantly decreased in patients with Plasmodium vivax in peripheral blood smear after completion of antimalarial therapy. The parasite clearance was hastened in the patients who were receiving primaquine for radical cure. G6PD testing should be made widely available so that primaquine can be given more safely. Though our study has few limitations like the number of study population is less and we did not take any parameters to differenriate reinfection from relapse.

Conclusion

Presence of malaria parasites in peripheral blood smear of Plasmodium vivax patients after successful anti-malarial therapy is not uncommon. Use of G6PD level estimation widely and using primaquine are important steps to follow for successful therapy and need to be available and accessible widely.

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Original Article

Prevalence of Depression in Chronic Kidney Disease : An Observational Study

Shabbir Shekhli[1], Ravi Allichandi[2], Mudiyappa Herakall[2]

Background : Chronic Kidney Disease (CKD) is considered a leading health problem globally. The prevalence of depression is about 10 to 25% in this population and is associated with higher hospitalization rates and death rates. This study aimed to evaluate the prevalence of depression in all types of CKD patients.

Materials and Methods : This observational study was conducted in a Tertiary Care Centerin India over three months. Patients diagnosed with CKD were asked to answer pre-tested questions. The Hamilton score was used to grade the severity of depression.

Results : Among 50 study participants, 70% were males. Patients with CKD not on dialysis were 35 and on dialysis 15. Among the no-dialysis group, 60% had depression and in the dialysis group, 80% had depression.

Conclusion : We found that the frequency of depression was significantly higher in the dialysis group. The degree of depression is inversely proportional to the level of education status.

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Key words **: Chronic Kidney Failure, Depression, Renal Dialysis.**

The worldwide incidence of ESRD is increasing at about 7% per annum[1]. Chronic Kidney Disease (CKD) is a progressively debilitating and negatively impacts a patient's Quality of Life. It can affect individuals' psychological as well as physical well-being[2]. It is associated with psychiatric sequelae such as depression, anxiety, sleep disorders, mixed anxiety and depressive disorder, dementia and adjustment disorder[3]. Due to the irreversible nature of the disease, depression is common. Depression is reported to occur at any point during the progression of CKD. Factors that affect the risk of depression include Socio-economic factors, Education status and the Gender of the patient[4].

Evaluating depression in patients during the early stages of CKD becomes essential since it influences the Quality of life and mortality rates[5]. However, most of the studies assessed patients with terminal illness of the disease and only a few focused on pre-dialysis patients.

This study aimed to evaluate the prevalence of depression in CKD patients undergoing conservative treatment and hemodialysis.

Editor's Comment :

- Depression is common but underrecognized in patients with Chronic Kidney Disease (CKD).
- Early recognition by periodic screening and appropriate treatment will improve Quality of Life.

Materials and Methods

Study area : Single-center study was carriedout ina Tertiary Teaching Hospital.

Sample Size : *Fifty cases* — who were diagnosed with Chronic Kidney Disease.

Design of the study — Observational, questionnaire-based clinical study.

Duration of the study — Three months.

Procedure : The institutional ethical committee clearance was obtained. Patients have explained the design and nature of the clinical study. Taken written informed consent from study participants. All the patients were assessed according to the hamilton Rating Scale For Depression. Based on the score, the severity of depression diagnosed.

Inclusion criteria :

(1) Age :18-65 years.

(2) Patients who are diagnosed with Chronic Kidney Disease.

Exclusion criteria :

(1) Patients already on treatment for depression.

(2) Patients in delirium.

(3) Patients with a primary psychiatric disorder are on treatment for the same.

(4) Patients with debilitating neurological disorders or cerebrovascular accidents.

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Statistical Analysis :

Descriptive Analysis of all the explanatory parameters expressed in frequency, categorical variables as proportions and continuous variables as Mean & SD. Statistical Package for Social Sciences (SPSS) for Windows, Version 22.0.

Results

Among 50 study participants, 70% were male and 30% female (Fig 1).

In the male group, ten patients were on dialysis, and twenty-five were not on dialysis. Whereas in the female group, five were on dialysis and ten were not on dialysis (Table 1).

In the high-income group, 83% of patients had depression and in the low-income group, 72.7% had depression (Fig 2).

Among different types CKD, 80% had depression in dialysis and 60% had depression in no dialysis patients. The majority accounted for the moderate depression category (Table 2).

Regarding education status in depression with CKD patients, 68.4% completed formal education,80% had middle and metric education and 53.8% completed postgraduation (Fig 3).

Discussion

There is increasing evidence supporting the role of psychosocial factors such as depression, anxiety, and perceived social support in the pathophysiology of various chronic diseases, including CKD, where depressive disorders have been found to be associated with an increased risk of mortality and poor health-related Quality of Life[6,7].

We used the Hamilton Depression Rating Scale to diagnose the different stages of depression. The Hamilton Depression Rating Scale is one of many ways to stage depression and has recently been shown to be a valid alternative to other methods[8,9].

Watnick, *et al* (2003) study found that symptoms of depression were frequently observed at the early stages of dialysis treatment[10]. Hedayatti, *et al* (2009) found that 1 in 5 patients with CKD had experienced at least one major depressive episode in late-stage CKD. There was an independent association between depression and poor survival outcomes[11].

Chiang, *et al* showed that depression was 22.6% in patients with sleep disturbances, no regular exercise regimen and diagnosed with stage III or above CKD[12].

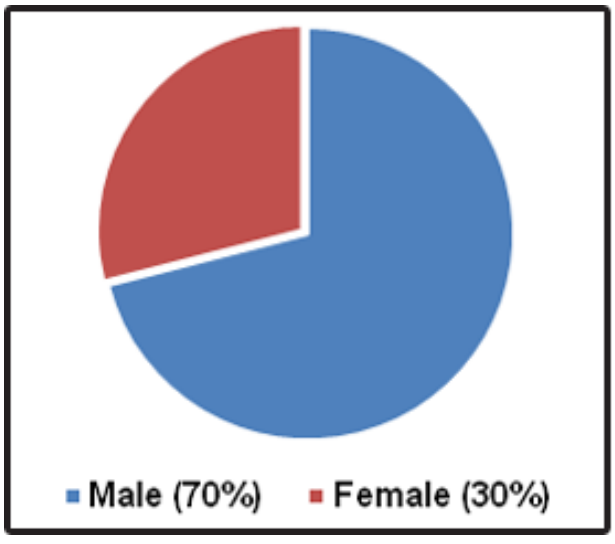

Fig 1 — Gender Distribution

Table 1 — *CKD Patients on Treatment*

Sex	No dialysis group	Mean age	Dialysis group	Mean age
Male	25	56.37±17.07	10	49.49 ±17.47
Female	10	49.36 ±19.17	5	44.17 ±17.83
Total	35	52.64±18.86	15	47.20±17.74

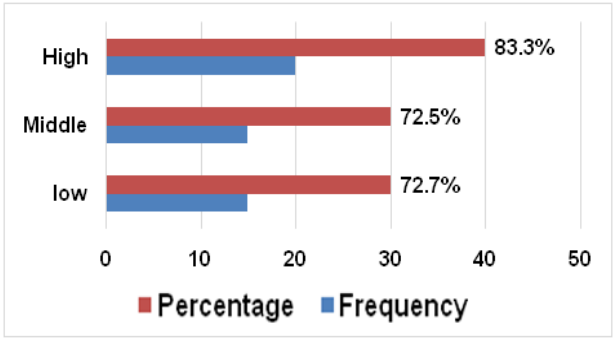

Fig 2 — Depression with Socio-economic Status

Table 2 — *Severity of Depression in CKD Patients*

Stages of depression	Pre-dialysis	Dialysis	p-Value
No Depression	14 (40%)	3 (20%)	
Mild Depression	10 (28.57%)	4 (26.6%)	<0.5
Moderate Depression	7 (20%)	6 (40%)	<0.5
Severe Depression	4 (11.42%)	2 (13.3%)	
Total (n)	35	15	

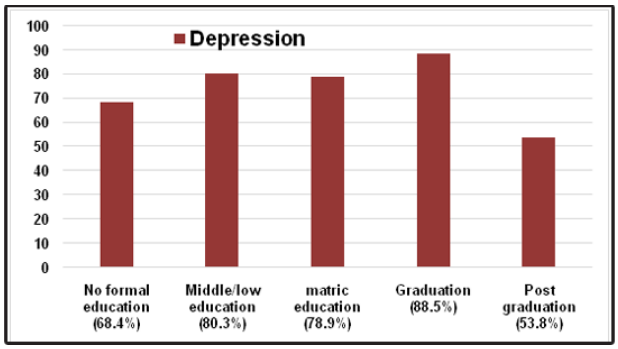

Fig 3 — Education Status in CKD Patients with Depression

In our study, the No dialysis group had 60% depression and the dialysis group had 80%. Results were similar in the Bhatti AB, *et al*. Study, which showed that in the dialysis group, 83.8% were in depression, while in the pre-dialysis group, only 61.3% of patients were in depression[13]. This result shows depression is a global health problem.

Limitations : (1) Single-center study. (2) Small sample size. (3) Short duration of the study.

Conclusion

In our study frequency of depression was significantly higher in the dialysis group. A higher level of education is associated with a lower frequency of depression. No significant association with income status. We conclude all types of CKD patients will have various degrees of depression and routine screening should be performed to identify and treat it in its early stages.

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Original Article

A Clinico-Anatomical Study on Primary and Secondary Infertile Females with Special Reference to Radiological Observations, Laparoscopic Findings and Endometrial Histology

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Background : Infertility in females may be attributed to a galaxy of factors. In order to pinpoint the exact aetiological factor, to contemplate the most rational therapy and last but not the least to appreciate the prognosis in a particular case, a thorough knowledge about the macro and microanatomy of female reproductive system is essential.

Aims and Objectives : To detect anatomical defects of female genital tract responsible for infertility by radiological observations and laparoscopic study and to study microanatomical changes of endometrium in infertile females.

Materials and Methods : The present study was conducted on 40 women who had attended the OPD of Obstetrics and Gynaecology Department and Infertility Clinic of RGKMC, Kolkata with the problem of either primary or secondary infertility and with normal semen analysis report of their husbands. The study was carried out over a span of almost one year (March, 2021- August, 2022).

Result : Out of 40 women studied, 25 women had normal hysterosalpingographic findings, 6 women had bilateral tubal blockage, 5 women had unilateral tubal blockage, in 2 women hydrosalpinx and only 1 case each had uterine anomaly in the form of unicornuate unicollis uterus and hypoplastic uterus.

Conclusion : Diagnostic laparoscopy, however, enabled to have a vivid picture of the gross anatomy as well as any existing pathology of the internal reproductive organs.

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***Key words* : Infertility, Hysterosalpingography, Laparoscopy, Endometrial histology.**

Infertility is seldom if ever a physically debilitating disease. During last two decades there has been marked increase in patient population in all Infertility clinics probably due to socio-cultural and environmental factors.

The male factors contribute 35% to 40% and in female factors to the 40% of the problem concerned while both impact 10-15%[1].

Malik E, *et al* (2000) did a retrospective study on primary and secondary infertile patients who had undergone HSG and found that 32 out of 102 patients (31.37%) had uterine pathology[2]. Age of the patient is to be noted. An woman reaches her maximum fertility potential at the age of 30, fertility potential begins to decline, at 38 years, clinical pregnancy is almost impossible after the age of 45 years[3].

Editor's Comment :

- Infertility in females may be attributed to a galaxy of factors. Out of 40 women studied, 25 women had normal hysterosalpingographic findings, 6 women had bilateral tubal blockage, 5 women had unilateral tubal blockage, in 2 women hydrosalpinx and only 1 case each had uterine anomaly in the form of unicornuate unicollis uterus and hypoplastic uterus.

Aims and Objectives

(1) To detect anatomical defects of female genital tract responsible for infertility by radiological observations and laparoscopic study.

(2) To study microanatomical changes of endometrium in infertile females.

Materials and Methods

After getting institutional ethical committee clearance, present study was conducted on forty subjects who had attended the OPD and Infertility Clinic of Obstetrics and Gynaecology Department, RGKMC, with the complaint of either primary or secondary infertility in the child bearing age. The investigating procedures which were undertaken for this study were

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hysterosalpingography, laparoscopy and endometrial histology.

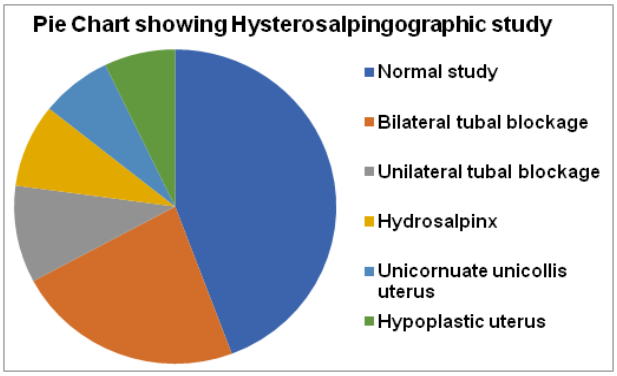
Study design was longitudinal analytical study and inclusion criteria were patients with complaint of primary or secondary infertility in the child bearing age span. Exclusion criteria was unwilling patients and those whose husband's semen analysis was abnormal.

Analysis and Result

Table 1 shows that the maximum number of infertile women belong to the age between 26-30 years (50%), next higher group was 21-25 years (30%).

Table 1 — *Distribution of Infertility Women*

Age group in years	Number of women	Percentage
20 and below	1	2.5
21-25	12	30
26-30	20	50
31-35	5	12.5
36 and above	2	5



Pie chart shows out of 40 women studied, 25 women had normal hysterosalpingographic findings, 6 women had bilateral tubal blockage, 5 women had unilateral tubal blockage, in 2 women hydrosalpinx, while only 1 case each had uterine anomaly in the form of unicornuate unicollis uterus and hypoplastic uterus.

Table 2 shows bilateral dye spillage in 29 cases (76.92%) and in 1 case of hydrosalpinx it was positive on one side (2.5%). It was negative in the remaining 9 cases (23.07%), indicating bilateral tubal blockage. In 1 case it was not attempted.

Fig 1 HSG shows Hydrosalpinx (5.26%), Figs 2 and 4 show bilateral tubal blockage (15.78%), Fig 3 shows unilateral tubal blockage (13.15%), Fig 5

Table 2 — *Bilateral Dye Spillage*

Number of Women	Result	Percentage
29	Bilateral dye spillage present	74.42
1	Unilateral dye spillage present	2.5
9	Dye test negative	23.07
1	Could not be done	2.5

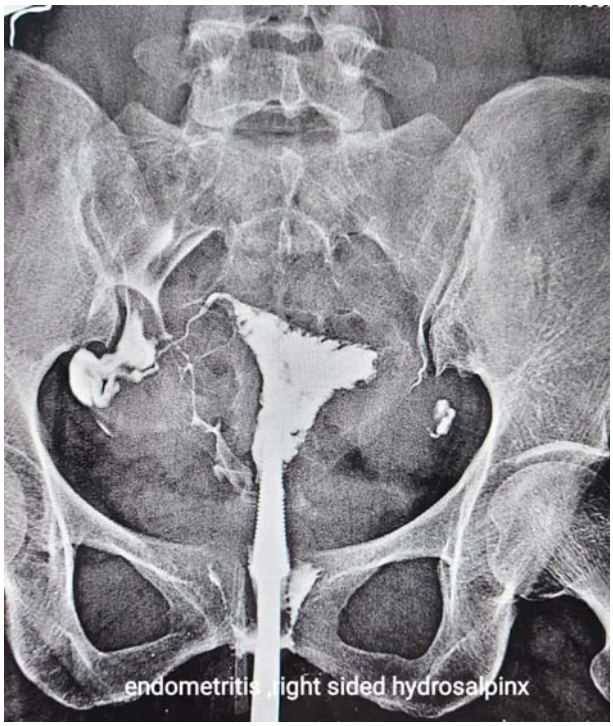


Fig 1

shows subtle arcuate fundus (2.63%) and Fig 6 shows hydrosalpinx (5.26%).

