Journal of the Vivekananda Institute of Medical Sciences

EDITORIAL BOARD

Journal of the
Vivekananda Institute of Medical Sciences

JOURNAL OF THE
VIVEKANANDA INSTITUTE OF MEDICAL SCIENCES
Instructions to Authors

All articles for publication in this journal must be contributed to it exclusively and, if accepted, will be subject of editorial revision. For reproduction elsewhere, previous permission of the Editors will be required and the customary acknowledgement must be made.

Statements and observations made and opinions or conclusions drawn in the articles are those of the authors and not the Editors.

Covering Letter :

A covering letter must be provided, stating the Title and identifying the Corresponding author with full contact details. Each author must sign the letter as evidence of consent for publication.

Manuscripts :

Manuscripts should be submitted as double-spaced Word Documents with default margins. They should be typed in Sylfaen Font; size 16 for Title, 14 for Headings and 12 for the text. Original articles should confirm to the conventional structure of introduction, methods, results, discussion, conclusion and references.

Original articles should not normally exceed 2000 words and should not have more than six tables or illustrations; they should report original research. Case reports should be limited to 600 words, with one table or illustration, and not more than five references. Letters should not exceed 400 words, and must be signed by each author. Articles on the organisation, operation and planning of medical care should be limited to 1500 words, with not more than four tables or figures.

Each manuscript should be arranged in this sequence; Title page; Abstract with Key words; Text; Acknowledgements; Ethical clearance and Conflict of Interest statement; References; Tables (each complete with title and footnotes on a separate page); legends for illustrations. Pages should be numbered.

Title page :

The title page should have the title of the article, concise and informative; initial(s) and surname of each author, with the highest academic degrees (not more than two degrees and/or diplomas) of each author, their designation and department alongside.

The second page should repeat the article title and carry the abstract and key words. The abstract should not exceed 200 words. Key words must be taken from MeSH, a maximum of 5 should be provided.

Appropriate scientific nomenclature giving both genus and species should be italicised, with an initial capital and abbreviation for the genus only, after a full spelling at first mention, thus: *Mycobacterium Tuberculosis,* the *Myco, Tuberculosis*. Drugs should be given their approved names, not their proprietary names. Spelling should confirm to the Oxford English Dictionary.

Numbers up to ten should be spelt, unless contrasted with other numbers. Larger numbers

should be in the form of numerals and not words, except when beginning a sentence, thus : "Fifteen patients out of a total 60 exhibited....."

Illustrations and tables :

A restricted number of illustrations will be reproduced, the photographic plates or drawings should be of good quality. An article should have not more than six tables or illustrations. Tables should be simple, brief and should not duplicate information in the text of the article. Illustrations should be used only when data cannot be expressed clearly in any other way.

All tables and illustrations should be separated from the text, but with their positions indicated. Tables should be numbered with Roman numerals, and figures with Arabic numerals. Tables with brief titles should be typed one to a page. The authors must obtain permission for reproduction of illustrations previously published.

As far as practicable, marking of lines and letters should be avoided; if absoltely necessary, separate sets of marked and unmarked prints should be drawn with black India ink on the white background. Original artwork, X-ray films, ECG tracing, etc. should be photographed and enlarged on glossy paper, identity of patients should be masked. The magnification of photomicrographs should be stated (e.g. x 200). All illustrations should accompany the manuscript with suitable legends, numbered and marked on the back with the author's name and article title.

Abbreviations should be avoided and, if used, should be explained in brief footnotes.

The author must obtain permission for reproduction of illustrations previously published.

References :

References should be appended to the article, numbered in the order of appearance in the text and must be in the Vancouver style. Authors must check their accuracy before submission. Names of journals and books must be itialicised.

Ethical Clearance & Conflict of Interest :

Must be specifically declared at the end of the text.

Books for Review :

Books for review should be sent to the Editor.

Correspondence :

All correspondence should be addressed to the Editor.

The Journal of the Vivekananda Institute of Medical Sciences is published by the management of the
Ramakrishna Mission Seva Pratishthan
99 Sarat Bose Road, Kolkata - 700026, India.
Phone : (033) 2475-3636 (4 lines).
E-mail : rkmspsm@gmail.com & rkmspsmvims@gmail.com.
Website : www.vimsrkmsp.org

Printed by : M/s. Shambhavi Forms Pvt. Ltd.

Editorial
Time for A New Direction

It is not easy being a general medical print journal in the age of social media, open access and medical pre-publication reviews. The Journal of the Vivekananda Institute of Medical Sciences began publication in 1977, and received its International Standard Serial Number (ISSN) in 1978. Now in its forty fourth year of publication it faces several challenges.

First and foremost is the COVID pandemic. The complete disruption in normal life arising from the National Lockdown affected publications across the country. The Journal was no exception, and now finds itself with a backlog of issues for 2020 to be published. The first of these is in your hands, and the next one, appropriately themed on the COVID pandemic, should be out within a reasonable timeframe.

Secondly, the stipulation from the National Medical Commission that publications as first, second or third author in Indexed journals are mandatory for faculty appointment and promotion, leaves the Journal struggling to attract original articles.

Thirdly, the seeming demise of traditional print journals. From the British Medical Journal to the New England Journal of Medicine, from the Lancet to the British Journal of Surgery, nearly all print journals are now offering readers attractive packages for online editions. Printed editions are still available, but copies go astray in the post, tend to accumulate without being read, and are increasingly held to be environmentally unfriendly.

The Vivekananda Institute of Medical Sciences is one of the 64 stand alone Post-graduate Institutes in India. At present we have 87 students enrolled in MD, MS or DNB courses. Each one of them has to produce a thesis or dissertation. Apart from this, unusual or complex cases are seen or admitted. The new undergraduate MBBS curriculum endorsed by the National Medical Commission envisages inculcation of an understanding of basic research methods in all medical students. The writing of an academic paper is a skill acquired over several years, and is of no use unless the resulting submission is published. Most indexed journals have an acceptance rate of less than twenty percent, and many of them no longer accept case reports. The need to publish forces consideration of the so-called predatory journals, which guarantee publication in return for a hefty fee, with little or no peer review.

The fundamental aim of an Institute journal should be to highlight the work occurring in the Institute itself. With this in mind we encourage Faculty to submit postgraduate dissertations completed under their guidance and reviews of treatment outcomes or innovative approaches. Students may submit reports of unusual and instructive cases, and papers submitted for the Annual Scientific Conference. We also welcome articles on the workings of the hospital itself: a new special interest clinic, or an innovative teaching approach. Once the School of Biological Sciences is fully established we look forward to publishing basic research as well.

The current issue, and some previous ones, may be viewed online at the VIMS website; we hope to gradually move to a completely online platform for ease of access and publication. We ultimately aim to get the Journal Indexed, but this will take time and effort.

I gratefully acknowledge the immense work done by all previous Editors of the Journal, without whose untiring nurturing the Journal may long since have withered away. Forty four years of continuous publication is no mean feat, even more so when one considers it is an entirely voluntary labour of love. I am acutely aware that I am standing on the shoulders of giants.

The journal requires the services of faculty as reviewers. Full instructions will be provided – no previous experience is required. If you are interested kindly contact the Executive Editor at Scicom2016@gmail.com. Any suggestions regarding the Journal are also welcome.

Prof. (Dr.) Ranjan Raychowdhury, Executive Editor; Department of ENT & Head Neck Surgery, RKMSP, VIMS

Original Article

A Study of Profile of Acute Kidney Injury in A Tertiary Care Hospital

Dr. Amitava Mazumdar,[1] Dr. Sujata Mazumdar,[2] Dr. Santa Subhra Chatterjee,[3] Dr. Tushar Kanti Pakira,[4] Dr. Soumik Mondal,[5] Dr. Sayan Malakar[6]

Abstract :

Objective : To evaluate different aetiologies, risk factors, comorbid illness and clinical presentations of acute kidney injury in a tertiary care hospital of Kolkata.

Methods : This is an observational prospective study of one and half years duration done in medical ward and ICU of VIMS Kolkata from 11 January 2018 to 30 June 2019. Patients admitted with various diseases (sepsis, acute gastroenteritis, heart failure, acute pancreatitis and post-operative hypotension etc) with history of decreased urine output and other signs of dehydration were evaluated clinically and their comorbid illness like diabetes mellitus, hypertension, chronic lung and liver diseases with their other risk factors were also studied. Sixty patients were further categorized according to RIFLE, AKIN and KDIGO criteria and compared.