Out of 40 women studied in this series, the endometrial histology of 5 cases (12.5%) were in proliferative phase and 34 cases (85%) were in secretory phase while only 1 (2.5%) case had hyperplastic endometrium.

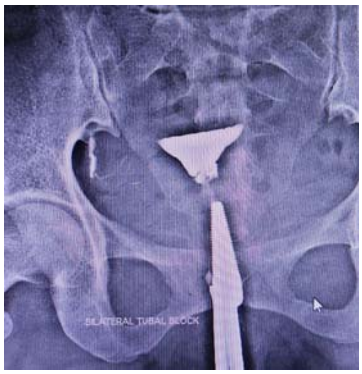


Fig 2

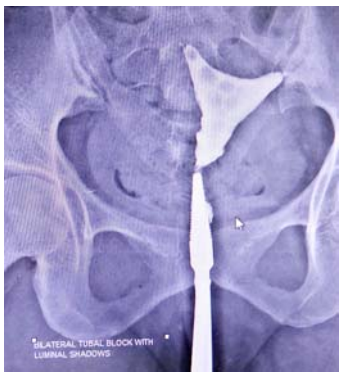


Fig 4

Discussion

Out of 40 infertile females investigated, there were patients of different age group. The maximum number of females (50%) belong to the age group between 26-30 years. The next higher incidence (30%) was observed in women between 21-25 years. Saini, *et al* found in their study that maximum infertile female were

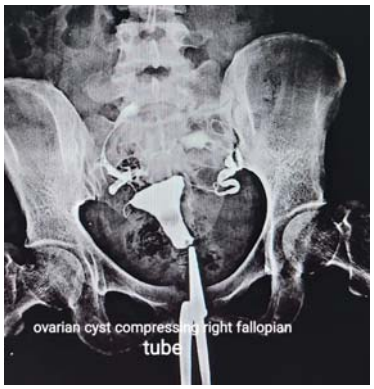


Fig 3

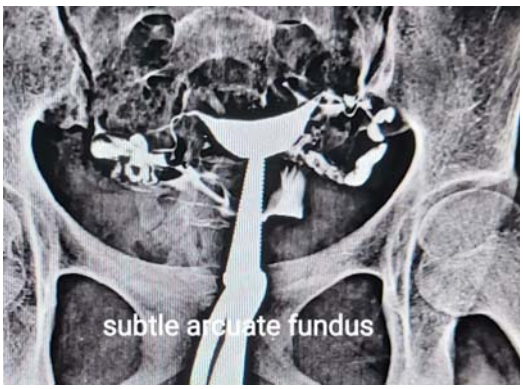


Fig 5

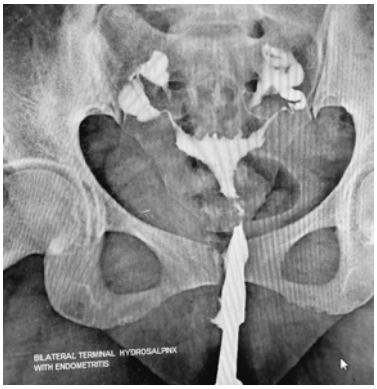


Fig 6

between 26-30 years of age group[4].

In the present study, normal HSG finding was noted in 60.52%, bilateral tubal blockage in 15.78%, unilateral tubal blockage in 13.15%, hydrosalpinx in 5.26%, hypoplastic uterus and uterine anomaly in the form of unicornuate unicollis uterus in 2.63% cases each.

Adrian C Schankath, *et al* found of 411 HSG examination, 226 (55%) were normal, 94 (23%) showed minor abnormalities and 5 (1.2%) were not diagnostic[5]. Malik E, *et al* did a retrospective study on primary and secondary infertile patients who had undergone HSG and found that 32 out of 102 patients (31.37%) had uterine pathology[6].

Regarding unilateral tubal block found in 13.15%, it can be stated that if dye goes through one tube rapidly and fails to enter the other tube, it usually means that the dye containing tube presents the path of least resistance. However, HSG has its limitations in determining the tubal, peritoneal and ovarian factors and diagnostic laparoscopy is the choice. Goynumer G, *et al* also found similar findings in their study[7].

Normal laparoscopic study was found in 40% women followed by adhesion among pelvic organs in 25% women. Clever O, *et al* also found normal laparoscopic finding followed by adhesion in their study subjects[8].

In the present study endometrium was curettated from all the 40 women and the histology revealed Secretory Endometrium in 85% and Proliferative Endometrium in 12.5% of the women. Girish, *et al* also found similar endometrial histological finding in their study[9].

Conclusion

Visualisation of the gross anatomy of the principal organs of the female reproductive system, mainly the uterus, ovaries and tubes along with any existing pathology of the same was achived by radiological observations comprising of Hysterosalpingography and Diagnostic Laparoscopy.

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Original Article

A Prospective Observational Follow-up Study of Infections in Post Renal Transplant Recipients in a Tertiary Care Hospital in Chennai

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Background : Infectious disorders are a major cause of concern in Renal Transplant Recipients (RTRs) leading to considerable morbidity and mortality. We studied the profile and outcomes of infectious disorders in a cohort of RTR.

Aim : To study the incidence of infections in Post Renal Transplant Recipients.

Materials and Methods : In this prospective, observational study, we evaluated all Renal Transplant Recipients who presented with the features of infection. We included all live related and deceased donor renal transplant recipients in a Tertiary Care Hospital in Chennai from August, 2018 to March, 2019. We also included every episode of significant infection in which therapy was initiated. Descriptive and analytical statistics were used to analyse the results.

Results : The study population (n = 50, 41 males and 9 females) had a mean age of 39.48 years (SD=14.3 years) and follow-up after transplant was one year. Among the 50 patients, 31 patients developed infections and 19 did not develop infections. Urinary Tract Infection (UTI, n=31) is the most common infection followed by systemic (n=5) and respiratory (n=4).

Conclusion : Infectious complications are very common in the post renal transplant period including UTI, systemic and respiratory.

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Key words **: Infections, Renal Transplantation, Urinary Tract Infection.**

Kidney transplantation offers a better Quality of Life over haemodialysis in patients with End-stage Renal Disease (ESRD). The survival after transplantation is determined by multiple factors, including pre-transplant co-morbidities, type of graft, and degree of immunosuppression[1]. The development of new immuno-suppressive drugs leads to a reduction in the mortality of Renal Transplant Recipients (RTRs). However, potent immunosuppression poses an additional risk of infectious disorders in the transplant recipients. One quarter of RTR develop a serious infection in the post transplant period that causes allograft dysfunction[2]. Infections occurring after transplantation account for half of the deaths and considerable morbidity in India[3,4]. Urinary Tract Infection (UTI) is the most common infection in the post transplant period followed by candidiasis and Tuberculosis (TB)[5]. Hepatitis B and C viral (HBV and HCV) infection, Cytomegalovirus (CMV) and Pneumocystis are also common infections that are encountered in RTR.

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Editor's Comment :

- Further studies with along term follow up will throw more light on infections in the Indian context.
- This study hopes to provide a base for surveillance of infection in kidney transplant recipients in the Indian scenario.

The spectrum of post transplant infections differs between the developed and developing nations. The risk factors prevalent in our country include tropical climate, poor hygiene and socio-economic status, high rates of endemic infections, late presentation, poor diagnostic techniques and lack of awareness in primary care physicians[6]. Renal transplantation centres are located in selected cities, which are unable to handle the volume of RTR[7]. Moreover, the transplant centres lay less emphasis on patients presenting with minor ailments such as fever and infection. Thus, more number of RTR will present to their local physicians for routine medical ailments[8]. It is essential for the local practitioners to identify the spectrum of infections that are common in RTR and direct appropriate therapy to improve the graft survival. The studies about the infectious complications in RTR are scanty from India[9,10]. Hence, we conducted this study to identify the profile of infectious disorders in RTRs.

Materials and Methods

The study was conducted in a Tertiary Care Hospital in Chennai. The study population included all patients

admitted to the hospital for renal transplantation during August, 2018 to March, 2019 was included for the study. The Study design was a prospective observational study and the study period was from August, 2018 to March, 2020. The Sample size was calculated based on studies reporting that infections are an important differential diagnosis in the event of allograft dysfunction due to their distribution throughout the post renal transplantation phase. Also studies quoting 80-86%[11] of allograft recipients had several episodes of infection throughout their post transplantation phase. Assuming that 86% of the subjects in the population have the factor of interest, the study would require a sample size of 47 for estimating the expected proportion with 10% absolute precision and 95% confidence.Taking drop-outs into consideration, the required sample were calculated as 50 cases.

Inclusion criteria :

(1) Live related and deceased donor Renal Transplant Recipients of the hospital, from August, 2018 to March, 2019.

(2) Every episode of significant infection in which therapy was initiated.

Exclusion criteria :

(1) Patient not willing to consent for this study.

Methodology :

Approval of thesis protocol was obtained from institute's scientific and ethical committee. After obtaining informed consent, all subjects were included in the study protocol. Detailed history was got and patients were examined and later followed up until 1 year after transplantation as outpatient, in wards if they were admitted and through phone and email.

Operational definitions used in the study —

(1) Urinary Tract Infections (UTIs) : Although the presence of bacteriuria would fulfil the criteria for UTI in Renal Transplant Recipient, other criteria, such as pyuria (>10 leukocytes/mm^3) and fever, were be used for diagnosing UTI. In the present study, the CDC criteria, eg, the clinical judgment of the physician in initiating therapy, was be used as a definition for infection UTI was considered to be catheter related if the infection occurred during urethral catheterisation or within 24 hour after catheter removal.

(2) Intra-abdominal infectious episodes included local or generalised peritonitis, abdominal abscess formation, cholangitis, and pancreatitis.

(3) Wound infection was defined as the presence of purulent discharge from a surgical wound.

(4) Cytomegalovirus (CMV) reactivation was defined by antigen detection or isolation of virus from any tissue or body fluid. The diagnosis of CMV disease was based on the presence of clinical symptoms (fever, malaise, arthralgia, myalgia and organ involvement) and detection of CMV in clinical samples (such as blood and Broncho alveolar lavage fluid).

Statistical data and analysis :

All the continuous variables were expressed as mean ± SD (if they follow Gaussian distribution). Other continuous variables which did not follow normal distribution were expressed as Median (Interquartile range). All the categorical variables were expressed either as percentage or proportion. Comparison of normally distributed continuous variables were done by independent sample't' test or ANOVA. Comparisons of non-normally distributed continuous variables were done by Mann-Whitney 'U' test or Kruskal Wallis 'H' test. Comparisons of categorical variables were done by Chi-square test or Fisher's Exact test based on the number of observation. Data entry was done in MS-Excel Spread sheet. Data validation and analysis were carried out by SPSS version 16.0. A two-sided p value <0.05 will be considered as statistically significant.

Observations and Results

The mean age of the study population was 39.48 years (SD=14.34 years) with the age ranging from 10 years to 68 years. Out of the 50 patients, 41 (82%) were male. Majority of the patients were from Tamil Nadu and 8 patients were from foreign countries. Many recipients belong to either O blood group (36%) or A blood group (36%) followed by the B blood group (26%). In the study group 14 (28%) were diabetic and 47(94%) were hypertensive (Table 1).

(A) Post Renal Transplant Infections : In the present study, 31 patients had infections and 19 did not have infection.

Table 1 — *Base Line Characteristics of Recipients of Renal Transplant*

Characteristics		N(%)
Age in years	<40	29 (58%)
	≥40	21 (42%)
Gender	Males	41 (82%)
	Females	9 (18%)
Nationality	Indian	42 (84%)
	Foreign	8 (16%)
Blood group	A	18 (36%)
	O	18 (36%)
	B	13 (26%)
	AB	1 (2%)
Co-morbidities	Diabetes mellitus	14 (28%)
	Hypertension	47 (94%)

(B) Episodes of Infections : In the present study, 17 patients had 1 infection, 7 patients had 2, 4 patients had 3 and 3 patients had 4 infections (Fig 1).

(C) Induction : 38 patients received induction and 12 patients did not receive induction.

Among those who received induction, 36 received ATG, 1 patient received Basiliximab and 1 received Alemtuzumab.

(D) Induction and Infection : Out of the 12 patients who did not receive induction, 6 developed infections and 6 did not. Of the 38 patients who received induction, 25 developed infections and 13 did not. But it was not statistically significant (p=0.32).

(E) Gender and Infection : 25 males and 6 females developed infections, whereas 16 males and 3 females did not develop any infection and it was found to be statistically insignificant (p=0.72).

(F) Diabetes and Infections : 12 diabetics developed infections and only 2 did not, 19 non-diabetic developed infections and 17 did not and this was found to be statistically significant (p=0.03).

(G) Hypertension and Infection : 2 hypertensive patients developed infection and 18 did not and 2 normotensive patients developed infection and 1 did not and it was not statistically significant (p=0.86).

(H) Duration of Diabetes and Infection : It was found that the mean duration of diabetes in the patients who developed infection was 17.75 years and in those who did not develop infection was 3 years. It was statistically significant (p=0.01).

(I) Duration of Dialysis and Infection : The mean duration of dialysis in those with infection was 2.35 years and that without infection was 1.53 years and it was statistically

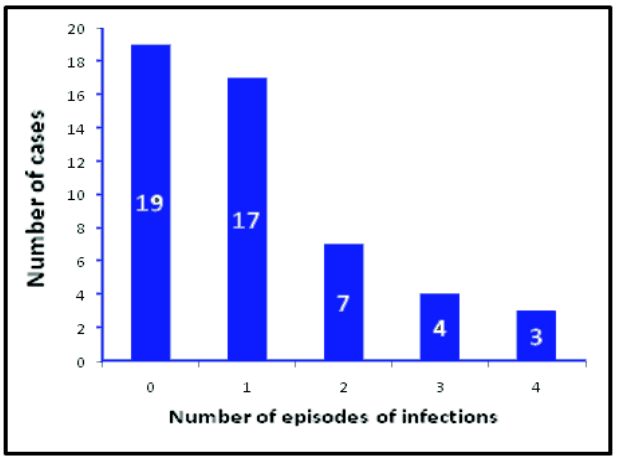

Fig 1 — Frequency of episodes of infection

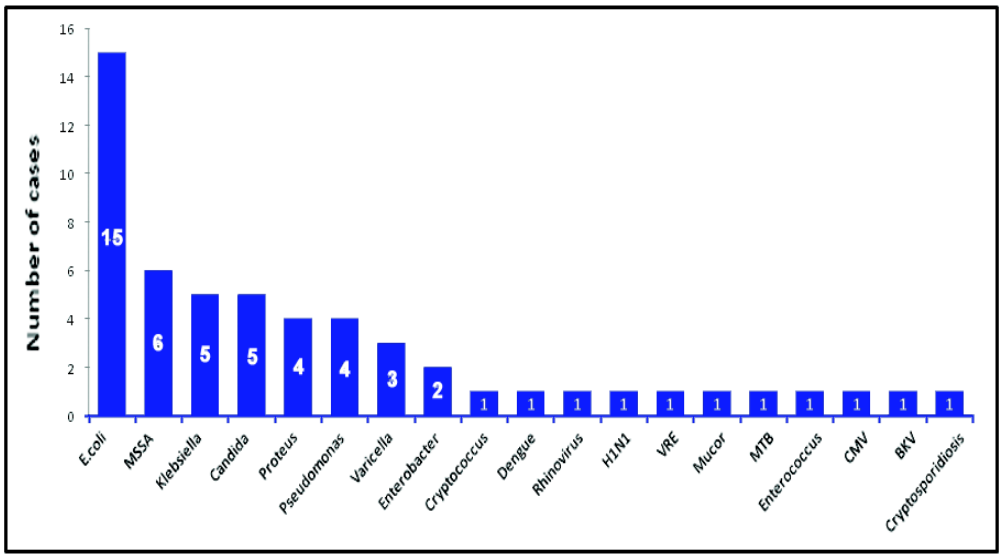

Fig 2 — Organisms Causing Infection

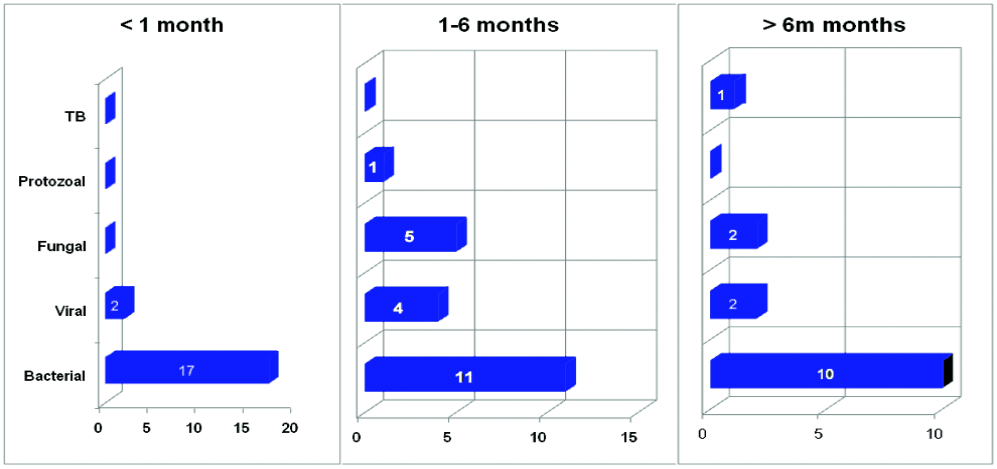

Fig 3 — Time Table of Infections according to Type of Organism

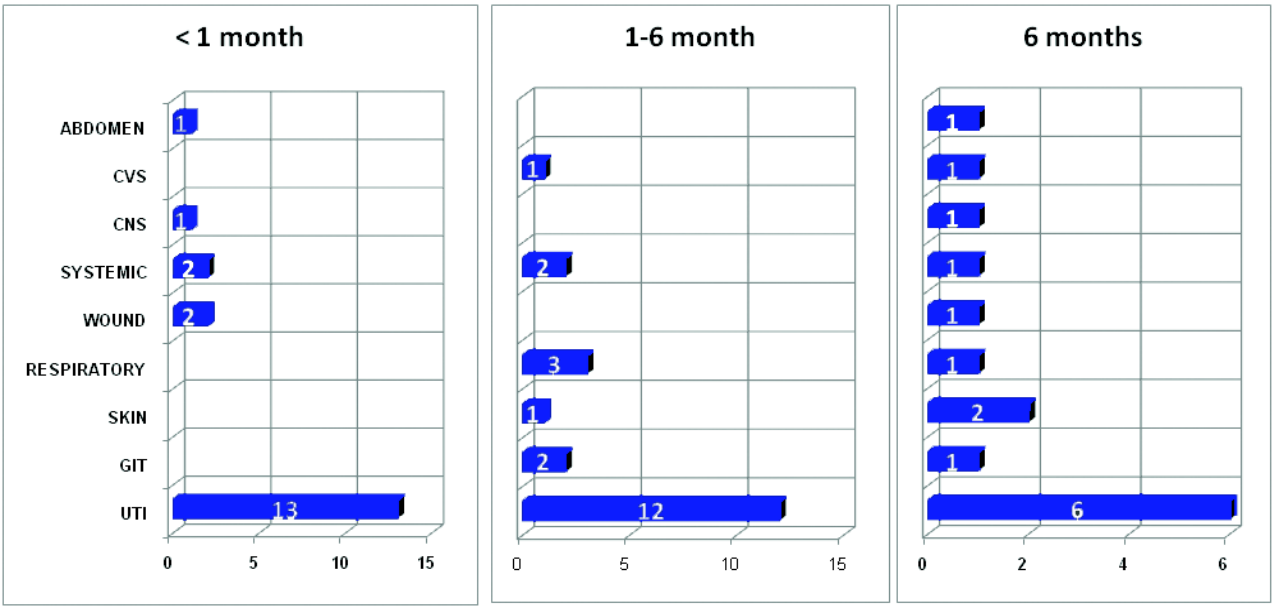

Fig 4 — Time table of Infections according to the Organ Involved

significant (p=0.04).

(J) Type of Transplant and Infection : Of the live transplant recipients, 16 developed infections and 16 did not. However, 15 deceased donor patients developed infections and only 3 did not and it was statistically significant (p=0.02).

(K) Basic Disease and Infections : It was found that all patients with diabetic nephropathy developed infections and it was found to be statistically significant (p=0.03).

(L) Serum Creatinine and Infections : The mean serum creatinine in patients with and without infection was the same at the end of 1 year of follow-up.

(M) Type of Infections : The commonest infection was urinary tract infections (n=31) followed by systemic infections (n=5) and respiratory infections (n=4)

(N) Duration of use of Urinary Catheter <5 days and >5 days: There were no significant difference between UTI and duration of urinary catheter of <5 or >5 days (p=0.94)

(O) Duration of Catheter and UTI: It was found that the mean duration of catheter in patients with UTI was 8.89 days and those without UTI was 6.45 days, but this was not statistically significant (p=0.29).

(P) Organisms causing Infections : *Escherichia Coli* was the most common cause of infection followed by methicillin sensitive *Staphylococcus aureus*, *Klebsiella* and *Candida* (Fig 2).

(Q) Graft Dysfunction and Infection : There were 19 episodes of graft dysfunction out of the 55 episodes of infections.

(R) Time Frame for Infections : We divided the time frame of infections into three groups, ie, <1 month, 1-6 months and >6 months. *Escherichia coli* were the most common organism causing infection in all the three time frames. Other bacteria were Enterobacter, Pseudomonas, Klebsiella, Proteus and MSSA. Viral infections such as Dengue and Rhinovirus were also reported.In the second time period also *Escherichia coli* was the commonest organism causing the infections. Vancomycin resistant Enterococci were reported. The viral infections which occurred during this period were due to BK virus Cytomegalovirus, H1N1 and Varicella. Fungal infections were prominent in this Fungal infections like Candida, Cryptococcus and Mucor were also reported. In the third time period, *Escherichia coli*, *Mycobacterium Tuberculosis* and Varicella were also reported (Figs 3 & 4).

Discussion

Demographic profile : The mean age of the study population was 39.5 years with a standard deviation of 14.3 years and the age ranged from 10 years to 68 years. In a study by Ram, *et al* the mean age was 34.4 years with a standard deviation of 11.4 years (range 10-60 years) and in the study by Arun Kumar, *et al* the mean age was 35.5 with a standard deviation of 10.4 years[11,12]. In 169 patients were retrospectively studied by Ram, *et al* and 45 patients by Arun Kumar, *et al* prospectively. We studied 50 patients prospectively (131,136). In our study 41 (82%) patients were male and 9 (18%) were female. In the study by Ram, *et al*, 136 (80.4%) were male and 33 (19.6%)

were female and in the study by Arun Kumar, *et al* 35 (77.8%) were male and 10 (22.2%) were female[11,12]. Most of the patients (54%) were in the age group of 20-40 years in our study group, similar to that in the study by Ram, *et al* (53.8%)(131).

Basic disease of the recipients :

Chronic interstitial nephritis (26%) was the most common cause of ESRD leading to transplantation followed by diabetic nephropathy (24%) and chronic glomerulonephritis (20%) in our study. In the study by Ram, *et al* chronic glomerulonephritis (69%) was the commonest cause followed by diabetes mellitus (15%) and chronic interstitial nephritis (12%)[11].

Donors : Mother followed by sister and spouse were the leading donors in our study, thus majority were females. In study by Ram, *et al* also mother and sister were the leading donors[11]. Arun Kumar, *et al* mentions that majority donors were females. Our study included 18 deceased donor renal transplantation (36%), but none were included in the study by Ram, *et al*, and only one was included in the study by Arun Kumar, *et al*[12].

Infection rate in the Post Transplant Period :

In this study 31 (62%) developed infections, whereas in the studies by Ram, *et al* and Arun Kumar, *et al* 86% and 73% developed infections respectively[11,12]. Infection rate was the lowest in our study, but the duration of follow up varied between the three studies.

Infections and Graft Dysfunction and Mortality:

In this study 55 episodes of infections were documented in those 31 patients, thus on average each patient 1.77 infections and in the study by Ram, *et al*, it was 2.8[11]. There were 19 (36%) episodes of graft dysfunction out of the 55 episodes of infection in our study. 93 (22.4%) episodes of graft dysfunction were reported in the study by Ram, *et al*[11]. In 2 patients died due to infection out of the 50 patients and thus mortality rate was 4%. In the study by Ram, *et al* the mortality rate was 2.4%[11].

Time frame of Infections : 19 (34.5%) infections occurred in the first 4 weeks, 20 (36.4%) occurred in the period between 1-6 months and 16 (29%) between 6 months and 1 year. However, in the study by Ram, *et al* majority occurred in the first four weeks (28.7%)[11].

UTI : UTI was the most common infection constituting 31 (62%) of the infections. UTI was the most common infection in the study by Ram, *et al*, occurring in 23.6% of the patients and in the study by Arun Kumar, *et al* it occurred in 33.3% of the cases[11,12]. *E coli* was the most common organism causing infection constituting 27.3% of all the infections, whereas it occurred in 12.6% of the infection in the study by Ram, *et al* (131) *E coli* caused 41.9% of all UTIs in our study, similar to study by Arun Kumar, *et al*, where it caused 33.3% of all the UTIs (136). The other organisms causing UTI were Proteus, Klebsiella, Enterobacter, Enterococcus and Pseudomonas.

CMV : CMV disease occurred in 1 patient causing leucopenia and pneumonitis in our study. It occurred in 28 patients causing 37 episodes in the study by Ram, *et al*, and in 6 patients in the study by Arum Kumar, *et al* (131,136). This discrepancy was probably due to difference in the follow up period of the three studies and valgancyclovir prophylaxis received by our patients for a period of 3 to 6 months. CMV was diagnosed by CMV PCR of blood and Broncho alveolar lavage fluid.

Tuberculosis : There was only 1 episode of pulmonary tuberculosis indicating a prevalence of 2%. In the study by Ram, *et al* the prevalence was 10.6%. The study by Arun Kumar, *et al* showed a prevalence of 17.8%[11,12]. There is considerable variation in the prevalence of TB in various studies ranging from 3.5% to 13.3%. This patient was diagnosed to have TB after he had persistent fever and cough for one month and CT chest was suggestive of TB and sputum for AFB was positive for him. It occurred after 8 months of transplantation.

Fungal infections : There were 7 episodes of fungal infections in our study. In the study by Ram, *et al*, 39 episodes of fungal infections were present[11]. In our study Mucormycosis of lung resulted in death of the individual. In 20% of patients affected by fungal infection died in the study by Ram, *et al*. We found no cases of Aspergillus and *Pneumocystis carinii* infection, unlike other studies. But there were 5 episodes of infection due to candida, where it resulted in candiduria, candidemia and also abdominal collection due to candida. One patient had severe oesophageal candidiasis. All the candidal infections were treated with fluconazole and all responded to the treatment and recovered from the infection. 1 infection was Crytpococcal meningitis, which presented with features of fever of unknown origin and was diagnosed by serum Crytpococcal antigen positivity and CSF showed positive for Indian ink stain and also Crytpococcal antigen. He was treated with amphotericin B and fluconazole and he recovered. In the study by Ram, *et al* a case of gastric Mucor has been described and the patient was treated with amphotericin B and the patient recovered.

Varicella Infection : There were 3 episodes of Varicella infection in our study. 1 occurred in the period

between 1-6 months and the rest occurred after 6 months. The infections were very severe and were treated with valacylovir. This stresses the need for routine testing Varicella antibody and immunisation if it is negative to prevent the infection and its complications. One patient had Varicella infection followed by pulmonary tuberculosis.

Dengue : One patient had Dengue infection leading to Leucopenia and Thrombocytopenia with NS1 and IgM Dengue positive tests. He recovered spontaneously. Another patient had pneumonia and was found to have Rhinovirus infection with bronchopneumonia. He also recovered with respiratory support. Both of these infections occurred within the first month after transplantation. 1 had H1N1 infection leading to severe pneumonia and was treated with oseltamivir. But he also had pulmonary Mucormycosis and succumbed to the infections.

Protozoa : There was one infection due to cryptosporidium causing persistent diarrhoea. It was diagnosed by analysis the stool sample. He was treated with Nitazoxanide and he responded to the treatment. There was also an episode of acute diarrheal disease caused by *E coli* which grew in stool culture and the patient responded to oral ciprofloxacin.

BK Virus : There was 1 case of BK viruria, who also had viremia. It was detected for unexplained azotemia and on evaluation was found to have BK virus in blood and urine. The patient was managed by adjustment of the immuno-suppressant dose and the viral load decreased considerably. BK virus is one of the emerging infections and routine screening for the virus may be necessary to prevent one of the preventable causes of graft dysfunction and also for managing the immuno-suppression, because BK virus indicates over immuno-suppression.

Factors Influencing Infections : 38 patients received induction out of the 50 patients. 36 received ATG, 1 received basilixmab and another received alemtuzumab. The infection did not carry an association with induction. Out of the 12 patients who did not receive induction, 6 developed infections and 6 did not develop infections. Out of the 38 patients who received induction 25 developed infection and 13 did not, but it was not found to be statistically significant. The mean dose of ATG in those who developed infection was 131.25 mg; whereas in those without induction was 121 mg. However it was not statistically significant.

Diabetes had a significant association with the study. 17 non-diabetics did not have any infections, and 19 had infections. However, only 2 diabetics did not have any infection and 12 had at least 1 episode of infection. The duration of diabetes also had a significant association with infections. The mean duration of diabetes in those who did not develop infection was 3 years and those who developed infection was 17.75 years. It was found to be statistically significant.

The mean duration of dialysis pre-transplant was also significant. In those who did not develop infections, the mean duration of dialysis was 1.53 years and in those with infection was 2.35 years and it was statistically significant.

The type of transplantation carried a significant association with infections. In live related (including spousal) transplantation, 16 developed infections and 16 did not develop infection. But, in the deceased donor renal transplantation, 15 developed infections and 3 did not develop infections and it was found to be statistically significant.

All diabetic nephropathy patients developed infections and it was found to be statistically significant. There were 2 episodes of infective endocarditis and both were caused by methicillin sensitive Staphylococcus aureus.

We tried to find the correlation between duration of catheter Post Transplant and UTI. The patients were divided into 2 groups. One group had catheter for $\leq$5 days and the other group had catheter for >5 days post transplant. It was found that in the first group 37.5% of the patients developed infections and in the second group 38.5% developed infections and it was not found to be statistically significant. The mean duration of urinary catheter in the post transplantation period was 6.45 days in the patients without UTI and 8.89 days with UTI, but it was not statistically significant. The mean serum creatinine at the end of 1 year of follow up in those patients who were alive at the end of transplantation (N-48) was 1.247 in the group who had infection and in the group who did not have infection also.

Drugs for Treating Infections :

Most of the Gram negative infections were treated with Cefoperazone sulbactam initially. MDR Klebsiella infections were treated with meropenem and colistin according to sensitivity. MSSA infections were treated with Co-amoxyclavulanic acid and cloxacillin. Varicella infections were treated with valacylovir. CMV infection was treated with ganciclovir. Crytpococcal infection and Mucormycosis were treated with amphotericin B.