Conclusion : Our study showed that with increasing age the incidence of AKI increases. Sepsis is the commonest cause of acute kidney injury followed by heart failure and diuretics induced dehydration. Diabetes mellitus and hypertension were the common risk factors of acute kidney injury. Only one patient needed hemodialysis. No significant difference was noted in different sub -classification of RIFLE, AKIN and KDIGO of acute kidney injury. No patient died during the study period.

Keywords : Acute Kidney Injury, Sepsis, Heart failure, Diuretics

Introduction :

Acute kidney injury (AKI), previously known as acute renal failure (ARF), was first described by the term 'ischuriarenalis' by William Herbeden in 1802[1]. During the First World War it was named as 'War Nephritis'[2]. The term Acute Kidney Injury (AKI) was used for the first time by William Mac Naider in 1918 in a situation of mercury poisoning, but became the preferred term in 2004 when ARF was redefined as AKI by RIFLE criteria[3]. The latest classification of AKI proposed by the Acute Kidney Injury Working Group of KDIGO (Kidney Disease Improving Global Outcomes) is the preferred definition, based on the previous two classification, and aims to unify the definition of AKI[4]. Acute Kidney Injury is an escalating clinical problem in hospitalised patients. Recent advances in AKI have improved knowledge of its pathogenesis, diagnosis, and prognosis. Early interventions proven to alter the natural history of established AKI in hospitalised patients and can prevent unfavourable outcomes and hospital stay. Recent estimates have suggested that AKI accounts for 1% of all hospital admissions, complicates 7% of hospitalizations, and is present in up to 20% of critically ill patients.

The definition and staging of acute kidney injury are mainly based on the risk, injury, failure, loss, end-stage kidney disease (RIFLE) criteria and the acute kidney injury network (AKIN) criteria.

[1,2]Associate Professor, [3]Ex-Assistant Professor, [4]Senior Resident, [5,6]Post Graduate Trainee, General Medicine, RKMSP, VIMS

Rifle criteria are classified in 5 categories -Risk, Injury, Failure, Loss, End Stage Renal Disease (ESRD) - based on GFR criteria and urine output criteria. **Risk -** increase in serum creatinine by 1.5 times of baseline or decrease of GFR by more than 25% of baseline or urine output less than .5 ml per kg body weight per hour for more than 6 hours. **Injury** - Increase in serum creatinine by 2 times of baseline or decease of GFR by more than 50% of baseline or Urine output less than 0.5 ml per kg of body weight per hour for more than 12 hours. **Failure** - Increase in serum creatinine by 3 times of baseline or decrease in GFR by more than 75% of baseline or absolute creatinine more than 4mg/dl or Urine output less than 0.3 ml per kg of body weight per hour for more than 24 hours OR anuria for 12 hours. LOSS-Persistent acute kidney injury for more than 4 weeks. ESRD - End stage renal disease or persistence of renal dysfunction for more than 3 months. According to **AKIN** (Acute kidney injury network) criteria 2007, AKI is categorized as: **Stage 1 -** rise of serum creatinine by 1.5 to 1.9 times of the baseline or more than 0.3 mg/dl increase from baseline, urine output-less than 0.5 ml/kg/hour for 6-12 hours; **Stage 2 -** rise of serum creatinine by 2-2.9 times of the baseline, urine output-less than 0.5 ml/kg/hour for more than 12 hours; **Stage 3 -** rise of serum creatinine more than 3 times of baseline or initiation or renal replacement therapy or in patients with less than 18 years of age decrease in eGFR to less than 35ml/min/1.73 square metre; urine output-less than 0.3 ml/kg/hour for more than 24 hours OR anuria for more than 12 hours.

KDIGO (Kidney injuries improving global outcomes) definition of acute kidney injury categorizes AKI into **Stage 1 -** rise in serum creatinine by 1.5 to 1.9 times of baseline OR creatinine increase by more than 0.3 mg/dl, urine output less than 0.5 ml/kg/hour for more than 6-12 hours; **Stage 2 -** rise in serum creatinine by 2-2.9 times of baseline, urine output less than 0.5 ml/kg/hour for more than 12 hours; **Stage 3 -** rise in serum creatinine by more than 3 times of baseline OR creatinine more than 4mg/dl OR initiation of dialysis, urine output less than 0.3ml/kg/hour for more than 24 hours OR anuria for more than 12 hours.

Among the etiological classes of acute kidney injury prerenal azotaemia (pre renal AKI), acute tubular necrosis (intrinsic renal AKI) and obstructive pathology (post renal AKI) are important causes. Among the comorbid conditions, chronic liver disease, diabetes mellitus, hypertension, collagen vascular diseases have been studied for predictors of acute kidney injury.

Methodology :

This prospective, observational, cross sectional study was conducted among sixty (60) patients admitted in medical ward, medicine ICU and post-operative HDU unit from 11th June 2018 to 30 the June 2019 at Ramakrishna Mission Seva Pratishthan (RKMSP), Vivekananda Institute of Medical Sciences, after approval from Institutional Ethics Committee. The objective of the study is to evaluate different aetiologies (sepsis, heart failure, acute gastroenteritis, cancer etc.) and clinical presentations of AKI in admitted patients. In addition, risk factors and comorbid illness were also evaluated.

Sixty patients were recruited with various clinical presentations like decrease urine output, dyspnoea, fatigue, drowsiness, fever and other various disease (sepsis, heart failure, over use of diuretics, acute gastroenteritis, acute

pancreatitis) causing AKI with risk factors like-dehydration, postoperative, hypotension, dehydration and comorbidities like-diabetes mellitus, hypertension, chronic lung disease and chronic liver disease-associated with AKI were studied. Patients with history of chronic kidney disease with or without maintenance hemodialysis and pregnancy were excluded from the study.

A detailed general examination with special reference to pulse, blood pressure, Jugular Venous Pressure, pallor, respiratory rate and signs of dehydration were noted. All other systems like cardiovascular, central nervous system, gastrointestinal system, locomotor system etc. were examined thoroughly. Laboratory investigations like complete blood count, C-reactive paper, renal function test, liver function tests, electrolytes, fasting blood sugar, post prandial sugar, glycated haemoglobin, malarial parasite in slides, malarial parasite dual antigen detection, Dengue IgM ELISA, Scrub typhus IgG/IgM, leptospira IgM were done. X-ray, electrocardiogram, ultrasonography of abdomen, computed tomography scan of abdomen, echocardiogram, urine routine examination, urine culture and sensitivity, blood culture and sensitivity testing, collagen vascular disease profile (Rheumatoid factor, Antinuclear antibody etc.) were done whenever necessary.

Acute Kidney Injury (AKI) sub-classification was done on the basis of RIFLE, AKIN, KDIGO criteria. For statistical analysis data were entered into a Microsoft excel spreadsheet and then analysed by SPSS (version 25.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data was summarized as mean and standard deviation for statistical analysis: numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. A p-value = 0.05 was considered statistically significant.

Results :

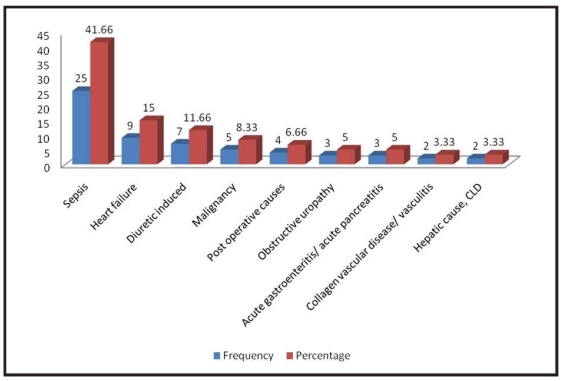
Sixty patients were clinically, biochemically, radiologically and with specific microbiological investigations evaluated. Out of 60 patients, 32 (53.4%) were above 60 years age. Of them, 16 (26.7%) patients were between 71 years and 80 years (Table 1).

Table 1 : Distribution of Age in years

Age in Years	Frequency	Percent
Less than equals to 30	3	5.0%
31-40	5	8.3%
41-50	4	6.7%
51-60	16	26.7%
61-70	10	16.7%
71-80	16	26.7%
81-90	6	10.0%
Total	**60**	**100.0%**

Forty patients (66.7%) were female and twenty patients (33.3%) were male. In our study among total 60 patients 22(36.7%) patients had sepsis, 6(10.0%) patients was on diuretics (furosemide, torsemide) 2(3.3%) patients had obstructive uropathy, 8(13.3%) patients had heart failure, 4(6.7%) patients had surgery, 3(5.0%) patients had acute gastro enteritis/Acute pancreatitis, 2(3.3%) patients had collagen vascular disease/vasculitis, one systemic lupus erythematosus and the other granulomatosis with

polyangiitis; 4(6.7%) patients had malignancy, 1(1.7%) patient had LVF and 2(3.3%) patients had hepatic disease (CLD, others). (Bar diagram 1).



Bar diagram 1: Showing Etiological Distribution of Acute Kidney Injury among study population

Out of 25 sepsis cases,18 patients (72%) had urosepsis followed by 5 cases(20 %)of pneumosepsis [P<0.05]. There was one case each of Intra-abdominal sepsis and meningitis (4% each).

Among comorbidities, 31 (51.7%) patients had T2DM followed by hypertension of 16 (26.7%) [P value<0.05] Among cardiac morbidities, 1 (1.7%) patient had CAD and 6 (10%) patients dilated cardiomyopathy. This study shows among total 60 patients renal cause of AKI was found in 36 patients (60%) followed by pre renal cause in 19 patients (31.6%) and 5 patients (8.33%) of post renal cause [P<0.05]. The mean hospital stay (mean+S.D) of patients was 11.4237+5.4495 days.

In this study all the three criteria of AKI (RIFLE, AKIN & KDIGO) showed similar and comparable results (Table 2). It is clear from tabulation regarding the grading as per RIFLE criteria on the basis of serum creatinine level that patients having RISK—28 (46%), INJUY-- 21(35%), FAILURE--10 (16.6%), LOSS-1 (1.66%), no patient entered into the end stage renal disease in total 60 patients. One patient who was in "Loss" stage as per RIFLE classification, underwent short term haemodialysis.

Table2: Comparison Among Rifle, Akin & Kdigo Criteria

Staging Criteria	RIFLE	AKIN	KDIGO
Risk (RIFLE) or Stage 1 (AKIN/KDIGO)	28(46%)	28(46%)	28(46%)
Injury (RIFLE) or Stage 2 (AKIN/KDIGO)	21(35%)	21(35%)	21(35%)
Failure (RIFLE) or Stage 3 (AKIN/KDIGO)	10(16.6%)	11(19%)	11(19%)
Loss (RIFLE)	1(1.66%)		
End stage renal disease (RIFLE			

In our study, out of 60 patients 25 patients (41.66%) had sepsis, and among them 10 patients (16.66%) and 12 patients (20%) were in "INJURY" and "RISK" category respectively whereas according to AKIN criteria out of 60 patients, 25 (41.66%) were in sepsis. Among them, 12 (20% of total) and 10 (16.66% of total) were in Stage-1 and Stage-2 respectively. This study reveals out of 60 patients, 7 patients (11.66%) received diuretics (furosemide and torsemide) and developed AKI and they were in "INJURY" and "RISK" category whereas out of 60 patients, 7 (11.66%) patients had undergone AKI due to diuretics use and most of them were is Stage-1 (3 no, 5% of total) and in Stage-2 (4 no, 6.66% of total) respectively as per AKIN

criteria. Out of 60 patients, 9 patients (15%) had heart failure and developed acute kidney injury. 28 patients (46.66%) were in RISK category and among them 8 patients (28.57%) had heart failure whereas according to AKIN criteria 9 patients (15%) had heart failure, 8 patients of them were in stage-1. In this study, according to KDIGO criteria 46% patients were in stage 1, 35% patients were in stage 2 and 19% patients were in stage 3. There was no mortality.

Discussion :

We conducted an observational, cross sectional, prospective study for 18 months on 60 patients in the Department of General Medicine ward, medical ICU and post-operative HDU units, who were diagnosed as AKI and were recruited for the study. Two important markers, serum creatinine level and urinary output' were monitored according to RIFLE, AKIN and KDIGO criteria. We found that AKI was more prevalent above age 50 years (80%). In one study in 2007 by Ali Khan, Simpson et all[5], based on 223390 population, median age group was found to be 76 years for AKI which corroborates well with our study. This study showed there was female preponderance for AKI. In our study also female preponderance was found because of increased evidence of urogenital sepsis in females. Among 60 patients of our study the etiological cause of AKI was evaluated and we found that sepsis was the most common cause (41.7%), followed by heart failure (15%), excess diuretics use (11.66%), malignancy-(8.3%), surgery (6.7%), obstructive uropathy (5%), acute gastro enteritis (5%), obstructive uropathy (5%), collagen vascular disease (3.3%) [one being granulomatosis with polyangiitis and another being systemic lupus erythematosus], chronic liver disease (3.3%). So, it is clear from our study that the most common cause of acute kidney injury is sepsis and the least common is chronic liver disease and collagen vascular disease / vasculitis. In a multicentric study done by Bagshaw, Uchino et al[6] 2007, sepsis was found to be the most common cause of oliguric renal failure among 1753 enrolled patients as 833 (47.5%) of patient developed acute kidney injury. In background of heart failure, AKI is also an important predictor of adverse outcome. In this study15% developed AKI who were cases of congestive heart failure. In the study by Gottlieb, Abraham et al[7] 72% developed increased serum creatinine during the hospitalization, with 20% developing an increase of > or = 0.5 mg/dL among 300 enrolled cases out of which 63% of cases were known cases of congestive heart failure during admission.We have found in our study that cases of post-operative AKI were 6.7%. Study done by Morgan E. Grams et al[8] on acute kidney injury after major surgery shows Postoperative AKI occurred in 11.8% of the 161,185 major surgery hospitalizations (stage 1, 76%; stage 2, 15%, stage 3 7%). Post-operative AKI also depends on several factors like proper resuscitation, operative field and skills etc. In our study we have observed that two (3.33%) acute gastro enteritis and one (1.66%) acute pancreatitis patient was diagnosed as AKI. A study by Atim, Pajaiet al[9] showed that Incidence of AKI due to diarrhea was 23%, and affecting males predominantly in 4th decade among 230 patients admitted with AKI. In ourstudy it was low because most of the patients with acute gastroenteritis were admitted either in infectious disease specialist hospital (NICED) or other government hospitals and medical colleges.

In our study prevalence of AKI in collagen

vascular disease and vasculitis is 3.3%. Two (3.33%) chronic liver disease (CLD) patients were diagnosed as AKI. A study by Slack et al[10] showed that the incidence of AKI in hospitalised patients with CLD was around 20%. There are three main causes of AKI in CLD: volume responsive pre-renal failure, volume unresponsive pre-renal failure with tubular dysfunction and acute tubular necrosis (ATN), and hepatorenal syndrome type 1.

In our study we found that three co-morbidities, T2DM, hypertension, and cardiac disease were related with AKI. Among these T2DM is related in 51.7% cases which is comparable to the result of the study by Hsiao, Yang et al[11] which showed that in the AKI group, 56.7% had diabetes mellitus. In our study 26.7% of cases were found to be hypertensive. The study by Hsiao, Yang et al[11] shows hypertension(54.6% versus 40.7%, P = 0.009). Another study by Bucuvic et all[5] shows Diabetes mellitus in 61.9%, high blood pressure in 44.4% among 477 adult patients admitted with AKI. The study reveals 60% of cases were of renal aetiology and 31.66% were of pre renal aetiology and 8.33% case due to post-renal aetiology. In our study we have observed 31.66% case due to pre-renal cause which is due to hypotension or intravascular volume depletion. This study shows that hypotension occurs in cases of heart failure. Hypotension with intravascular volume depletion seen in over use of diuretics (11.66%) and rest were due to acute gastroenteritis, acute pancreatitis, and chronic liver disease.

In one study by Santos, Zanetta et al[12] 88% of cases (524 cases out of 593) developed intrinsic renal AKI (acute tubular necrosis). This data also corroborates with our study as the cases of renal causes of AKI was more than those of pre renal and post renal. Only one patient needed short term haemodialysis and there was no mortality. As per RIFLE classification 46% cases are in risk category, 35% cases are in injury category, 16.6% cases are in failure category and loss category includes 1.66% cases. Basically, this classification is for the determination of severity of the disease and planning of treatment and prognosis of the disease. In our study we found in AKIN classification of AKI patients are in stage-1 (46%), stage-2 (35%), stage-3 (19%). We find out the similar result and similar out-come as we found in RIFLE classification.