Conclusion

We have analysed the profile of infection in the

Renal Transplant Recipients in our study. In 62% of the patients developed infections. Infections were associated with diabetes mellitus, deceased donor renal transplantation and duration of dialysis in the Pre-transplantation period. The duration of urinary catheter did not carry statistical significance to correlate with Urinary Tract Infections. There was no difference in the incidence of infections in those receiving induction therapy and those not induction therapy.

Majority of the infections were UTI. *E coli* was the most common cause of infections in our group. We divided the Post transplant period into <1 month, 1-6 months >6 months. 34.5% of infection occurred during first period, 36.4% during the second period and 29.1% occurred during the third period. There were 19 episodes of graft dysfunction out of 55 episodes of infections. There were 2 deaths in our group. One died due to pulmonary Mucormycosis and another died due to infective endocarditis due to MSSA and severe Pseudomonas bacteraemia with pneumonia. Most of the Gram negative infections were treated with Cefoperazone sulbactam initially. MDR Klebsiella infections were treated with meropenem and colistin according to sensitivity. MSSA infections were treated with Co-amoxyclavulanic acid and cloxacillin. Varicella infections were treated with valacylovir. CMV infection was treated with ganciclovir. Crytpococcal infection and Mucormycosis were treated with amphotericin B.

Further studies with more number of patients and further follow-up beyond one will be necessary to elucidate the full spectrum of infections in Indian conditions.

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Conflicts of interest : There are no conflicts of interest.

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Original Article

Etiologies of Space Occupying Lesions of Liver among Patients Presenting in a Tertiary Care Center in India

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Background : Liver Space Occupying Lesions (SOL) in tropical regions may be caused by infectious as well as non-infectious etiologies. We aimed to determine the prevalence of different etiopathology of hepatic SOL and their clinical presentations with relation to common risk factors mostly in tropics.

Materials and Methods : Observational study was done over 12 months on 57 patients aged above 13 years with hepatic SOL evident on either Ultrasonography or Computed Tomography (CT) of abdomen.

Results : Amoebic liver abscess (29.82%) turned out to be the most common cause followed by Pyogenic liver abscess (17.54%), Hepatocellular carcinoma (17.54%) and other minor causes such as hepatic metastasis, hydatid cyst, hepatic simple cyst, tubercular liver abscess and hemangioma. Majority of these patients presented with either pain in right upper quadrant of abdomen (78.94%) or fever (57.89%). Both the symptoms were present in 49.12% cases. Clinical examination revealed hepatomegaly (85.96%) and liver tenderness (70.18%) in most of the cases. However, other clinical findings were pallor (57.90%), jaundice (14.03%), oedema (28.07%) and splenomegaly (17.54%).

Conclusion : Majority of liver SOL was amoebic liver abscess followed by pyogenic liver abscess and hepatocellular carcinoma. Right lobe of liver was involved in majority of patients.

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***Key words* : Liver, Space Occupying Lesion, Hepatocellular Carcinoma, Amoebic Liver Abscess, Pyogenic Liver Abscess, Tubercular Liver Abscess.**

Liver Space Occupying Lesions (SOL) may be benign, malignant as well as of infectious origin (bacterial, amoebic or parasitic)[1]. They can be broadly classified into cystic or solid[2].

Common causes of cystic lesions include infections like Pyogenic Liver Abscess (PLA), Amoebic Liver Abscess (ALA), hydatid cyst of liver and tumors like simple cyst and polycystic liver disease.

On the other hand, solid lesions are often caused by infections like tuberculosis, syphilitic gumma, liver fluke (fasciola, clonorchis, opisthorchis) and tumors like Hepatocellular Carcinoma (HCC), adenoma, fibronodular hyperplasia, hemangioma, metastatic disease, lymphoma and regenerative nodule.

PLA are generally associated with older age (>50 years) and co-morbid conditions like diabetes, renal failure and alcoholic liver disease[2,3]. Causative organisms of PLA may include *E coli, Klebsiella pneumoniae, Streptococcus milleri, Staphylococcus aureus, Burkholderiapseudomallei*[2].

ALA may be solitary or multiple and often occur in the right hepatic lobe (75%) caused by *Entamoeba histolytica*[2].

Editor's Comment :

- Majority of SOLs is infective followed by malignancy. Infective SOLs are usually cystic, whereas solid SOLs are usually malignant. Among infections amoebic liver abscess is most common followed by Pyogenic then Tubercular, hydatid cyst. Amoebic liver abscess found among alcoholics whereas Pyogenic abscess is more common among diabetics. HCC is more common than secondary hepatic metastasis.

Liver hydatid cysts may be classified into different stages based on radiological features. They may have calcified pericystic walls, septa as well as daughter cysts[2].

The evaluation of a liver SOL includes non-invasive tests, such as serology, blood parameters, tumor markers and microbiologic assessment. Imaging modalities include abdominal Ultrasonography (USG); Contrast Enhanced Computed Tomography (CECT) or Magnetic Resonance Imaging (MRI) with contrast. Diagnosis of HCC in Chronic Liver Disease is supported by radiographic findings and elevated levels of Alpha-fetoprotein (AFP). Radiographic features of HCC include hyper-vascular lesions due to neo-vascularization[2,4].

In Asia and Sub-Saharan Africa incidence of HCC is the highest, mostly due to high prevalence of Hepatitis B (HBV) infection. HCC is also associated

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with Hepatitis C viral infection. HCC has a strong male pre-ponderance[5].

In 2018 National Viral Hepatitis Control Programme (NVHCP-INDIA) reported that chronic HBV infection accounts for 40-50% of HCC and 20-30% cases of liver cirrhosis in India. Chronic HCV infection accounts for 12-32% of HCC and 12-20% of liver cirrhosis[6].

Materials and Methods

The Observational study was conducted in the time period of July, 2020 to June, 2021. Our study involved patients of all sex with age more than or equal to 13 years having evidence of liver SOL in either Ultrasonography or Computed Tomography (CT) of abdomen. The participants were recruited after obtaining informed consent. Ethical committee approval was obtained from the Institutional Ethics Committee.

All patients were diagnosed with confirmed hepatic SOL by abdominal USG or CECT.Etiology of liver SOL was confirmed by histopathological examination and microbiological analysis. Aspirated materials were cultured and examined under microscope with proper staining. All Tubercular Liver Abscess (TLA) lesions were confirmed radiologically. Histopathological examination and CBNAAT were used to diagnose tubercular infection. HCC was confirmed by histo-pathological features, radiological assessment and level of tumor markers. Hepatic secondaries were detected by CT scan.

The statistical analysis was performed with the R software package version 4.1.2 by the R Foundation for Statistical Computing. Comparison of findings was done by 't' test for continuous variables and McNemar's test for categorical variables. Between groups analysis was done by Fisher's Exact Test. The test for predictive value of the variables was done using regression models. The p-value of less than 0.05 was taken as significant and a p-value of less than 0.001 was taken as highly significant.

Results

A total number of 57 patients were recruited. The mean age of the study population was 53.50 years. 75.44% of the study participants were male, 38.60% patients had history of alcohol intake and 19.30% patients had history of smoking.

Majority of these patients presented with pain in right upper quadrant of abdomen (78.94%) or fever (57.89%) and 49.12% patients presented with both. Other presenting symptoms were weight loss (22.80%), cough (19.29%), dyspepsia (12.28%), abdominal distension (10.52%) and vomiting (8.77%).

Physical examination findings included pallor (57.90%), jaundice (14.03%), clubbing (7.01%) and oedema (28.07%). During abdominal examination we found hepatomegaly (85.96%), liver tenderness (70.18%) and splenomegaly (17.54%). Hepatic encephalopathy developed in 5.26% patients and 21.05% patients had ascites.

Among the 57 participants 17 (29.82%) had ALA, 10 (17.54%) had PLA and 10 (17.54%) had HCC. Other causes of hepatic SOL were hepatic metastasis (10.53%), hydatid cyst (10.52%), hepatic simple cyst (8.77%), TLA (3.51%) and hemangioma (1.75%)(Fig 1).

Right lobe of liver was involved in 52.63% patients (Fig 6). In 68.42% patients, there was single liver SOL and the size was more than 5 cm in 57.64% patient.

Among the 57 participants, 38 (66.67%) had cystic and 19 (33.33%) had solid non-cystic SOL in liver. Causes of cystic SOL were ALA, PLA, hepatic simple cyst and hydatid cyst or Cystic Echino-coccosis. Non-cystic or solid space occupying lesions include HCC, hepatic secondary metastasis, TLA and hemangioma (Table 1).

Among 57 participants 13 (22.80%) were diabetic and 11 (19.30%) were HIV positive. In diabetic patients PLA (61.54%) was most common. Other lesions were ALA (30.76%) and secondary hepatic metastasis (7.70%). Among 11 HIV positive patients, common causes of hepatic SOL were ALA (36.36%), HCC (36.36%), TLA (18.18%) and secondary liver metastasis (9.10%)(Table 2).

Most of the pathological lesions of liver were seen in HIV infected patients with low CD4 count (<200 cells/μL) (63.63%)(Table 3).

In immuno-competent patients the most common

Table 1 — *Distribution of Cystic / Solid (Non-cystic) lesions according diseases (n=57)*

Cystic / non-cystic	Lesions	Number (n=57)	%
Cystic	ALA	17	44.73
	PLA	10	26.32
	Hepatic simple cyst	5	13.16
	Hydatid cyst	6	15.79
Non-cystic	Hepatocellular Carcinoma (HCC)	10	52.63
	Secondary metastasis	6	31.59
	Tubercular Liver Abscess/lesion (TLA)	2	10.52
	Hemangioma	1	5.26

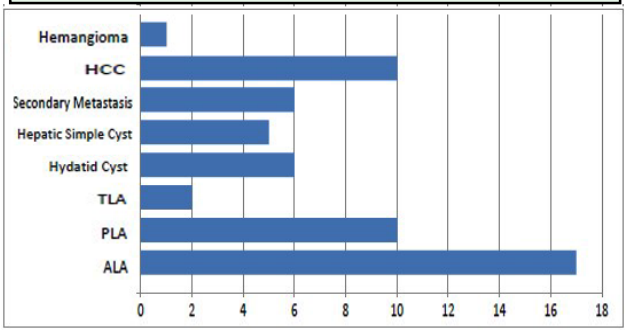

Fig 1 — Distribution of study population according to Diseases (n=57)

Table 2 — *Distribution of liver SOL according to diseases associated with Diabetes (n=13) and HIV (n=11)*

Comorbidities	Lesions	Number	%
Diabetes (n=13)	PLA	8	61.54
	ALA	4	30.76
	Secondary metastasis	1	7.70
HIV (n=11)	ALA	4	36.36
	HCC	4	36.36
	Secondary metastasis	1	9.10
	Tubercular abscess	2	18.18

etiology was ALA (27.27%) followed by HCC, hydatid cyst, simple cyst, secondary malignancy, PLA and hemangioma.

Among 57 patients 17 (29.82%) were diagnosed with ALA. Twelve (70.59%) patients were male and remaining were female. Ten patients (58.82%) had history of alcohol consumption. Out of 17 patients 4 were diabetic (23.53%) and 4 were HIV positive (23.53%).

All of them had enlarged liver with liver tenderness. Eight of 17 ALA cases were anemic (Hb <10 gm %), 13 patients had raised Total Leukocytes Count (TLC >12000 cells/cmm). Three patients had raised level of total bilirubin, SGPT as well as prothrombin time. Among four diabetic patients two had raised HbA1c level with the values being 9.2% and 9.9% respectively. All ALA were microbiologically confirmed. In 14 cases Leishman Giemsa staining showed plenty of degenerated hepatocytes, necrosis, plenty of neutrophils and both cyst and vegetative forms of *Entamoeba histolytica*. In one case *E histolytica* was identified by saline wet mount preparation under microscope and remaining 2 cases were treated empirically based on clinical and radiological findings. Stool sample from all patients were examined for ova, parasite, cyst and among them 3 (17.65%) had *E histolytica* trophozoites and 3 had cyst also.

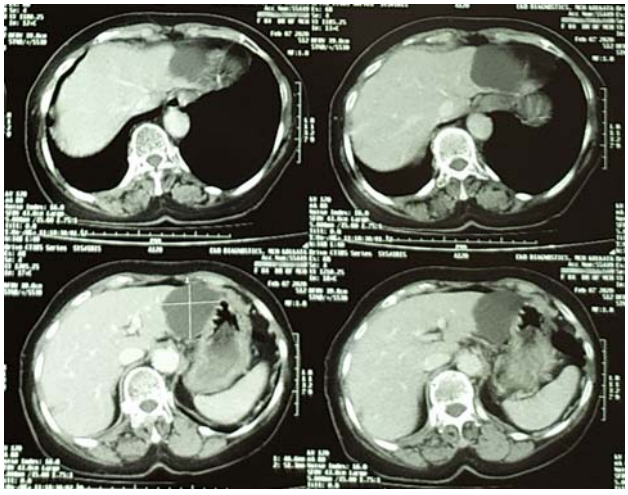

Fig 2 — A well-defined non enhancing thin-walled cystic lesion (86×84×75 mm) is seen in left lobe (segment2 and 3) of liver suggestive of amoebic liver abscess

Table 3 — *Distribution of Liver SOL associated with HIV positive status according to CD4 count (n=11)*

CD4 Count (cells/μL)	ALA	TLA	HCC	Secondary hepatic metastasis
<50	0	1	1	1
50-100	0	1	2	0
101-200	1	0	1	0
201-500	2	0	0	0
>500	1	0	0	0

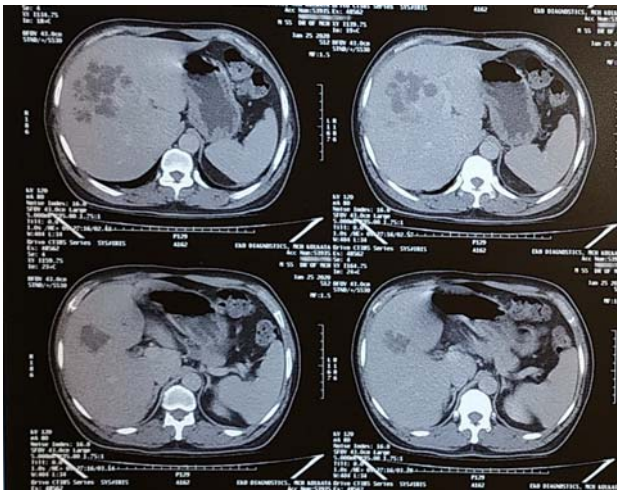

Fig 3 — Multiple small decreased attenuating lesions in right lobe and largest one is 63×54 mm. (pyogenic liver abscess)

Among the 57 participants 10 (17.54%) had PLA. Among them 8 were male and 2 were female. All patients presented with complaints of fever and 9 had associated complaints of pain in the right upper quadrant of abdomen.

Average size of lesion in PLA was 6 cm. Out of 10 patients of PLA, 6 patients (60%) had right lobe and 4 patients (40%) had bi-lobar involvement of PLA. In 50% patients the number of lesions was 2, 40% patients had a single lesion and in 10% patient had 3 cystic lesions were present in liver.

In culture we found *Klebsiella pneumonae* (40%), *E coli* (20%), *Staphylococcus aureus* (10%), *Burkholderiapseudomallei* (10%) and 20% patients had no growth. Only one patient had *Staphylococcus aureus* growth in blood (Table 4).

Among 57 patients two had TLA (3.51%) and both of them were immunocompromised male (CD4 counts 45 cells /μL& 62 cells /μL respectively). Both of them presented with low grade fever with an average duration of 4 weeks, pain abdomen and weight loss. One of them had bronchiectasis. Both patients had a history of chronic alcohol abuse, anemia and hepato-splenomegaly. One of them had splenic abscess. Average size of the lesions was 4 cm and all were confined in right lobe of liver. One of them had multiple retroperitoneal lymph nodes.