AKIN classification actually a modified version of the RIFLE classification and was released in order to increase the sensitivity and specificity of AKI diagnosis. Our result of RIFLE Vs AKIN is as Risk: Stage-1=46%: 46%, Injury : Stage2 = 35% : 35% Failure: Stage-3 =16.6%:19%. From this analysis it is obvious that in spite of some theoretical benefit for diagnosis of AKI practically AKIN classification does not provide any extra benefit than RIFLE classification. In our study, as per KDIGO classification we found the same result like AKIN classification.

Limitations of The Study :

This study was conducted in small number of patients with a smaller number of acute gastroenteritis cases as these patients are usually admitted in the Infectious Disease Hospital of the state. Snake bite cases were also not available in our study.

Conclusion :

The study of profile of acute kidney injury in a tertiary care hospital, conducted on 60 patients over one and half year duration shows that with increasing age the incidence of AKI increases. Sepsis is the commonest risk (cause) followed

by heart failure and then drugs-diuretics and commonest comorbidity is T2DM followed by hypertension (51.7%). Most of the patients as per RIFLE classification were in Risk stage followed by Injury stage followed by failure stage and only 1 patient among our study group entered into loss stage, needed short term haemodialysis and survived. The high incidence of sepsis is due to increase number of female patients presenting with urinary tract infection. Most patients were in RISK category of RIFLE classification followed by INJURY and FAILURE category. No significant difference was noted with RIFLE, AKIN and KDIGO classification of acute kidney injury in our study.

However, this study was conducted in small number of patients and further multicentric studies with a larger sample size are required to establish exact conclusions.

Conflict of Interest : None

Ethical Clearance : Institutional Ethics Committee.

References :

1. Yavuzerkoza et all. Current Concepts And New Insights in Acute Kidney Injury, January 2016. 16-3.289.
2. Jay L Koyner, 2 Amit X Garg, 4 Heather Thiessen-Philbrook, 4 Steven G Coca, 1 Lloyd G Cantley, 1 Aldo Peixoto, 1 Cary S Passik, 3 Kwagnik Hong. Adjudication of etiology of acute kidney injury: experience from the TRIBE-AKI multi-center study. BMC Nephrol. 2014; 15: 105.
3. Arghya Majumdar. Sepsis induced Acute Kidney Injury. Indian J Crit Care Med. 2010 Jan-Mar; 14(1): 14–21.
4. Sean M. Bagshaw, Shigehiko Uchino, Rinaldo Bellomo, Hiroshi Morimatsu, Stanislao Morgera, MietSchetz, Ian Tan, Catherine Bouman, Ettiene Macedo, Noel Gibney, Ashita Tolwani, Heleen M. Oudemans-van Straaten, Claudio Ronco, John A. Kellum and; for the Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators. Septic Acute Kidney Injury in Critically Ill Patients: Clinical Characteristics and Outcome. CJASN May 2007, 2 (3) 431-439.
5. Ali T, Khan I, Simpson W, Prescott G, Townend J, Smith W, MacLeod A. Incidence and outcomes in acute kidney injury: a comprehensive population-based study. Journal of the American Society of Nephrology. 2007 Apr 1;18(4):1292-8.
6. Sean M. Bagshaw, Shigehiko Uchino, Rinaldo Bellomo, Hiroshi Morimatsu, Stanislao Morgera, Miet Schetz, Ian Tan, Catherine Bouman, Ettiene Macedo, Noel Gibney, Ashita Tolwani, Heleen M. Oudemans-van Straaten, Claudio Ronco, John A. Kellum and; for the Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators. Septic Acute Kidney Injury in Critically Ill Patients: Clinical Characteristics and Outcomes. CJASN May 2007, 2 (3) 431-439.
7. Gottlieb SS, Abraham W, Butler J, et al. The prognostic importance of different definitions of worsening renal function in congestive heart failure. J Card Fail. 2002; 8:136–141.
8. Morgan E Grams, Yingying Sang, Josef Coresh, Kunihiro Matsushita, Zoltan S Zabo. Acute Kidney Injury After Major Surgery: A Retrospective Analysis of Veterans Health Administration Data. Volume 67, Issue 6, June 2016, Pages 872-880.
9. Atim E Pajai, Kalpana S Meheta. Study on AKI due to diarrhoea in Tertiary Care Centre in India. 2017-24-volume 45:57.
10. Andy Slack Andrew Yeoman Julia Wendon. Renal dysfunction in chronic liver disease Critical Care volume 14, Article number: 214 (2010).
11. Chih-Yen Hsiao, Huang-Yu Yang, Meng-Chang Hsiao, Peir-Haur Hung, and Ming-Cheng Wang. Risk Factors for Development of Acute Kidney Injury in Patients with Urinary Tract Infection. PLoS One. 2015; 10(7): e0133835.
12. Santos WJ, Zanetta DM, Pires AC, Lobo SM, Lima EQ, Burdmann EA. Patients with ischaemic, mixed and nephrotoxic acute tubular necrosis in the intensive care unit–a homogeneous population? Crit Care. 2006;10(2): R68.

Original Article

Clinical Evaluation of Poisoning in A Tertiary Care Hospital in Kolkata – A Study

Dr. Sujata Mazumdar[1], Dr. Amitava Mazumdar[2], Dr. Sayan Choudhury[3]

Abstract :

Background : Poisoning is one of the common causes of emergency admissions at hospitals all over the country. This study aims to analyze the type of poisoning, clinic-epidemiological and biochemical features, course and outcome of patients and factors affecting the outcome.

Methodology : This was an observational, prospective study conducted at a tertiary care, teaching, urban hospital for a period of 5 years in between 1st March 2013 to 28th February 2018. We noted demographic profile, nature and class of poison, clinical manifestations, investigations and outcome. Association between qualitative variables was assessed by Chi-Square test, Fisher's exact test and Binary Logistic Regression.

Results : Among 250 patients, mortality was 4.8%. Common agents of poisoning used were unknown chemicals seen in 100 patients (40%), followed by pesticides (organophosphate and organochloride) and rodenticides (72 patients, 28.8%), corrosives (muriatic acid and H_2SO_4) (28 patients, 11.2%), benzodiazepines (26 patients, 10.4%), kerosene (14 patients, 5.6%) and antipsychotics (10 patients, 4%). Ventilator support was needed in 6 patients (2.4%). Hospital stay for 20 patients (8%) was less than 5days, for 180 patients (72%) was 5-10 days and for 50 patients (20%) it was more than 10 days. Deranged liver function test was present in 35 patients (14%). Deranged renal function test was present in 27 patients (10.8%).

Conclusions : Poisoning was predominant in married young males from lower economic class. The most common type of poisoning was suicidal, route was oral and agent was unknown chemicals. Corrosive poisonings associated with high mortality.

Keywords : Poisoning, Emergency admissions, Biochemical features.

Introduction :

Poisoning is a problem of all socio-economical strata of India. A poison is a substance that causes damage or injury to the body and endangers one's life due to its exposure by means of ingestion, inhalation or contact. Acute poisoning is defined as acute exposure (less than 24 hours) to the toxic substance. Acute poisoning may be due to suicidal, accidental or homicidal causes leading to significant morbidity and mortality.

Acute poisoning forms one of the most common causes of emergency hospital admissions and it is the fourth common cause of mortality in India.[1] According to WHO more than three million poisoning cases with 2,51,881 deaths occur worldwide annually, of which 99% of total poisonings occur in developing countries, particularly among agricultural workers.[2] Recent date from National Crime Bureau of India shows poisoning accounted for 7.50% of all causes of unnatural deaths in the year 2007.[3] However, due to under reporting of poisoning cases and lack of updated database like Toxic Exposure Surveillance System (TESS) in India, the above

[1,2]Associate Professor, [3]Post-graduate Trainee, Department of General Medicine; RKMSP, VIMS

mentioned figure may be considered to be the tip of the iceberg.[4] Pattern of poisoning differs from country to country and different socio-economical groups and regions. Acute pesticide poisoning is one of the most common causes of international deaths worldwide.[5] In developed countries analgesic and antidepressants are common causes of acute poisoning.[6] Pesticides are used commonly in Asian region for self-poisoning particularly in rural areas.[7,8] There is strong need for generating regional clinic-epidemiological data on poisoning, which will be helpful in planning the prevention and management of poisoning.

India is an agriculture-based country. That is why agricultural poisons (pesticides and rodenticides) are common poisons in rural India.[9,10] Pattern of poisoning in India shows regional differences due to variety of factors. Therefore, periodic studies are necessary to understand the prototype of poisoning in each region so they will act as a useful planning tool for providing healthcare facilities to reduce the poisoning associated mortality.

Hence the present study was undertaken to explore the pattern of poisoning, clinical profile and outcome of patients presenting with poisoning in a tertiary care, teaching hospital in Kolkata. The primary objectives being to study the pattern of poisoning, the clinical presentation of the patients admitted with poisoning and secondary objectives were to determine the various agents (nature and class) used for poisoning and to determine the outcome of poisoning in these patients and factors affecting the outcome.

Materials and Methods :

This was an observational, prospective study. All patients admitted in a tertiary care, teaching hospital with poisoning during the study period of 5 years in between 1st March 2013 to 28th February 2018 were enrolled in the study after obtaining valid written informed consent from patient or from legally acceptable relatives. The data collected for each patient included were demographic profile of patients, nature and class of poison, clinical manifestations, time interval between poisoning and hospitalization, duration of hospital stay, requirement of mechanical ventilation, investigations, and outcome. The diagnosis of poisoning was based on history given by the patients or relatives, clinical examination and necessary biochemistry.

All patients admitted to the medical unit with history and clinical feature suggestive of poisoning, patients of age >18 years, patients of either sex and in whom all the relevant history and data was available were included in the study; whereas, patients of food poisoning and adverse drug reactions were excluded. Relevant history includes nature of poison which could be unknown chemicals, pesticides (organophosphate and organochloride) and rodenticides, corrosive (muriatic acid and H_2SO_4) etc.

Sample size was calculated as 250 with the prevalence of vomiting 80% based on the study by Rajasuriar R et al using the formula $n=Z^2p(1-p)/d2$, where n is the size of the sample; Z is the z statistics for the desired level of confidence; p is the estimate of expected proportion with the variable of interest in the population; d is the half width of the desired interval.[11] However, we enrolled 250 cases for the present study.

Statistical Analysis :

Qualitative data was represented in form of

frequency and percentage. Association between qualitative variables was assessed by Chi-Square test, with Continuity Correction for all 2 X 2 tables and by Fisher's exact test for all 2 X 2 tables where Chi- Square test was not valid due to small counts. In presence of small counts in tables with more than two rows and/or columns, adjacent row and/or Column data was pooled & Chi-Square Test reapplied. Continuity Correction was applied for all 2 X 2 tables after pooling of data. Quantitative data was represented using mean ± SD, median, odds ratio, and 95% confidence interval. Comparison of Qualitative data measured between group categories, was done using unpaired t-test, if the data passed 'Shapiro- Wilk test Normality test' or by Mann-Whitney U test if the data failed 'Normality' test.

Binary Logistic Regression was used to assess between Outcome as dependent variable and a set of independent (Predictor) variables. Results were graphically represented where deemed necessary. Appropriate statistical software, including but not restricted to MS Excel, PSPP version 1.0.1 was used for statistical analysis. An alpha value (p-value) of <.05 was used as the cut-off for statistical significance.

Table 1: General Characteristics of Study Population

Parameter (N=250)	Number	Percentage(%)
Gender		
Male	151	60.4
Female	99	39.6
Age (in years)		
18 to 30	100	40.0
31 to 40	75	30.0
41 to 50	45	18.0
51 to 60	20	8.0
>60	10	4.0
Marital status		
Married	190	76.0
Unmarried	60	24.0
Socioeconomic status		
Lower	180	72.0
Middle	62	24.8
Upper	8	3.2
Type of poisoning		
Suicidal	238	95.2
Accidental	12	4.8
Route of poisoning		
Oral	250	100.0
Time of presentation at emergency (hours)		
<3	180	72.0
>3	70	28.0
Hospital stay (days)		
<5	20	8.0
5-10	180	72.0
>10	50	20.0
Mechanical ventilator		
Required	6	2.4
Not required	244	97.6
Agent of poisoning		
Unknown chemicals	100	40.0
Pesticides and rodenticides	72	28.8
Corrosive	28	11.2
Benzodiazepine	26	10.4
Kerosene	14	5.6
Antipsychotics	10	4.0
Mortality		
Total	12	4.8
Corrosive	6	2.4
Pesticides and rodenticides	4	1.6
Unknown chemicals	2	0.8

Results :

During the study period, 250 patients were analyzed, out of them, 151 (60.4%) were males and 99 (39.6%) were females. The most common age group amongst study population was 18 to 30 years (100 patients, 40%). 238 (95.2%) patients presented with suicidal type of poisoning while 12 (4.8%) patients presented with accidental poisoning. The route of poisoning in all of the study population (100%) was oral ingestion. Common agents of poisoning used were unknown chemicals seen in 100 patients (40%), followed by pesticides (organophosphate and organochloride) and rodenticides (72 patients, 28.8%). The demographic and other study parameters and mortality are mentioned in Table1. 180 patients (72%) presented at emergency within 3 hours of poisoning and 70 patients (28%) presented after 3 hours of poison ingestion. Ventilator support was needed in 6 patients (2.4%) (Table 1).

Table 2: Clinical Presentation of Various Poisoning

Clinical features	Number	Percentage(%)
Vomiting, pain abdomen	70	28
Vomiting, breathlessness, headache	55	22
Vomiting, pain abdomen, altered sensorium	38	15.2
Vomiting, altered sensorium	32	12.8
Vomiting, headache	29	11.6
Altered sensorium	16	6.4
Pain abdomen	10	4
Total	**250**	**100.0**

The most common clinical features amongst study population were vomiting (80.7%) and pain abdomen (47.3%) followed by altered sensorium (36.7%) and breathlessness (22%) (Table 2).

Ventilator support was required in 6 (2.4%) patients, 4 of them (1.6%) were victim of pesticide (organophosphate and organochloride) poisoning and 2 of them (0.8%) were of unknown chemical poisoning. Deranged liver function test was present in 35 (48.6%) cases of pesticides (organophosphate and organochloride) and rodenticides poisoning, 13 cases (13%) of unknown chemical poisoning and 2 cases (7.6%) of Benzodiazepine poisoning. Deranged renal function was present in 27 cases (37.5%) of pesticide and rodenticides poisoning, 44 cases (44%) of unknown chemicals and 2 cases (7.6%) of Benzodiazepine poisoning.

The mortality rate in the present study was 4.8% (12 patients) and survival rate was 95.2% (238 patients). The parameters which show significant association with mortality are more days of hospital stay, corrosive poisoning and need for mechanical ventilation.

Binary Logistic Regression test was applied between 'Outcome' as dependent variable and a set of independent (Predictor) variables and it interpreted that, agent of poisoning (Overall), use of other agents for poisoning and deranged renal function were statistically significant predictors of mortality (Table 3).

Table 3: Binary Logistic Regression between 'outcome' as dependent variable and a set of independent (predictor) variables

Outcome	Internal Value
Died	1
Survived	0

Variables in The Equation

Variables	B	S.E.	p- value
Age (years)	-0.013	0.010	0.197
Sex (Female)	0.237	0.339	0.483
Marital status (Married)	-0.656	0.411	0.111
Socioeconomic class	-	-	0.639
Socioeconomic class (Lower)	-0.854	0.628	0.174
Socioeconomic class (Middle)	-0.816	0.704	0.246
Type of poisoning (Suicidal)	-0.124	0.371	0.737
Agent of poisoning	-	-	0.000263
Agent of poisoning (Chemicals)	0.693	0.536	0.196
Agent of poisoning (BZD overdose)	-19.795	19947.861	0.999
Agent of poisoning (Pesticides)	-0.145	0.578	0.802
Renal Function (Deranged)	0.812	0.387	0.035708
Liver Function (Deranged)	-0.327	0.428	0.445
Constant	1.183	1.058	0.264

B – Coefficient for the constant in the null model (also called "Intercept"), S.E. – Standard error around the coefficient for the constant, Exp (B) – Exponentiation of the B coefficient, BZD: Benzodiazepines.