Ten patients (17.54%) out of the total study population had HCC. Eight were male. Majority of the HCC patients presented with complaints of pain abdomen (90%) and the remaining had fever (30%), jaundice (30%), weight loss (50%), melena (30%) and hematemesis (10%). Two patients (20%) developed hepatic encephalopathy. Four patients (40%) had history of alcohol use and 3 were smoker. Nine patients (90%) had enlarged liver. Alpha-feto protein level was raised in all patients and the mean value was 1700.70 ng/ml. Isolated HBsAg were reactive in 4 patients. Four patients were HIV positive and 2 of them were co-infected with Hepatitis C and 1 was co-infected with Hepatitis B (Table 5). Among them1 had previously diagnosed Non-alcoholic Fatty Liver Disease (NAFLD) and 1 had alcoholic CLD.

All cases of liver SOL were solid tumors. Out of 10 HCC patients 4 had bi-lobar involvement and the remaining patients had isolated right (30%) and left (30%) lobe involvements. Six patients had lesions more than 5 cm in size. Four patients had retroperitoneal, peri-portal lymph nodes as well as Para-aortic lymph nodes. HCC was common in those patients with chronic viral Hepatitis B infection and high HBV viral load (>20000 IU/ml copies).

Among 57 patients, 6 (10.53%) had secondary metastasis of liver. The primary sites of malignancy were adeno-carcinoma of colon (33.33%), adeno-carcinoma of lung (16.66%), adeno-carcinoma of stomach (16.66%), breast (16.66%) and cholangio-carcinoma (16.66%) (Table 6). Among 6 patients, 4 were male and 5 of them presented with pain in right quadrant of abdomen and history of weight loss (more than 10% in last 6 months). One female patient was diabetic and 1 had chronic Hepatitis B infection. One male patient was HIV positive who was diagnosed with adenocarcinoma of colon.

One patient with adeno-carcinoma of colon and secondary metastasis in liver also had splenomegaly with retroperitoneal lymph nodes. All 5 patients had normal Alpha Feto-Protein (AFP).

Three patients had only left lobe lesion and remaining had bi-lobar involvement. Lesion size was less than 5 cm in 4 patients and 2 had more than 5 cm. Liver echo texture was altered in 2 patients and 3 patients had ascites.

Five patients (1 female, 4 male) were diagnosed with hepatic simple cyst (8.77%) and all of them were asymptomatic. No abnormalities were detected in Liver Function Test and AFP level was within normal limits. Size of all simple cysts was less than 5 cm and majority (80%) of them were confined to the left lobe.

One 67-year, male with chronic liver disease was diagnosed with hemangioma (<5 cm) in right lobe of liver during routine work up of chronic liver disease.

Six patients (4 male and 2 female) were diagnosed with hydatid cyst (10.53%). Five of them were from

Table 4 — Distribution of Pyogenic Liver Abscesses according organisms identified (n=10)

Organisms	Male	Female	%
Klebsiella pneumoniae	4	0	40
E coli	1	1	20
Staphylococcus aureus	1	0	10
Burkholderiapseudomallei	1	0	10
No growth	1	1	20
Total	8	2	100

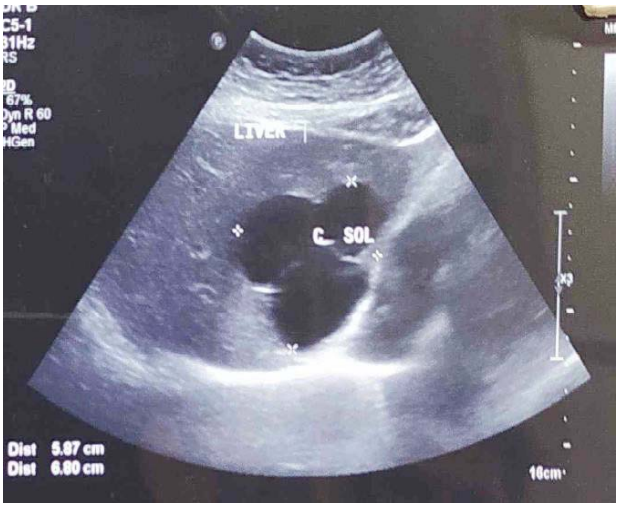

Fig 4 — Septate cystic SOL on left lobe of liver measuring 58mm×68mm (Hydatid cyst)

Table 5 — *Distribution of HCC according to association of Chronic Viral Hepatitis (n=10)*

Patients	Male	Female	%
Isolated Chronic Hepatitis B infection	3	1	40
Isolated HIV positive	1	0	10
HIV-HCV Co-infection	2	0	20
HIV-HBV Co-infection	0	1	10
NAFLD	1	0	10
Alcoholic CLD	1	0	10
Total	8	2	100

Fig 5 — Amoebic liver abscess

Table 6 — *Distribution of secondary Metastatic lesions in liver according to Primary Sources (n=6)*

Primary sites	Male	Female
Breast	0	1
Adenocarcinoma of Lung	1	0
Cholangiocarcinoma	0	1
Adenocarcinoma of Stomach	1	0
Adenocarcinoma Colon	2	0
Total	4	2

rural area and all of them presented with pain in the right upper quadrant of abdomen with enlarged liver. Four (66.67%) had high Echinococcal Antibody (IgG). All lesions were confined to the right lobe of liver. The mean diameter of the lesions was 6.83 cm. At the end of 3 months of medical treatment the lesion size was decreased by 50% in all cases and calcification of cyst wall seen in 5 cases.

Fever (p=0.005), alcohol (p=0.007), raised total bilirubin (p=0.003), altered albumin globulin ratio (p=0.004) were found to have predictive value in ALA.

In PLA right upper quadrant pain abdomen (p=0.030), low grade fever (p=0.044), diabetes (p=0.0001), increased TLC (p=0.003), raised FBS (p=0.0001), raised ESR (p=0.020), increased CRP (p=0.001), prolonged prothrombin time (p=0.033), more than one cystic liver SOL (p=0.041) had significant predictive value.

Fever (p=0.042), weight loss (p=0.328), jaundice (p=0.018), oedema (p=0.004), splenomegaly (p=0.007), low platelet count (p=0.006), SGOT (p=0.045), low albumin (p=0.002), altered albumin globulin ratio (p=0.007), prolonged prothrombin time (p=0.002), high LDH (p=0.003), high uric acid (p=0.016), low sodium (p=0.012) and HBsAg reactive status (p=0.001) had significant predictive value in HCC.

Weight loss (p=0.005), melena (p=0.011), jaundice (p=0.019), oedema (p=0.043), raised total bilirubin (p=0.046), low albumin (p=0.008), high globulin (p=0.007), altered albumin globulin ratio (p=0.008), high ALP (p=0.030), high ESR (p=0.015), prolonged prothrombin time (p=0.014), high LDH (p=0.003), high uric acid (p=0.003) and presence of retroperitoneal lymph node (p=0.002) had significant predictive value in secondary hepatic metastasis.

Discussion

Among the 57 participants 17 (29.82%) had ALA, 10 (17.54%) had PLA and 10 (17.54%) had HCC. Other causes of hepatic SOL were hepatic metastasis (10.53%), hydatid cyst (10.52%), hepatic simple cyst (8.77%), TLA (3.51%) and hemangioma (1.75%).

Most common presentation was pain in right upper quadrant of abdomen (78.94%) or fever (57.89%) and most of them had both (49.12%). Other presenting symptoms were vomiting (8.77%), dyspepsia (12.28%), weight loss (22.80%), cough (19.29%) and abdominal distension (10.52%).

Thirty-eight (66.67%) had cystic and 19 (33.33%) had solid non-cystic SOL in liver. Causes of cystic SOL were ALA, PLA, hepatic simple cyst and hydatid cyst (cystic echinococcosis). Non-cystic or solid space occupying lesions include HCC, hepatic secondary metastasis, TLA and hemangioma.

In the study by Jha, *et al* at Kolkata[7] it was found that 88% patients with liver SOL had ALA. There was correlation between the occurrence of liver abscesses and addiction to alcohol and history of Diabetes Mellitus. The most common cause of liver SOL in our study was ALA (29.82%) and there was correlation between the occurrence of ALA and alcohol consumption (58.82%) and diabetes (23.53%) similar to their study.

Vineet Jain, *et al*[8] found that ALA (86%) was more common over PLA (14%) which is similar to our findings. They also showed that abscesses were found mainly in right lobe (76%) as single SOL (66%). Complications include ascites (12%) and pleural effusion (6%). In our study 66.67% patients had liver abscess in right lobe and 22.22% patients had bi-lobar involvement. Only 3.70% patients had ruptured liver abscess requiring surgical intervention. No other complication was found.

Soumik Ghosh, *et al* at New Delhi[9], found the incidence of TLA to be 7.5%. In our study we found 2 cases with TLA (3.51%).

Neeraj Dhameja, *et al*[10] found that Fine needle Aspiration Cytology (FNAC) was safe and rapid diagnostic tool for hepatic mass. In our study 19 patients with solid non cystic liver SOL underwent FNAC. None of them suffered any complication.

Sudhamshu KC, *et al*[11] found 83 patients (81.31%) with single lesion among a total number of 102 patients. We also found that the most common lesions were solitary (68.42%). In their study the most common organisms were *E coli* followed by *Klebsiella* sp, *S aureus*, *Pseudomonas aeruginosa* and *Acenetobacter*. In our study most common organism was *Klebsiella pneumonae* (40%) followed by *E coli* (20%), *Staphylococcus aureus* (10%), *Burkholderiapseudomallei* (10%) and the other 20% patients had no growth.

In 2021 a study from New Delhi, India by Jindal, *et al*[12] found that the most common etiologies of liver abscess were ALA (81%) and PLA (10.3%). Compared with ALA, patients with PLA were in older age group, more often had multiple and bi-lobar abscesses with local complications. Nearly 68.96% Liver abscess were solitary, 68.96% localized to the right lobe of liver. In our study we found that most common cause of liver SOL was ALA (29.82%) followed by PLA (17.54%) and HCC (17.54%). In our study, patients with PLA were in

51-60 years age group, more often 60% had multiple and bi-lobar (40%) abscesses.

Sahid Imam Mallick, *et al* at Kolkata[13] found that the commonest cause of liver SOL was metastatic adenocarcinoma (32.55%) followed by ALA and PLA (20% and 15% respectively). In contrast, we found that most common cause of liver SOL in our study population was ALA (29.82%).

Takahisa Sato, *et al*[14] in 2009 detected 243 treatment naïve cases of HCC among 1,431 patients with chronic Hepatitis C. Out of 243 HCC cases 221 patients were first detected by Ultrasonography. HCC was first detected by CT scan in 22 cases. In our study 9 patients with HCC were screened by CT scan and the remaining 1 with USG.

In 2018, Jennie Engstrand, *et al*[15] performed a retrospective population-based study. Liver metastasis was diagnosed in 272 out of 1026 (26.5%) patients with colorectal carcinoma within 5 years of diagnosis of the primary lesion. Liver metastases were more extensive for right-sided cancer. In our study, among 57 patients, 6 (10.53%) had secondary metastasis of liver and primary sites of malignancy were adenocarcinoma of colon (33.33%), adenocarcinoma of lung (16.66%), adenocarcinoma of stomach (16.66%), breast (16.66%) and cholangiocarcinoma (16.66%). In 2 cases of hepatic secondary malignancies primary sites were right side adenocarcinoma of colon.

Our study population size was small. We did not find any uncommon cases of Liver SOL such as polycystic liver disease, syphilitic gumma, liver fluke infestation or tumors like adenoma, fibronodular hyperplasia or primary hepatic NHL. We did not perform any immuno-histochemistry. We could not estimate human hepatocyte growth factor, and insulin-like growth factor, lens culinaris agglutinin-reactive AFP and des-gamma carboxyprothrombin and glypican-3.

Conclusion

The most common lesion was ALA (29.82%) followed by PLA (17.54%), HCC (17.54%) and other causes of hepatic SOL were hepatic metastasis, hydatid cyst, hepatic simple cyst, TLA and hemangioma.

Fever, alcohol, raised total bilirubin and altered albumin globulin ratio were found to have predictive value in ALA. In PLA right upper quadrant pain abdomen, low grade fever, diabetes, increased TLC, raised FBS, raised ESR, increased CRP, prolonged prothrombin time and more than one cystic liver SOL (p=0.041) had significant predictive value.

TLA was common in HIV patients with low CD4 counts.

Fever, weight loss, jaundice, oedema, splenomegaly, low platelet count, SGOT, low albumin, altered albumin globulin ratio, prolonged prothrombin time, high LDH, high uric acid, low sodium and HBsAg reactive status had significant predictive value in HCC. In secondary hepatic metastasis weight loss, melena, jaundice, oedema, raised total bilirubin, low albumin, high globulin, altered albumin globulin ratio, high ALP, high ESR, prolonged prothrombin time, high LDH, high uric acid and presence of retroperitoneal lymph node had significant predictive value.

Further study with larger sample size on this subject may reveal better quality evidences.

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Original Article

Statin Intake and Thrombotic Events in Indian Patients — A Cross Sectional Study

Ankita Sharma[1], Aruna Donepudi[2], Mekala Padmaja[3]

The present cross-sectional study was planned to evaluate the incidence of (cardiovascular or stroke) events in patients on statin therapy using data collection form which included patient details such as medical history, treatment history and events occurred. Statin use was stratified to record the occurrence of primary event in patients using statin prophylactically and the occurrence of re event in the patients using statin in therapeutic manner. We enrolled 103 patients out of which thrombotic events occurred in 10 patients (9.7%). Among the 10 patients, 7 (6.7%) patients had Coronary Artery Disease (CAD) while 3 (2.9%) patients had stroke with statin use. Our study got similar incidence of major clinical events with statin use as in literature.

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Key words **: Statin, Cardiovascular events, Stroke.**

Globally, an estimated 17.9 million people died from Cardiovascular Disease (CVD) in 2016, representing 31% of all deaths. Of these deaths, 85% were due to heart attacks and stroke. The factors which contributed to cardiovascular diseases were high systolic blood pressure, air pollution, high total cholesterol, high fasting plasma glucose, high body-mass index and rapid population ageing during that period. The India Global Burden of Disease (GBD) Collaborators noted that ischaemic heart disease and stroke have made the largest contribution to the total burden of mortality in India in 2016, at 28·1% which increased by 34·3% from 1990 to 2016[1]. Asian Indians have the highest risk of premature Coronary Artery Disease (CAD) and diabetes. Available evidence supports the use of statin therapy for primary prevention in Asian Indians at a younger age and with lower targets for Low-density Lipoprotein Cholesterol (LDL-C) and Non-high-density Lipoprotein (non-HDL-C) than those currently recommended for Americans and Europeans. Early aggressive statin therapy offers the greatest potential for reducing the continuing epidemic of CAD among Indians[2].

In adults at high risk of CVD without prior CV events, statin therapy is associated with reduced risk of all-cause and cardiovascular mortality and CVD events. Benefits appear to be present across diverse demographic and clinical subgroups- men and women, young and old, and in people with and without diabetes or prior diagnosis of CVD. Greater absolute benefits are seen in patients at higher baseline risk and do not appear to be restricted to patients with marked hyperlipidaemia[3,4]. Several reviews and meta-analysis have demonstrated the incontrovertible benefits of statin therapy in patients with CVD[5,6]. The updated 2013 Cochrane review showed overwhelming benefits of long-term statin therapy in primary prevention by demonstrating highly significant reductions in all-cause mortality, Major Adverse Cardiovascular Events (MACE) and the need for Coronary Artery Revascularization Procedures (CARPs) by 25-60%[7]. The US Preventive Services Task Force (USPSTF) concluded that adults who smoke or have dyslipidaemia, diabetes, or hypertension and a 10% or greater 10-year CVD event risk are most likely to benefit from statin use[3].