Discussion :

In India acute poisoning is one of the most common causes of emergency hospital admissions and mortality. There are many regional differences in the pattern of poisoning and the factors contributing to the mortality and morbidity in India. For that reason, periodic region wise studies are necessary to formulate standard protocol for prevention, management and reduction of poisoning associated mortality.

In the present study, 250 poisoning patients were studied during 5 years of study period from 1st March 2013 to 28th February 2018. Amongst the study population there was young male predominance with common age group being 18 to 30 years (40%) and 31 to 40 years (30%). This finding is in agreement with the study conducted by Patil et al that resembles the age pattern of poisoning which was found by other researchers.[12-17] Studies mention that people of this age group are suffering from stress of the modern lifestyles.[12-17] Higher suicidal rate was found among males (140 cases, 58.8%) than females (98 cases, 41.1%) which were similar with other studies done by Sharma et al and others.

In the present study, poisoning was seen in all socioeconomic groups; however, it was more

commonly seen with lower economic class (180 patients, 72%). This finding is in conformity with other studies which mention lower socioeconomic status contributed 20-64% of the poisoning study population.[18,19]

In the present study, the route of poisoning in all cases was found to be oral (100%). 95.2% of the study population had suicidal type of poisoning, while 4.8% had accidental poisoning. In our study 72% of patients presented within 3 hours of poisoning and 28% of patients presented after 3 hours. The delayed presentation could be due to the fact that majority of the cases were referrals and hence a lot of time could have lapsed during the transport. This highlights that the outcome in these patients depends on multiple factors and time interval between poisoning and presentation to the hospital is one of them.

In the present study, the most common agent of poisoning amongst study population were unknown chemicals (40%), followed by pesticides and rodenticides (28.8%), corrosive ingestion (mostly muriatic acid and H_2SO_4) (11.2%), Benzodiazepine overdose (10.4%), Kerosene poisoning (5.6%) and antipsychotic (4%). Among the pesticides commonly used compounds were organophosphate and organochlorine.

Significant numbers of patients were with unknown poisoning which due to household products like phenol, bleaches; drugs like antihistaminics, paracetamol, oral hypoglycemic agents, antiepileptics, antipsychotics. Easy availability of these products makes them responsible for higher incidence of poisoning. Similarly in the study conducted by Patil et al demonstrated highest frequency of poisoning occurred with household products followed by pesticides.[12] Malangu N et al reported that household unknown chemicals were responsible for the highest number of accidental poisoning[20]. In our study, we got no patient with methyl alcohol poisoning.

In the present study, the most common clinical features amongst study population were vomiting (80.7%), followed by pain abdomen (47.3%), altered sensorium (36.7%) and breathlessness (22%). In this study, deranged liver function test was present in 35 (48.6%) cases of pesticides and rodenticides poisoning, 13 cases (13%) of unknown chemical poisoning and 2 cases (7.6%) of Benzodiazepine poisoning. Deranged renal function was present in 27 cases (37.5%) of pesticide and rodenticides poisoning, 44 cases (44%) of unknown chemicals and 2 cases (7.6%) of Benzodiazepine poisoning. 6 patients (2.4%) mostly of corrosive poisoning (muriatic acid and H_2SO_4) required ventilator support which was due to aspiration chemical pneumonitis.

Death analysis : In the current study, 95.2% patients recovered while death occurred in 4.8% patients. Poisoning with corrosives (mostly muriatic acid and (H_2SO_4) were associated with high mortality in 6 patients (50% of total deaths), followed by pesticides (organophosphate and organochloride) and rodenticides in 4 patients (33.3% of total deaths) and 2 patients (16.6% of total deaths) with unknown chemicals. Low mortality in our study is probably due to early presentation at emergency, absence of methyl alcohol poisoning which is associated with high mortality and a smaller number of patients developing multi-organ failure. Anthony et al mention that duration of hospital stay, ventilator requirement, type of poison and the quantity, comorbid conditions are some of the major determinants of outcomes in patients with poisoning.[17]

The present study was not free from limitations as it was a prospective observational single centre study. Also, there were no cases of methyl alcohol poisoning in this study. For better validation of results and generalization of findings randomized controlled study at multiple sites (urban/rural) done in future will help in formulating national and regional standard protocols for prevention and management of poisoning in India.

Conclusion :

In the urban city of Kolkata, poisoning was predominant in male persons below 40 years of age of lower socioeconomic status. 175 patients (70%) below 40 years were admitted. The most common type of poisoning was suicidal, oral route of poisoning was observed in all of the cases. Significant numbers of patients were admitted with unknown poisoning which could be due to chemicals like phenol, bleach; drugs like antihistaminics, paracetamol, antiepileptics, oral hypoglycemics. Vomiting and pain abdomen were the most common clinical features. Overall mortality in the current study was 4.8% with corrosive poisoning were associated with highest mortality followed by pesticides and rodenticides. Duration of hospital stay was significantly associated with mortality and agent of poisoning and deranges renal function were predictors of mortality.

In urban areas education and awareness of the general population regarding chemical poisoning with household chemicals is essential to reduce the incidence of poisoning. Authorities should take initiatives in preventing and controlling such mishaps and strict execution of law for sale and usage of these chemicals. Identifying early symptoms of suspected poisoning, effective early management, recognizing nature of poisoning and suspected complications is required to improve the morbidity and mortality. Implementation of effective preventive strategies, counseling for managing stress and strain of life, formulating standard management protocol, prompt and specific effective treatment will go a long way to win battle against poisoning in India.

Conflict of Interest : None

Ethical Clearance : Institutional Ethics Committee.

References :

1. Unnikrishnan B, Singh B, Rajeev A. Trends of acute poisoning in south Karnataka. KUMJ. 2005; 3(2):149-54.
2. WHO. Guidelines for poison control. Available from http://www.who.int/ipcs/publications/training poisons/guidelines
3. Deaths A. Suicides in India 2008. New Delhi: NCRBMA; 2009. Available from: http://ncrb.nic.in/ADSI2008/suicides.
4. Centres for disease control. Toxic exposure and surveillance system. Available from: http://www.cdc.gov/Mmwr/preview/mmwrhtml/su5301a74.htm
5. Konradsen F, Dawson AH, Eddleston M, Gunnell D. Pesticide self-poisoning: thinking outside the box. The Lancet. 2007 Jan 20;369(9557):169-70.
6. McClure GM. Suicide in children and adolescents in England and Wales 1970–1998. The BJP. 2001 May; 178(5):469-74.
7. Eddleston M. Patterns and problems of deliberate self-poisoning in the developing world. Qjm. 2000 Nov 1; 93(11):715-31.
8. Chan YC, Fung HT, Lee CK, Tsui SH, Ngan HK, Sy MY, Tse ML, Kam CW, Wong GC, Tong HK, Lit AC. A prospective epidemiological study of acute poisoning in Hong Kong. HKJEM. 2005 Jul; 12(3):156-61.
9. Chan YC, Fung HT, Lee CK, Tsui SH, Ngan HK, Sy MY, Tse ML, Kam CW, Wong GC, Tong HK, Lit AC.

A prospective epidemiological study of acute poisoning in Hong Kong. HKJEM. 2005 Jul; 12(3):156-61.

10. Banerjee I, Tripathi SK, Roy AS. Clinico-epidemiological profile of poisoned patients in emergency department: A two and half year's single hospital experience. IJCIIS. 2014 Jan; 4(1):14.
11. Rajasuriar R, Awang R, Hashim SB, Rahmat HR. Profile of poisoning admissions in Malaysia. Human & experimental toxicology. 2007 Feb; 26(2):73-81.
12. Patil A, Peddawad R, SAHAY VV, Gandhi H. Profile of acute poisoning cases treated in a tertiary care hospital: a Study in Navi Mumbai. Asia Pac J Med Toxicol 2014; 3:36-40.
13. Raghu K, Shreevani P, Kumar SS, Gopal S, Shaik MV, Ahammed B. Incidence and outcome of poisoning patients in a tertiary care teaching hospital. AJPT. 2015; 3(7):23-6.
14. Erickson TB, Thompson TM, Lu JJ. The approach to the patient with an unknown overdose. Emergency medicine clinics of North America. 2007 May 1; 25(2):249-81.
15. Maharani B, Vijayakumari N. Profile of poisoning cases in a Tertiary care Hospital, Tamil Nadu, India. JAPS. 2013 Jan 1; 3(1):91.
16. Khosya S, Meena SR. Current trends of poisoning: An experience at a tertiary care hospital Hadoti region, Rajasthan, India. J Clinic Toxicol. 2015; 6:298.
17. Anthony L, Kulkarni C. Patterns of poisoning and drug overdosage and their outcome among in-patients admitted to the emergency medicine department of a tertiary care hospital. IJCCM: Peer-reviewed, Official Publication of ISCCM. 2012 Jul; 16(3):130.
18. Sharma BR, Harish D, Sharma V, Vij K. Poisoning in northern India: changing trends, causes and prevention thereof. Medicine, science and the law. 2002 Jul; 42(3):251-7.
19. Pokhrel D, Pant S, Pradhan A, Mansoor S. A comparative retrospective study of poisoning cases in central, zonal and district hospitals. KUJSET. 2008; 4(1):40-8.
20. Malangu N, Ogunbanjo GA. A profile of acute poisoning at selected hospitals in South Africa. SAJEI. 2009 Jan 1; 24(2):14-6.

Original Article

Awareness Regarding Arsenic Pollution in West Bengal : A Hospital Outpatient Survey

Mr. Argha Nath[1], Ms. Sankalita Sarkar[2], Dr. Ranjan Raychowdhury[3], Dr. Ajanta Haldar[4]

Abstract :

Background and Objectives : Arsenic pollution is a major health hazard. Contaminated drinking water is the source of this pollution which results in various diseases of skin, heart and lung as also cancer. The residents of arsenic affected areas should be aware of the safe intake level of arsenic through water set by World Health Organization (WHO). The present study has been carried out to assess the extent of awareness regarding this public health issue among patients attending the Outpatient clinics of a Tertiary Level Teaching Hospital and to create awareness amongst them with respect to arsenic pollution, its harmfulness, sources and also preventive measures.

Method : A total of 960 patients participated in this survey from different districts of West Bengal and data was collected by administered questionnaire.

Results : Our findings reveal widespread lack of knowledge regarding arsenic pollution and indicate that females are less aware in comparison to males.

Interpretation & conclusion : For improving this situation, urgent sustained public awareness campaigns involving both print and electronic media are required, preferably targeted female members of the society.

Keywords : Arsenic; Awareness; Public health; Survey; WHO.

Introduction :

Arsenic is a heavy metal naturally present in the groundwater of a number of countries. Over the decades arsenic poisoning has become one of the most severe environmental health hazards worldwide[1]. There are more than 30 countries affected by arsenic poisoning including India, Bangladesh, Argentina, USA, Chile, China, Finland and Mexico[2]. Arsenic is found in two forms in our bodies: organic arsenic, which is not harmful to health and is removed from our body by excretion and theinorganic arsenic, which isresponsiblefor arsenic toxicity.

Acute arsenic toxicity may lead to symptoms like vomiting, abdominal pain, encephalopathy and watery diarrhoea with blood whereas long term exposure or chronic arsenic toxicity may show thickening of skin, darker skin, heart disease, numbness and finally a significant probability of cancer[3]. According to the International Agency for Research on Cancer (2004), the European Chemical Bureau (2007) and the US Environmental Protection Agency (2007) inorganic arsenic is a human carcinogen causing cancer in various part of the body like lung, urinary bladder etc.

In West Bengal environmental heavy metal toxicity is documented in various districts[2]. Heavy metals include arsenic, lead, mercury, chromium, nickel, cadmium, copper and aluminum[4]. District wise arsenic pollution can be divided into two categories: highly affected

[1]Junior Research Fellow,[2]Research Assistant,[3]Professor, Dept. of ENT Head & Neck Surgery, RKMSP, VIMS; [4]Professor, Dept. of Genetics, RKMSP, VIMS, Kolkata

and mildly affected districts. Out of 23 districts 6 districts are highly affected and 5 districts are mildly affected[5].

To reduce the public health risk the Government and Non-Government Organizations (NGOs) have started awareness camps and sealed many contaminated ground water sources. In 2013 there was a study of some villages in North 24 Parganas to assess the knowledge of the local people regarding arsenic[6]. Current survey has been carried out to assess the awareness regarding the public health issue among patients attending the Outpatient Clinic of a Tertiary Level Teaching Hospital.

Aims and Objectives :

1. To assess awareness regarding arsenic pollution among representatives of the society attending a tertiary level teaching hospital.
2. To assess the knowledge of those individuals about the harmful nature of arsenic.
3. To observe their views regarding the source of arsenic pollution.
4. To elucidate their perceptions regarding prevention of arsenic pollution.

Methodology :

a) Study design : An administered questionnaire (Annexure I).

b) Study setting : Department of Ear-Nose & Throat (ENT) and Maxillo-facial Outpatient clinics of a tertiary level teaching hospital in Kolkata.

c) Duration: Three months (1st December, 2018 to 28th February, 2019)

Results :

A Total of 960 individuals were surveyed of whom 481 were male and 479 were female, aged between 10 to 80 years. The majority of participants were from Kolkata, South 24 Parganas, North 24 Parganas, Howrah, Hooghly, Midnapur and Nadia (Table-I).

Sl. No.	Districts	Male	Female	Total
1	Kolkata	226	258	484
2	South 24 Parganas	87	81	168
3	North 24 Parganas	39	35	74
4	Howrah	35	35	70
5	Midnapur	31	19	50
6	Hooghly	25	22	47
7	Nadia	17	15	32
8	Bardhaman	5	6	11
9	Murshidabad	8	1	9
10	Malda	3	1	4
11	Bankura	1	3	4
12	Jhargram	1	1	2
13	Birbhum	1	1	2
14	South Dinajpur	1	0	1
15	Alipurduar	0	1	1
16	Purulia	1	0	1
Total	**16 Districts**	**481**	**479**	**960**

Table I: Total male and female sample distribution in 16 districts of West Bengal

Table-II shows the level of individual awareness regarding arsenic pollution in various districts of West Bengal.

Serial No.	Districts	Male		Female		Total
		Aware	Not aware	Aware	Not aware	
1	Kolkata	119	107	120	138	484
2	South 24 Parganas	43	44	32	49	168
3	North 24 Parganas	22	17	16	19	74
4	Howrah	16	19	17	18	70
5	Midnapur	14	17	5	14	50
6	Hooghly	14	11	14	8	47
7	Nadia	7	10	6	9	32
8	Bardhaman	1	4	4	2	11
9	Murshidabad	3	5	1	0	9
10	Malda	3	0	1	0	4
11	Bankura	0	1	0	3	4
12	Jhargram	1	0	1	0	2
13	Birbhum	1	0	1	0	2
14	South Dinajpur	1	0	0	0	1
15	Alipurduar	0	0	0	1	1
16	Purulia	1	0	0	0	1
Total	**16 Districts (51.14%)**	**246 (48.86%)**	**235 (45.51%)**	**218 (54.49%)**	**261**	**960**

Table II : Level of awareness regarding arsenic pollution in various districts of West Bengal.

In total it was found that 51.14% of males and 45.51% of females surveyed were aware about arsenic pollution in this state.

Table-III shows the percentage of people (both male and female) aware that arsenic is a human health hazard.

Male		Female	
Aware about harmfulness	**Unaware about harmfulness**	**Aware about harmfulness**	**Unaware about harmfulness**
46.78%	53.22%	42.80%	57.20%

Table III: Percentage of people who have the conception about harmfulness of arsenic

Information was collected from people about whether they knew the sources of arsenic pollution or not (Table-IV).

Serial No.	Districts	Male		Female		Total
		Aware of pollution source	Unaware of source	Aware of pollution source	Unaware of source	
1	Kolkata	105	121	107	151	484
2	South 24 Parganas	40	47	29	52	168
3	North 24 Parganas	21	18	17	18	74
4	Howrah	17	18	12	23	70
5	Midnapur	15	16	5	14	50
6	Hooghly	14	11	13	9	47
7	Nadia	7	10	6	9	32
8	Bardhaman	2	3	4	2	11
9	Murshidabad	4	4	1	0	9
10	Malda	3	0	1	0	4
11	Bankura	0	1	0	3	4
12	Jhargram	1	0	1	0	2
13	Birbhum	1	0	1	0	2
14	South Dinajpur	1	0	0	0	1
15	Alipurduar	0	0	0	1	1
16	Purulia	1	0	0	0	1
Total	**16 Districts**	**232 (48.23%)**	**249 (51.77%)**	**197 (41.13%)**	**282 (58.87%)**	**960**

Table IV: Distribution of people of various districts who are aware and unaware about the source of arsenic pollution

Overall only 48.23% male were aware of the source of arsenic pollution and in case of females it is 41.13%.