Clinical trials using statins have demonstrated a reduction in stroke, particularly in patients with established Coronary Artery Disease due to lipid lowering and pleiotropic effects. The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial provided evidence of the benefit of statin therapy among patients with a Transient Ischemic Attack (TIA) or stroke within the previous 6 months[8]. The Heart Protection Study (HPS)[9,10] and the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT)[11] study

Editor's Comment :

- This cross sectional aimed to study the incidence of (cardiovascular or stroke) events in patients on statin therapy. Thrombotic events occurred in 10/103(9.7%) patients despite being on statin therapy for a period of 2 years and more. Our results were similar to the reported incidence of major clinical events with statin use as in literature.

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provide strong support for the role of statin therapy in reducing risk of stroke in patients with average or relatively low LDL cholesterol levels. However, HPS study, found no reduction in the risk of stroke among patients with prior cerebrovascular disease. On the contrary, an increase in the incidence of haemorrhagic stroke was observed among patients treated with simvastatin (40 mg)[9,10]. In primary prevention studies, the use of statins is not associated with an increased risk of intracranial bleeding while there may be an increased incidence of haemorrhagic stroke with high dose statins in patients with a previous cerebrovascular event. Patients who suffer from stroke while on statins should not discontinue statins. Statin-naive patients are associated with better survival and improved functional outcome when statins were administered during the acute phase of stroke. In contrast, statins do not confer any benefit in patients with acute ischemic stroke who receive thrombolysis.

However, there is no available Indian literature about the occurrence of clinical events (cardiovascular or stroke) in patients on statin therapy. The present study is planned to evaluate the incidence of (cardiovascular or stroke) clinical events in patients on statin therapy.

Material and Methods

The study was conducted in the Department of Clinical Pharmacology & Therapeutics in collaboration with Department of Cardiology & Neurology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana State. It was a cross sectional study with a sample size of 103. Patients aged between 30-70 years and who were on statin therapy for at least 2 years were included and patients less than 2 year of statin therapy and pregnant and lactating women were excluded from the study.

Methodology :

Study was started after Institutional Ethics Committee(IEC) approval. The patients attending the Outpatient Departments of Cardiology and Neurology on statin therapy for the last 2 years, were included in the study. Written informed consent was taken from all patients prior to the study. Medical history, treatment history and events occurred were collected in a data collection form. Use of statin was stratified into therapeutic or prophylactic based on the indication. The occurrence of primary event in patients using statin prophylactically and the occurrence of re-event in the therapeutic group were recorded in this study.

Statistical analysis :

Data was presented as Mean ± SD. P value < 0.05 was kept as significant.

Results

We enrolled 103 patients in the study who were subdivided into therapeutic group (54 patients) and prophylactic group (49 patients). Amongst them 71 (68.9%) patients were male and 32 (31.1%) were female. Average age of the patient population was 57.8 years. The patients with hypertension were 65 (63.1%), with diabetes 66 (64.1%) and with dyslipidaemia 59 (57.3%). Patients on Rosuvastatin were 68 (66%) and patients on Atorvastatin were 35 (34%). Most commonly used dose was 10 mg for both atorvastatin and rosuvastatin in both the therapeutic and prophylactic group. Average duration of statin use was 4.4 years. Thrombotic events occurred in 10 patients (9.7%) out of 103 patients. Out of 10 patients, 7 (6.7%) patients had CAD while 3 (2.9%) patients had stroke with statin use. The characteristics of study population were shown in Table 1.

Table 1 — *Characteristics of Study Population (n=103)*

Characteristic	Therapeutic (n = 54)	Prophylactic (n = 49)
Age (mean) in years	60.23	55.5
Men : Women	41:13	30:19
Duration of statin use in years	4.51	4.29
Type of statin (A : R)	19:35	16:33
Co-morbidities :		
Diabetes	28/54 (51.8%)	38/49 (77.5%)
Hypertension	34/54 (62.9%)	31/49 (63.2%)
Dyslipidaemia	14/54 (25.9%)	45/49 (91.8%)
Thrombotic event	7/54 (12.9%)	3/49 (6.12%)
M : F	5:2	3:0
CVD	5/54 (9.25%)	2/49 (4.1%)
Stroke	2/54 (3.7%)	1/49 (2%)

Discussion

In our study, we have concentrated on occurrence of thrombotic events of either cardiovascular or stroke after the use of statin for at least 2 years. Our results were consistent with a cohort study by Lee, *et al* which reported major events such as stroke, Acute MI or death in 5.6% of patients maintained on statin compared to 7.8% who discontinued statin[12]. In our study 12.9% patients in the therapeutic group had re-event compared to 5.6% of the above study. The variation in the rate of major events was high in our study which could be due to a small sample size of our study. A meta-analysis done by Guiterrez, *et al* concluded that statin therapy was associated with reduced risk of cardiovascular or cerebrovascular events (14.9% in the statin group *versus* 18.2% in the placebo group)[13].

In our study, cardiovascular events occurred in 7/103 (6.7%) patients maintained on statin out of which

5 patients belonged to the therapeutic group and 2 patients belonged to the prophylactic group. The study by Lee, *et al* evaluated the effect of statin on MI and cardiac procedures such as stenting or endartectomy, the incidence of these events was similar in both statin continued and statin discontinued group. In the meta-analysis by Guiterrez, *et al* MI event rate was 7.2% in the statin group as compared to 10% in the placebo group. Rate of cardiac intervention was 10.9% in the statin group compared to 14.2% in the placebo group.[13]

Stroke occurred in 3/103 (2.9 %) patients in our study out of which 2(3.7%) patients belonged to the therapeutic group and 1 (2%) patient belonged to the prophylactic group. In the study by Lee, *et al* 4.4% events of recurrent stroke were reported in statin continued group patients as compared to 6.2% events in the patients who discontinued statin[12]. In a retrospective observational study by Choi, *et al* cardioembolic stroke patients were analysed which showed a reduction in mortality but no effect on the incidence of recurrent stroke with the use of statin. 9.8% patients in non-statin group compared to 8% patients in the statin group had a recurrent stroke. Also, there was no beneficial effect of statin therapy on recurrent stroke in patients with non-cardioembolic stroke[14]. The meta-analysis by Guiterrez, *et al* reported 4.6% stroke in the statin group compared to 5.4% in the placebo group[13].

Conclusion

In conclusion, our study also got similar incidence of major clinical events with statin use as in literature.

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Conflict of interest : All authors declare there is no conflict of interest.

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Case Report

Refractory Pure Red Cell Aplasia Secondary to Parvovirus B19 in an Immunocompetent Patient : A Challenging Case Report

Shyam Murti Bohare[1], Rajshekhar Lohar[2], Ashish Sanjay Chaudhari[2], Ujjawal Kumar Shriwastav[2], Prabhat Rijal[2], Ravi Kant[3]

This report presents a case of acquired Pure Red Cell Aplasia (PRCA) of a 36-year-old immunocompetent woman after parvovirus B19 infection. Following the fever, she developed severe anaemia and dyspnoea which necessitated frequent blood transfusions. Despite extensive diagnostics, including bone marrow biopsy, initial oral prednisolone and recombinant erythropoietin yielded limited results. Subsequent Intravenous Immunoglobulin (IVIG) treatment did not show significant improvement, challenging the traditional understanding of Parvovirus B19-related PRCA. This case emphasizes the necessity for further research into its diverse clinical manifestations and optimal management strategies.

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Key words **: PRCA, Anaemia, Parvovirus B19, Immunocompetent, Human Parvovirus B19.**

Pure Red Cell Aplasia (PRCA) is a disorder of Red Blood Cells characterized by severe anaemia, reduced reticulocytes in peripheral blood and virtually absent mature erythroblasts in the bone marrow. However, other cell lineages usually remain unaffected. Paul Kaznelson first described it in 1922. The congenital form of PRCA was described by Diamond and Blackfan in 1938.

PRCA is classified as congenital and acquired. The former is a lifelong disorder associated with congenital abnormalities; the acquired type can be further classified as primary and secondary PRCA. Primary-acquired PRCA is idiopathic, while secondary-acquired PRCA is associated with autoimmune diseases, lymphoprolife rative disorders, infections (parvovirus B19), neoplasms (thymoma being the best-known), pregnancy and drugs[1].

Case Report

A 36-year-old, regularly menstruating homemaker without any co-morbidities, addiction, or high-risk behaviour, presented to the OPD with a history of Acute-onset Fever (101-102°F) with chills and myalgia without diurnal variation, which occurred 6 months ago and lasted for 7 days,resolved with over-the-counter medications. The fever was not associated with headache, sore throat, productive cough, abdominal pain, burning sensation during micturition, rashes, and joint pain.

After ten days of fever resolution, she gradually developed Shortness Of Breath (SOB), initially occurring on exertion. Over three months, her SOB worsened from mMRC grade I to grade III, without cough, orthopnea, or paroxysmal nocturnal dyspnea. SOB was associated with regular palpitations during exertion without a history of syncope and chest pain. She was evaluated elsewhere and diagnosed with severe anaemia (haemoglobin 2g/dL) and received multiple blood transfusions every 15-20 days due to the recurrence of similar symptoms.

Editor's Comment :

- Diagnosis of PRCA should be considered in the case of treatment-resistant anaemia. Acquired PRCA is commonly associated with Parvovirus B19 infection and usually has a good prognosis. However, in a handful of cases it may not respond to the conventional treatment including oral prednisolone and IVIG. Refractory cases necessitate patient counselling, intermittent blood transfusions, and long-term follow-up for comprehensive care.

On examination, her vital signs were stable, heart rate of 98 beats per minute, blood pressure of 100/60 mmHg, respiratory rate of 20 breaths per minute, temperature of 98.5°F and oxygen saturation of 99% on room air. Her general physical examination was unremarkable except for severe pallor.Cardiovascular, respiratory, gastrointestinal and neurological examinations were non-contributory.

Upon further evaluation, a complete hemogram revealed severe anaemia and the peripheral smear showed normocytic normochromic anaemia. Subsequent investigations demonstrated decreased reticulocyte count despite adequate levels of vitamin B12, folic acid and ferritin (Table 1). These findings raised concerns regarding the possibility of acquired PRCA. To confirm the diagnosis, a bone marrow biopsy was done, which revealed cellular marrow (Fig 1) with reduced erythroid precursor, along with the presence of a few giant proerythroblasts (Fig 2). To determine the aetiology of PRCA, Anti-nuclear Antibody (ANA) was negative, High-resolution Computed Tomography (HRCT) thorax was

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Table 1 — *Various relevant laboratory parameters*

Laboratory parameters									
Investigations	Reference range	D 01	D 19	D 23	D 30	D 32	D 35	D 45	D 48
Haemoglobin	11.5 – 15 gm/dL	4.5	3.4	9.4	9.24	8.3	7.7	7.7	8
Total Leucocyte Count	4-11 x 10^3/L	5.8	5.3	7.1	7.4	9.85	7.4	7.30	13.30
Differential Count (N/L/M)	40-80/20-40/2-10 %	44/47/6	53/40/4	49/43/6	73/22/4	54/28/12	49/42/6.1	79/5.7/16	65/27/5
Platelets	150-450 x 10^3/mm^3	433	276	321	371	410	371	458	337

Peripheral blood smear : Normocytic normochromic RBCs with mild anisocytosis, Normal counts with mild lymphocytosis. Adequate platelets. No blood parasites were seen.
Bone marrow aspiration and biopsy : Cellular bone marrow with reduced erythrocyte component with occasional giant pronormoblasts seen ;
Vitamin B12: >2000 pmol/L (156-672 pmol/L) ; **Folic acid:** 12ng/mL(> 5.38 ng/mL) ;
Reticulocyte count: <0.2% ; **Ferritin :** 364 ng/mL (10-291 ng/mL) ;
DAT & IAT: negative ; **ANA- IFA:** negative (<1:80) ; **Viral markers:** Non-reactive ;
Stool occult blood: Negative ; **Parvovirus IgG:** 0.95 (< 0.9) ; **Parvovirus IgM:** 3.84 (< 0.9)

N Neutrophils; L Lymphocytes; M Monocytes; DAT Direct antiglobulin test; IATIndirect antiglobulin test; ANA Antinuclear antibody; IFA Immunofluorescence assay; IgG Immunoglobulin G; IgM Immunoglobulin M

done for the possibility of thymoma and was ruled out. Viral markers were found to be negative, while parvovirus serology was positive. Hemoglobinopathies were ruled out by performing haemoglobin high-performance liquid chromatography.

She was treated with oral prednisolone (1mg/kg) along with subcutaneous recombinant EPO. The patient did not exhibit improvement and necessitated blood transfusions every fortnight. Consequently, IVIG was given (0.4mg/kg/day) for 5 days. Despite these therapeutic interventions, there was no significant improvement and the patient currently requires recurrent blood transfusions at intervals of every 3 to 4 weeks.

Discussion

Multiple cases were reported in the literature of parvovirus B19-associated PRCA in immuno-compromised patients. To the best of our knowledge, this is the first case of parvovirus B19-associated chronic PRCA in an immunocompetent non-pregnant adult.

Parvovirus is a compact, non-enveloped, single-stranded DNA virus that exhibits an affinity for erythroid progenitor cells. Parvovirus B19 member of the *erythrovirus* genus belongs to the *Parvoviridae* family. It is the only known parvovirus pathogenic to humans and can cause fifth disease in immunocompetent individuals[2], transient aplastic crisis in patients with haemolytic disorders[3], chronic infection in immuno-compromised patients can lead to chronic pure red cell aplasia. In pregnant women leads to congenital infections and hydrops fetalis[4]. Rarely, immuno-competent adults may manifest with symmetric polyarthropathy mimicking rheumatoid arthritis.

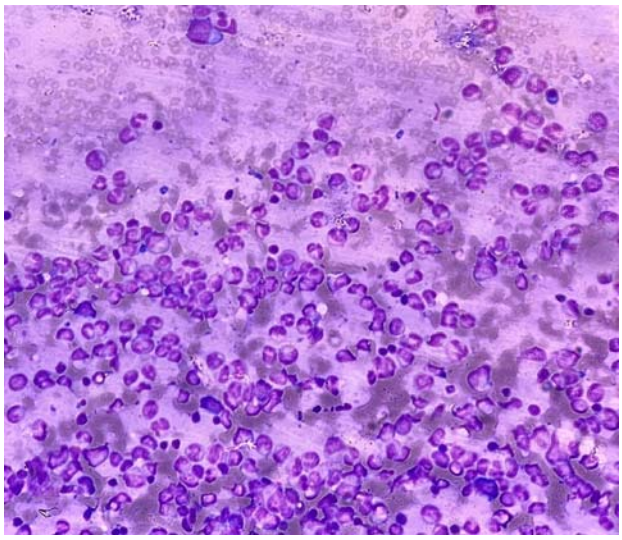

Fig 1 — Bone marrow aspirate showing adequate myeloid series with all stages of maturation. No erythroid lineage cells are seen. Magnification x200 (Leishman stain)

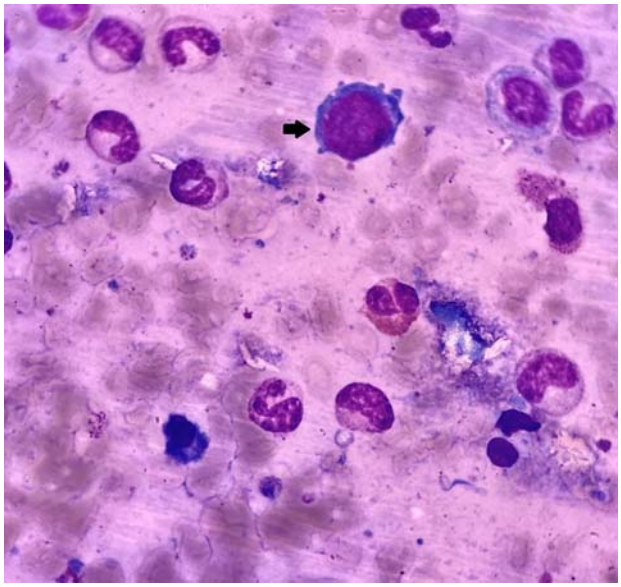

Fig 2 — Bone marrow aspirate showing giant proerythroblast displaying high nucleocytoplasmic ratio, round nucleus, fine chromatin, prominent nucleoli with scant basophilic cytoplasm showing cytoplasmic protrusion. Magnification x400 (Leishman stain)

Parvovirus primarily transmits through the respiratory route and infrequently via blood transfusions and vertical transmission. Following infection in healthy adults, viremia occurs after one week, accompanied by mild symptoms such as pyrexia, malaise, myalgia and pruritus. In the 2nd week of infection peak viremia and production of IgM followed by IgG antibodies occur. Around 3rd week, a second symptomatic phase occurs which manifests as rash, pruritus or arthralgia. PRCA is a self-limiting condition. IgM antibodies typically persist for about 3 months but can be detected for an extended duration, while IgG antibodies provide lifelong protection against secondary infections[6-7].

PS shows normocytic normochromic anaemia with reticulocyte count <10000/µL. WBCs and platelets are normal, sometimes relative lymphocytosis, thrombocytosis or thrombocytopenia[1]. Diagnosing PRCA requires a bone marrow examination, there are absence or near absence of erythroblasts (<1% on marrow differential count). Rarely, a few proerythroblasts or basophilic erythroblasts (up to 5%) may be present. "Giant proerythroblasts" with vacuolated cytoplasm and pseudopodia may suggest parvovirus B19 infection but are not definitive for diagnosis[8]. Confirmation involves anti-parvovirus B19 IgM presence and positive peripheral blood PCR for high parvovirus B19 load.

Management of PRCA depends on the treatment of the underlying cause. Initially, supportive care is given to maintain haemoglobin levels above 7 gm/dL. Definitive treatment is IVIG at 0.4 g/kg/day over five days. Alternatives include corticosteroids, cyclosporin A, cyclophosphamide, anti-thymocyte globulin, alemtuzumab and rituximab[9].

Conclusion

An atypical presentation of PRCA following Parvovirus B19 infection in an immunocompetent adult may not respond to the conventional therapeutic interventions including oral prednisolone and IVIG.This warrants further research to refine management strategies for this uncommon manifestation of PRCA.

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Conflict of Interest : No conflict of interest.

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Case Report

Uncommon Presentation of Adenocarcinoma of Cervix

Neetu Ramkumar Soni[1], Parul Gupta[2]

Early detection and treatment of cancer is very essential for its complete cure. We present a case who came to physician for leg pain, which turned out to be Deep Venous Thrombosis and later associated with adenocarcinoma of cervix diagnosed in early stage by gynecologist. Hence, physicians and general practitioners play a very important role in suspicion of cancer and detailed evaluation for early diagnosis.

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Key words **: Adenocarcinoma of Cervix, Deep Venous Thrombosis, Early Diagnosis of Cancer.**

Early detection and treatment of any cancer is very much necessary for complete cure in most cases. Here we present a case of 45 years old female who presented to physician for deep venous thrombosis and then evaluated by gynecologist in view of menorrhagia. Timely and detailed evaluation revealed presence of suspicious growth over cervix which turned out to be adenocarcinoma of cervix and complete surgical excision was possible.

Case Report

45 years old female came in OPD for right leg pain and swelling since 20-25 days. On examination, her vitals were stable. Her right leg had calf tenderness and edema. Right lower limb venous Doppler suggested Deep Venous Thrombosis (DVT) for which patient was advised anticoagulation treatment and further workup, but they refused treatment. 10 days later, she again presented in OPD for profuse bleeding per vaginum. Patient denied consuming or taking any anticoagulation therapy after the first visit. Patient was hemodyanamically stable and clinical examination revealed pallor. She was admitted and investigated. In view of low hemoglobin of around 6 gm%, she received blood transfusion. Also, Injection Tranexa and oral progesterone were required to control bleeding. Her total leucocyte count and platelet counts were normal. So also, her Renal Function Test (RFT), Liver Function Test (LFT) and coagulation profile was within normal limits. Left lower limb swelling was also noticeable during this admission for which Doppler was planned. Left venous Doppler showed left lower limb acute DVT. Her Computed Tomography (CT), pulmonary angiography was done which showed pulmonary thromboembolism involving segmental branches of pulmonary arteries.

With bilateral lower limb DVT and Pulmonary embolism, she was investigated further. Her Antinuclear Antibodies (ANA) profile was negative for antibodies. She was advised thrombophilia profile but patient refused due to financial constraints. By day 3, menorrhagia was controlled, patient was stabilized with 3 units of blood transfusion and anticoagulation in form of Low Molecular Weight Heparin 0.6 ml SC twice a day started. Patient could now be examined in detail by gynecologist who found a small fragile growth on the cervix. Biopsy was taken from the mass which turned out to be adenocarcinoma in situ. MRI pelvis revealed bulky uterus with 5.9 X 3.8 X 3.7 cm ill defined lesion involving anterior wall of cervix & adjoining lower body of uterus. No obvious extraserosal extension seen.

Editor's Comment :

- Early Detection of cancer can be curative. Venous Thromboembolism can be a marker of underlying malignancy. Though it is a poor prognostic marker in gynecological malignancies, early diagnosis and treatment can offer complete cure.

With this diagnosis, a possibility of extensive thrombosis with pulmonary embolism secondary to adenocarcinoma was thought. Patient was subjected to total hysterectomy with bilateral salpinoopherectomy with lymph node dissection (Fig 1). Histopathology of the specimen showed poorly differentiated adenocarcinoma cervix and lymphnode invasion was not seen. Further Immunohistochemistry (IHC) marker study was done and it reconfirmed primary cervical malignancy. Patient received chemotherapy and is stable without recurrence 1 year post surgery follow up.

Discussion

Many a times patients present with unprovoked acute venous thromboembolism. Such cases needs to be evaluated for occult or undiagnosed malignancy. Several cohort studies have suggested that the incidence of cancer among patients who present with unprovoked Venous Thromboembolism (VTE) is more than 3 times higher than among patients with a provoked VTE and there is evidence that more than 40% of these cancers are metastatic at the time of diagnosis[1]. The incidence of thromboembolism in cervical cancer patients was around 11.7%[2]. In various studies amongst all gynecological

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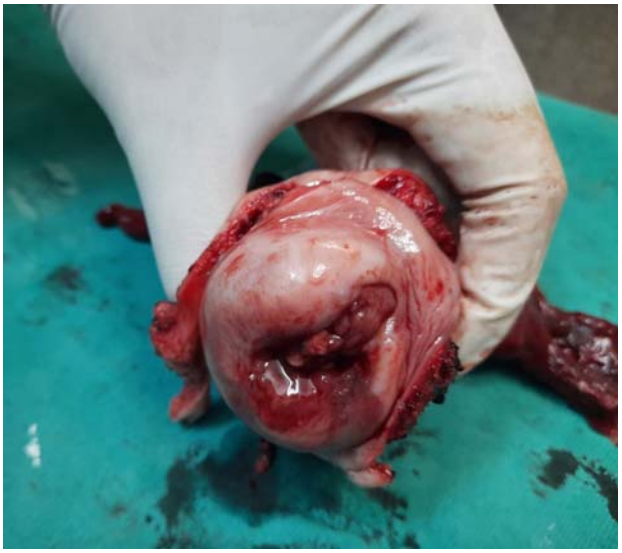

Fig 1 — Specimen after Hysterectomy showing growth on the Cervix

malignancies, endometrial carcinoma was most commonly found to be associated with risk of Deep venous thrombosis, with cervical cancer being second on list sharing its position with ovarian carcinoma.

The diagnosis of venous thromboembolism is a poor prognostic factor in patients with locally advanced cervical cancer[3]. Hence, the importance of early diagnosis and treatment in such patients for possibility of complete cure.

There are multiple causative factors for increased risk of venous thromboembolism. This includes activation of coagulation cascade directly by cancer cells or compression of the vein by the tumor mass leading to venous stasis and thus thrombus formation. Also, treatment of cancer itself can lead to venous thromboembolism. Patient can have inherent tendency for thrombus formation that can lead to same.

Overall, VTE represents aggressive tumor behavior and poor patient condition and is an independent prognostic factor for decreased survival in women with cervical cancer[4]. But our patient presented early, so could be treated and complete cure could be offered.

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Drug Corner

Assessing the Therapeutic Effectiveness and Tolerability of Lincomycin Injectables in Skin and Soft Tissue Infections and Surgical Site Infections : A Comprehensive Real-World Evidence Study

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

Objective : The open-label, observational, real-world evidence study evaluated the effectiveness and tolerability of Lincomycin injection in patients with Surgical Site Infections (SSI) or Skin and Soft Tissue Infections (SSTI).

Methodology : A total of 214 patients above 18 years of age, diagnosed with impetigo, folliculitis, or minor SSTI, were enrolled and received Lincomycin 600 mg (intramuscular or intravascular). The primary outcomes included the evaluation of signs and symptoms associated with SSI and SSTI wound healing and post-operative pain after the treatment with Lincomycin injection. Secondary outcomes included 30-day readmission rates and adverse events.

Result : Lincomycin 600 mg injectable significantly improved mean symptom score for fatigue, cellulitis, redness, and pain around the infectious area. Additionally, complete resolution of folliculitis and scar formation was observed after Lincomycin treatment ($P<0.05$). The drainage of fluid also significantly decreased. No major adverse events related to Lincomycin administration, such as diarrhoea or Clostridium Difficile Infection (CDI), were reported throughout the study period. Moreover, no patients required readmission, indicating that Lincomycin was generally well-tolerated without significant risks or adverse effects.

Conclusion : The study supports Lincomycin injection as an effective and safe option for treating SSI and SSTI.

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***Key words* : Surgical Site Infection, Skin & Soft Tissue Infection, Lincomycin Injection, Surgery.**

Skin and Soft Tissue Infections (SSTIs) result from a compromise of the skin's defences and microbial invasions and interactions therein. Since SSTIs are usually caused by bacteria, viral, fungal, or parasitic aetiologies[1]. In India, there are minimal data on the prevalence of SSTIs and only few studies have been done till date with one study reporting an incidence rate of 18.21/1000 person years in a tertiary care hospital in South India[2,3]. SSTIs are associated with risk factors such as diabetes, compromised immune system, trauma, obesity, injury, chronic skin conditions, etc[4]. SSTI can also be caused by other factors, such as viruses (eg, herpes simplex virus), fungi (eg, Candida or dermatophytes causing fungal infections) or parasites (eg, scabies mites). However, bacterial infections, particularly those caused by Staphylococcus spp. and Streptococcus spp. Staphylococcus aureus and Streptococcus pyogenes, are the most common culprits in SSTIs[5]. There are various types of SSTI, each characterized by specific symptoms, affected tissue such as cellulitis, folliculitis, abscesses, etc[6]. Severe infections often present with intense pain, rapidly spreading redness, significant swelling, systemic signs of infection (eg, high fever, rapid heart rate), diarrhoea, tissue destruction, fatigue and anaphylactic reactions[7].

The treatment options for SSTI depend on the specific type and severity of the infection, as well as individual patient factors. Therefore, antibiotics are a mainstay in the treatment of bacterial SSTI. Commonly used antibiotics include penicillin's, cephalosporins, macrolides and fluoroquinolones. In severe cases or when resistant bacteria are suspected, intravenous antibiotics may be necessary. Pain associated with SSTI can also be managed with acetaminophen and anti-inflammatory drugs (NSAIDs)[8]. While current treatment options for SSTI are generally effective, there are some limitations and challenges that healthcare professionals may encounter. Antibiotic resistance is a significant concern in the treatment of SSTI whereas some antibiotics have a narrower spectrum of activity, meaning they are effective against specific types of bacteria [9].

Lincomycin was isolated from the Streptomyces lincolnensis strain in 1962[10]. Lincomycin has been utilized in both its oral and injectable forms for the treatment of Respiratory Tract Infections (RTI), Skin and Soft Tissue Infections (SSTI) and Surgical Site Infection (SSI), bone and joint infections (osteomyelitis and septic arthritis) and oro-dental infections. It has

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proven to be particularly valuable in cases involving strains of bacteria that produce Penicillinase (an enzyme that inactivates penicillin) or those that are resistant to Erythromycin (another antibiotic). Therefore, Lincomycin serves as an effective antibiotic for combating infections caused by specific antibiotic-resistant strains[11]. This study aims to evaluate effectiveness and tolerability of Lincomycin injectable 600 mg/ml in the treatment of Surgical Site Infection (SSI) and Skin and Soft Tissue Infection (SSTI).

Materials and Methods

Study design :

This was an open label, observational, real-world evidence study that assessed the effectiveness and tolerability of Lincomycin injection. Data was collected using a standardized case report form that included demographics, treatment dose and duration, symptom improvement, clinical condition, comorbidities, complications and details of concomitant medication.

Study participants :

Patients with SSI or SSTI were prescribed Lincomycin injection 600 mg (intramuscular or intravascular). Patients of either gender above 18 years of age, who were undergoing surgical operation and clinically diagnosed with impetigo, folliculitis, or minor SSTI including secondarily infected eczema presumed to be caused by Staphylococcus aureus were included. Pregnant or breastfeeding women were excluded. Patients with known sensitivity to Lincomycin or Clindamycin, signs of systemic infection (such as fever) or with evidence of abscess or cellulitis at the site of treatment were also excluded.

Outcome measures :

The primary outcome measures included evaluation of signs & symptoms associated with SSI (reduction in severity, signs of infection at surgical site, wound healing, postoperative pain) & SSTI (erythema, purulence, crusting, oedema, redness, swelling, warmth, and pain) after Lincomycin injection with incision and drainage after the end of original planned course. It also added therapy to the patients after hospital discharge. Secondary outcomes included change in wound size from baseline, SSI & SSTI related 30-day re-admission and incidence of adverse events such as (allergic contact dermatitis, antibiotic resistance and anaphylaxis. Safety outcomes included adverse effects reported by the patients and any abnormal findings reported through routine investigations. Data was collected from baseline till end of treatment.

Statistical analysis :

A sample size of 214 patients was considered adequate for the study. Descriptive statistics was used to present the data in mean and percentage. Paired t-test and Wilcoxon Sign Ranked Test were used to test significance.

Results

Demography and baseline data :

A total of 214 patients were enrolled for the study, comprising 62.15% of males and 37.85% of females. The distribution of patients across different age groups is summarized in Table 1, with the maximum number of patients belonging to the age group of 21-40 years (59.35%). Patients received Lincomycin injections at a dosage of 600 mg/ml. Majority of the patients in our study presented with various diagnoses including abscess, appendicitis, cellulitis, post-surgical infections and diabetic foot infections (Table 1).

The mean duration of treatment with Lincomycin injection was found to be 6 days (30.37%), with a minimum to maximum ranging from 5-10 days (Fig 1).

Effectiveness :

The results pertaining to ESR, WBC and Hb values in patients treated with injectable Lincomycin (IV + IM) are presented in Table 2. There was a significant change observed in mean ESR and WBC from 21.40mm/hr, 18388.57 million/mm^3 to 8.50 mm/hr and 8974.29 million/mm^3 respectively ($P<0.05$) (Table 2).

Symptoms such as fatigue, cellulitis, redness and pain around infectious area were reduced from 0.38, 2.11, 1.97, 2.35 to 0.02, 0.07, 1.03, 0.08 respectively. Also, folliculitis (0.80) and scar (0.01) formation completely reduced after the Lincomycin treatment

Table 1 — *Demographics details of patients*

Age wise distribution		
Age Group	No of Patients (N=214)	Percentage
< 20 Years	20	9.35%
21-30 Years	64	29.91%
31-40 Years	63	29.44%
41-50 Years	47	21.96%
51-60 Years	12	5.61%
61-70 Years	6	2.80%
> 70 Years	2	0.93%
Gender wise distribution		
Male	133	62.15%
Female	81	37.85%
Diagnosis based distribution		
SSTI	17	7.94%
Abscess	30	14.02%
Wound Infection	4	1.87%
Cellulitis	62	28.97%
Diabetic foot infection	15	7.01%
Injury	5	2.34%
SSI	8	3.74%
Appendicitis	14	6.54%
Post surgical infection	7	3.27%
Others	52	24.30%

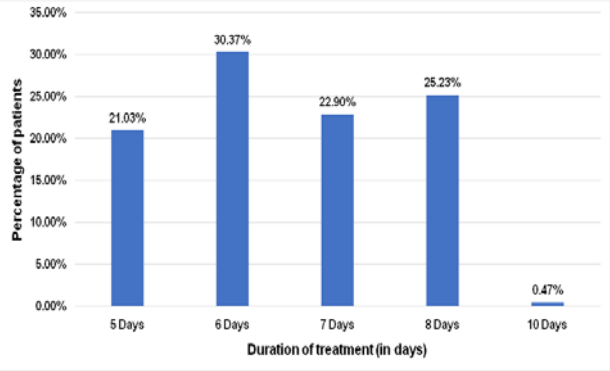

Fig 1 — Duration of Treatment

(P<0.05). The drainage of fluid was also decreased from 2.2 to 1.01.The graphical representation of the outcomes is presented in Fig 2.

Tolerability :

The tolerability of Lincomycin injection was assessed and it was found to be safe and well tolerated by the patients. Throughout the study period, no major adverse events related to Lincomycin administration such as diarrhoea or CDI were reported. Re-admission was not observed in any patient.

Discussion

The findings of our study support the use of Lincomycin as an effective treatment option for SSTI. The significant reduction observed in various outcomes and their related parameters, such as fatigue, pain, cellulitis, folliculitis and redness, indicate the therapeutic benefits of Lincomycin in managing these infections. These results align with previous studies highlighting the efficacy of Lincomycin in treating Respiratory Tract Infections (RTI), SSTI and bone infections.

The present study demonstrated that Lincomycin injection has a generally favourable safety profile in the study population, with a low incidence of adverse events. The most reported adverse events, such as diarrhoea and pain around the area, were typically mild and self-limiting, indicating good tolerability of the drug. Severe adverse reactions were rare and no unexpected safety concerns were identified. These findings contribute to the body of evidence supporting the safety and tolerability of Lincomycin in clinical practice.

Several studies have investigated the role of Lincomycin in different clinical settings, demonstrating its efficacy in treating diabetic foot infections and reducing the risk of SSI and SSTI. A study conducted in 2013 in China focused on the prevention of central venous catheter infections in the ICU setting. The study randomized 172 patients with central venous catheters into trial and control groups. The trial group received

Table 2 — *Mean values for ESR, WBC, Hb*

Parameter		Mean	N	SD	P-Value
ESR (mm/hr)	BT	21.40	10	16.02	0.008
	AT	8.50	10	4.95	
WBC (million/mm^3)	BT	18388.57	35	4527.42	0.000
	AT	8974.29	35	2016.31	
Hb (g/dL)	BT	11.37	13	0.84	0.717
	AT	11.30	13	0.78	

BT : Before Treatment; AT : After Treatment

Lincomycin combined with heparin sodium, while the control group received normal saline and heparin sodium. The trial group showed significantly lower incidence rates of infection at 1-2 weeks (2.33%) and 2-3 weeks (5.81%) after catheterization compared to the control group (10.47% and 15.12%, respectively). The total incidence of infection was also significantly lower in the trial group (9.30%) compared to the control group (30.23%). The positive rate of blood culture was significantly lower in the trial group (12.50%) compared to the control group (53.85%). These findings highlight the efficacy of Lincomycin combined with heparin sodium in reducing central venous catheter infections[11].

Furthermore, a study involving 40 randomly allocated patients evaluated the effect of intra-abdominal lavage with an antibiotic solution containing Lincomycin and gentamicin in decreasing the risk of postoperative infections after colorectal cancer surgeries. Group 1 patients underwent lavage with normal saline followed by gentamicin-Lincomycin solution, while Group 2 patients underwent lavage with normal saline only. The study found a significant difference in the incidence of postoperative wound sepsis between the two groups, with a lower incidence in Group 1 (5%) compared to Group 2 (45%). The isolated organisms in Group 1 were Pseudomonas, while Group 2 had cases of *E coli*, Pseudomonas, Klebsiella and Enterobacter infections. These findings suggest that intra-abdominal lavage with Lincomycin and gentamicin may reduce the risk of postoperative infections in colorectal cancer surgeries[12].

These studies collectively support the efficacy of Lincomycin in preventing central venous catheter infections, treating diabetic foot infections and reducing postoperative infections in colorectal cancer surgeries. However, it is important to consider the specific study designs, patient populations and limitations of each study when interpreting the results. Further research and well-designed clinical trials are necessary to validate.

Like any other study, our research has certain limitations that should be acknowledged. The study design and methodology may have inherent limitations, such as the lack of a control group or a relatively small

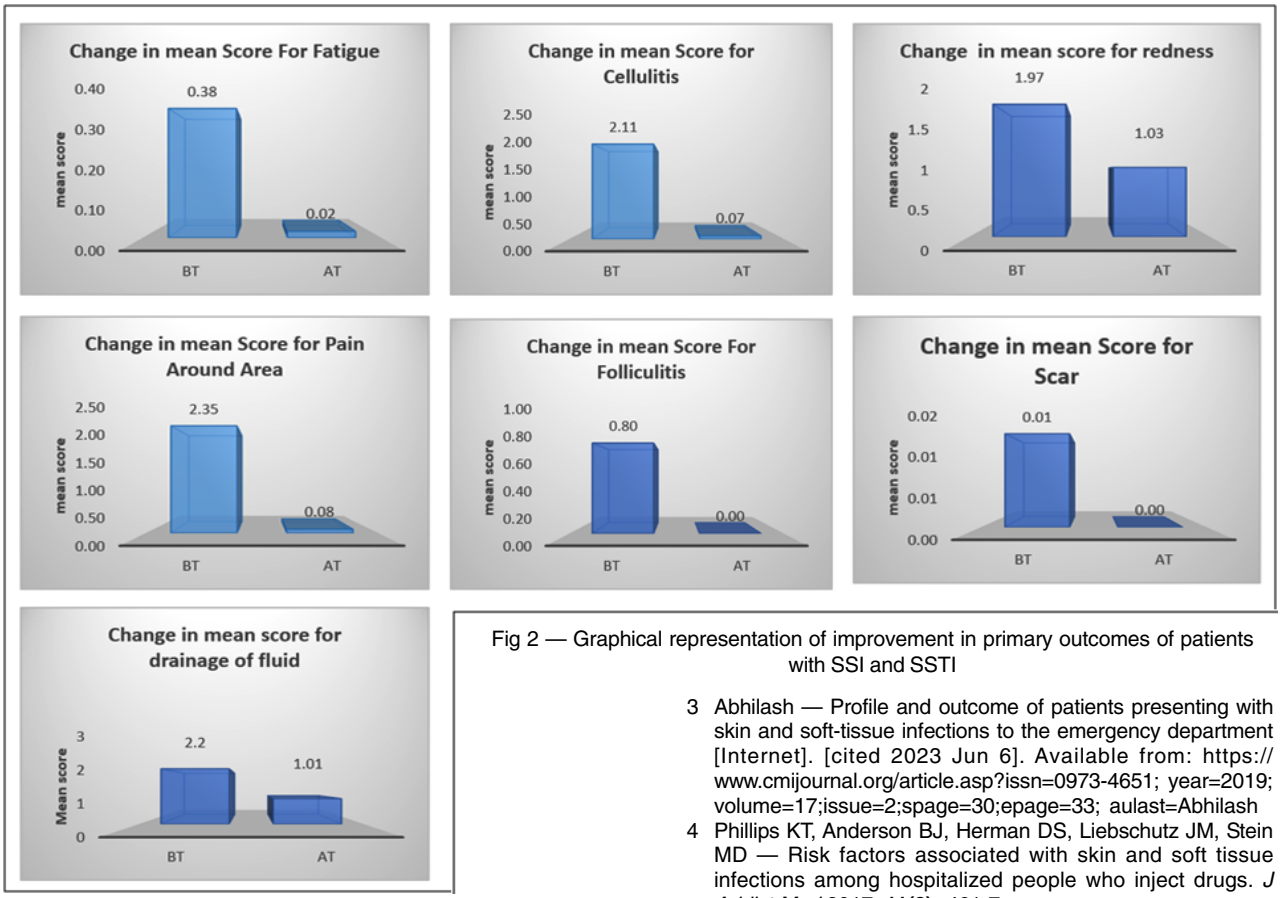

Fig 2 — Graphical representation of improvement in primary outcomes of patients with SSI and SSTI

sample size. Future research should focus on larger, well-designed studies to further investigate the effectiveness, tolerability and optimal dosage regimens of Lincomycin injection in various patient populations and indications.

Conclusion

In this real-world study, Lincomycin 600 mg injectables has shown to be effective and well-tolerated in the treatment of SSI and SSTI.

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

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Conflict of Interest : No

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Letters to the Editor

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

The Clinical Utility of Atypical Lymphocytes, Large Immature Cells, and Rising Hematocrit in Predicting Dengue Fever Severity

Sir, — I am writing to draw attention to the clinical significance of atypical lymphocytes, large immature cells, and rising hematocrit in predicting the severity of Dengue fever — an issue of paramount importance in the field of infectious diseases.

Acute febrile illnesses, particularly Dengue fever, are prevalent from August to November. Dengue, a mosquito-borne viral hemorrhagic fever, poses a potential threat to life, primarily affecting tropical and subtropical regions. The risk of severe Dengue is heightened during secondary infection with a different serotype, where antibodies induced during primary infection facilitate enhanced viral entry into cells, triggering severe manifestations such as vascular leakage, fluid accumulation, thrombocytopenia, and hemorrhagic shock.

Natural History of Dengue Fever : Dengue fever progresses through three stages: the acute febrile phase, the critical phase following defervescence, and the recovery phase. Severe Dengue, marked by complications like vascular leakage and thrombocytopenia, typically arises in the critical phase with an increase in hematocrit and a decline in platelet counts. There is a clinical imperative to devise metrics to predict severe Dengue, aiming to comprehend its underlying pathophysiology.

Prognostic Factors : Several markers have been explored for prognostic purposes, with a focus on atypical lymphocytes, large immature cells, and rising hematocrit. Atypical lymphocytes, as proposed by Claire, *et al* (2019), demonstrate a correlation with Dengue severity. These immune cells, exhibiting anomalies under microscopic examination, could be valuable in assessing the efficacy of the immune response.

Large immature cells, indicating bone marrow response, and rising hematocrit levels, reflective of hemoconcentration, offer insights into the severity of vascular leakage and fluid accumulation during Dengue infection. These factors hold promise as early indicators of disease progression, facilitating timely intervention.

Conclusion : In conclusion, the clinical utility of atypical lymphocytes, large immature cells, and rising hematocrit in predicting Dengue fever severity presents a promising avenue for further research and application in clinical settings. If validated through rigorous research, these metrics could become valuable tools for identifying patients at risk of severe complications during the critical phase. Early recognition and intervention based on these markers may not only improve patient outcomes but also guide resource allocation in Dengue-endemic regions.

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Publication Spree in Medical Colleges. Where does this lead us in long term ?

Sir, — Publication in the medical colleges are on their all-time high pick. Writing on same topic by multiple authors which are making spree to journal for publication. There are several strange bedfellows are existing which influence the medical research publication practices[1]. As Banerjee A said very well that, you can bring a horse to water, but can'tmake it drink. We are facing a similar situation. Earlier it was only for promotion in colleges, but now with accreditation and ranking competitions, it is now mandatory for all to do publications in respected journals.

The result is now a mad rush. It has now gone beyond "Publish or perish"[2,3]. With institutes publishing articles in hundreds not having an appropriate infrastructure, questions must be asked but the genuinity of the articles. With the data generated from these publications, can a policy making body rely? To writing one research paper need a many thing. Start from thought of hypothesis and review literature and take few months to years to complete one research article. Hard work, team work and passionate work can be a fruitful and useful for the field, society and humanity but today in race of quantitative work, the qualitative work going to vanish.

How many path breaking publications have come from these forced publications?Can one enlighten. Forced publications have led to increase in predatory journals, plagiarism etc[4]. Most of the good data comes from a handful of people who are in genuine love for research and work exclusively towards that. Research work planning, performing and collecting data is not enough to complete the publication, Good language and writing skill all required to convey you research work to journals as well as others[5]. Donning multiple hats at one time doesn't do any good. If this madness does not stop, we will be sitting on a pile of truck load of garbage soon.

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Exploring the Potential of Artificial Intelligence in Diagnostic Microbiology

Sir, — Artificial Intelligence (AI) refers to the creation of a computer system capable of performing work that requires human intervention, including learning from data, recognising patterns, making decisions, and solving problems. The notion of AI traces its origins to the 1950s when British scholar A. Turing envisioned the concept that machines could evolve into smart devices, and their intelligence could be tested. John McCarthy and Marvin Minsky introduced the term Artificial Intelligence in the year 1956[1].

Use of AI in diagnostic Microbiology laboratory : Various tasks in diagnostic microbiology can be integrated with AI which includes various activities like analysis of microscopic images, screening of slides for micro-organisms, culture identification and interpretations, antimicrobial susceptibility testing and interpretation along with identification of mechanism responsible for Antimicrobial Resistance (AMR). AI systems can also be useful in molecular laboratories identifying infectious organisms.

There are algorithms used for culture identification such as Chromogenic Media Image Detectionin which positive cultures can be detected with very high specificity and sensitivity. Another algorithm is Growth versus No-growth discrimination by colony counting method*;* this algorithm is best applied on samples that may be received in bulk in the laboratory particularly urine samples for culture examination[2,3]. Recently, the BD Kiestra™ TLA system automates the microbiology process, from sample processing, plate transportation and incubation, to digital imaging. A deep Convolutional Neural Network (CNN) is utilized for culture analysis by investigating the urine samples through their images[4]. Colony recognition and application of expert rules*;* help in an easy and rapid reading of culture plates and better discriminate the negative from positive cultures[2,3].

Computer vision technology in AI can assess the screening for Vancomycin-resistant *Enterococcus* (VRE) and Methicillin-resistant *Staphylococcus Aureus* (MRSA). Early detection and timely intervention for such bacterial organisms are crucial for treatment and also to prevent their further spread in hospital environments[3].

Microorganisms like acid-fast bacilli and protozoan-like malarial parasites can be identified by using computer vision with high precision. Furthermore, Mathison *et al*. have reported computer vision as an effective AI tool for detecting protozoal parasites and helminthic ova in trichrome-stained stool smears[5].

AI can be utilized to predict antimicrobial resistance in vitro. Peiffer-Smadja N, *et al* 2020, have shown the application of AI algorithms to predict resistance to aminoglycosides in *Escherichia coli* and *Staphylococcus aureus*[6].

Matrix-assisted laser desorption ionization-time-of-flight mass spectrometry (MALDI-TOF MS) could be improved by merging it with AI for the identification of microorganisms and the prediction of antimicrobial resistance[7].

The molecular methods allow us for detailed and very precise study of microorganisms like early identification, mutations and presence of AMR genes etc. AI algorithms are effectively used for the enhancement of results in this study.

Thus, the implementation of AI in diagnostic microbiology enhances precision in microorganism identification, image analysis, and antimicrobial resistance prediction. After rigorous training and validation, AI proves to be cost-effective, utilizing existing laboratory computers for image analysis[8]. While AI partially replaces human involvement, challenges like interpretability of results, transparent models for reliability[2], scarcity of comprehensive datasets, and robust validation techniques are challenges to be tackled to reveal its complete potential in microbiology.

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