Table-V reveals the number of people with knowledge of preventive measures for arsenic pollution.

Serial No.	Districts	Male		Female		Total
		Aware of preventive measures	Unaware of preventive meaures	Aware of preventive measures	Unaware of preventive measures	
1	Kolkata	76	150	83	175	484
2	South 24 Parganas	28	59	20	61	168
3	North 24 Parganas	18	21	11	24	74
4	Howrah	8	27	7	28	70
5	Midnapur	7	24	3	16	50
6	Hooghly	11	14	11	11	47
7	Nadia	5	12	4	11	32
8	Bardhaman	1	4	3	3	11
9	Murshidabad	3	5	1	0	9
10	Malda	3	0	1	0	4
11	Bankura	0	1	0	3	4
12	Jhargram	0	1	1	0	2
13	Birbhum	0	1	1	0	2
14	South Dinajpur	1	0	0	0	1
15	Alipurduar	0	0	0	1	1
16	Purulia	1	0	0	0	1
Total	**16 Districts**	**162 (33.68%)**	**319 (66.32%)**	**146 (30.48%)**	**333 (69.52%)**	**960**

Table V : Awareness of preventive measures against arsenic pollution in West Bengal.

Only 33.68% males and 30.48% females surveyed were aware of the preventive measures to protect against arsenic pollution.

Discussion :

Arsenic Exposure :

In the environment, sources of arsenic may be natural or anthropogenic. Natural sources are leaching of ambient arsenic in ground water from sediments containing arsenic bearing minerals; leaching and percolation of arsenic in soils. Anthropogenic sources are agrochemicals, wood preservatives, industrial sources, mineral processing, acid mine drainage, burning of fossil fuels etc. The main source of arsenic which affects the human body is from drinking water. How arsenic contaminates the drinking water is still a topic of debate. According to the Geological Survey of India and the Central Ground Water Board, the Ganga-Brahmaputra drainage pattern is responsible for sedimentation of arsenic in

West Bengal and the source of the metal are the coal fields and highlands of Chotonagpur-Rajmahal[7]. Other than drinking water there are a few other factors also, such as inhalation of gases and dust; weathering of minerals and ores; sea foods; absorption of arsenic in plants (more concentrated in vegetables, rice, apple, grape juice etc.) and volcanic ashes.

Effect of arsenic poisoning on human health:

Inorganic arsenic is a confirmed carcinogen and may be present in drinking water anywhere across the globe. This chemical contaminant is highly toxic for human health. There is another form of arsenic also found i.e. organic arsenic, which is less harmful to health.

According to WHO there are 140 million people in 50 countries using drinking water containing arsenic at levels above the WHO provisional guideline (safe limit of daily intake of arsenic, which is less than 10 g/L). Ingested elemental arsenic is absorbed in a very low quantity and largely eliminated unchanged. Organic arsenic is rapidly and almost completely eliminated via the kidneys. A daily intake of more than 10 g/L, can lead to a toxic outcome in the body. Inorganic arsenic (As^{III} and As^{V}) accumulates in the skin, bone, liver, kidney and muscle[5].

In acute arsenic poisoning the immediate symptoms are vomiting, abdominal pain and diarrhoea, followed by muscle cramps, numbness of the limbs and, in extreme cases, death. The first symptom of long term toxicity is the pigmentation change of skin, formation of lesions and hard patches on the palms and soles of the feet. Later this can lead to cancer of the lung, bladder etc. Developmental effects, diabetes, pulmonary disease and cardiovascular disease may also be found in patients with long term ingestion of inorganic arsenic[1]. According to some studies arsenic is also associated with adverse pregnancy outcomes and infant mortality, with an impact on child health[8].

Situation in West Bengal : During the 1990s there were a few cases of skin disorder reported from Murshidabad, North 24 Parganas, South 24 Parganas, Nadia and Bardhaman, due to arsenic contaminated groundwater. Presently according to WHO report in West Bengal out of 23 districts, six districts are highly affected and five districts are mildly affected [Fig. 1]. Highly affected districts are Malda, Murshidabad, Nadia, North 24 Parganas, South 24 Parganas and Kolkata whereas mildly affected districts includes Purba Bardhaman, Hooghly, Howrah, East Midnapur and some part of West Midnapur. Remaining districts are generally arsenic free. The level for arsenic in highly affected zones is generally greater than 50 g/L and in case of lower affected zones it ranges between 10-50 g/L. Groundwater with high concentration of arsenic generally occurs within 20-80 metre depth zone. There are more than 26 million of people who are potentially at risk from drinking arsenic contamination water in West Bengal[2].

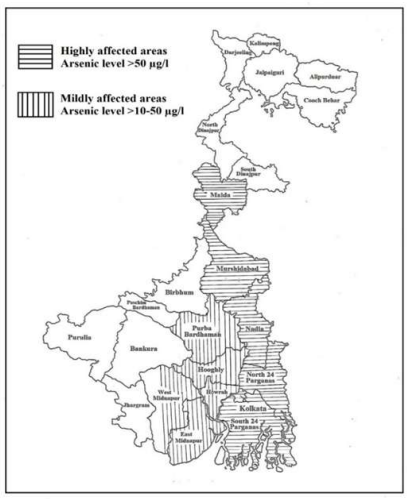


Fig.1: Arsenic affected districts of West Bengal (WB)

that only 34.14% [illegible]

eard of arsenic pollution,
females the percentage is

nple of 960 adults 46.78%
emales were found to be
ental effect and potential
ganic arsenic such as skin
disease) in human body.

als that in spite of increase
isoning, the basic concept
arsenic pollution remains
he people surveyed. About
87% females have no idea
rsenic pollution.

results were found when
ontrol of arsenic poisoning
population sample of 960
nales and 30.48% females
re of the control measures,
than one third of the total.

Annexure I

ARSENIC AWARENESS SURVEY

১। বয়স ঃ ২। লিঙ্গ ঃ

৩। ঠিকানা ঃ

৪। আপনি কি আর্সেনিক দূষন সম্পর্কে সচেতন ?

৫। এটা কি শরীরের পক্ষে ক্ষতিকারক ?

৬। কিভাবে আর্সেনিক আমাদের শরীরে ছড়িয়ে পড়ে ?

৭। কিভাবে আমরা আর্সেনিক দূষন নিয়ন্ত্রন করতে পারি ?

Original Article

A Study on Hepatic Involvement, Thrombocytopenia and Hematocrit in Dengue

Dr. Amitava Mazumdar[1], Dr. Sujata Mazumdar[2], Dr. Sayan Choudhury[3]

Abstract :

Objective : The purpose of this study was to assess the pattern of hepatic involvement, thrombocytopenia and hematocrit in patients with dengue fever and time taken for clinical/biochemical recovery.

Methods : This is a retrospective study done in a tertiary centre. A total of 111 patients with documented dengue fever, with IgM antibody (ELISA) positive report who were admitted between January 2018 to December 2018. The aminotransferase levels, platelet counts and hematocrit were measured on day 1, 4 and 7. Patients were assessed clinically on day 1, 4, 7 or till discharge/death accordingly.

Conclusion : Out of 111 patients with dengue infection, 98 had either thrombocytopenia or hepatic involvement or both. Majority of patients with thrombocytopenia, hepatic involvement and hematocrit >45 recovered between 4-7 days of admission. Statistically significant correlation of platelet count and aminotransferase levels and increased hematocrit with recovery or death of the patient was seen in our study.

Keywords : Hepatic involvement, Thrombocytopenia, Hematocrit, Dengue fever.

Introduction :

Dengue fever was first reported by Benjamin Rush in 1780 as “break bone fever”. Dengue is an acute vector borne disease caused by flavivirus, which is a RNA virus presenting as four antigenically distinct serotype (DENV 1-4). It is transmitted by the bite of Aedes aegypti mosquito. The clinical spectrum varies from Asymptomatic stage, Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS).[1] The clinical features in symptomatic patients range from fever, arthralgia, myalgia, thrombocytopenia presenting as petechial rash, gum bleeding and bleeding from muco-cutaneous orifices to severe dengue hemorrhagic shock syndrome. About 3.9 billion people in 128 countries are at risk of infection with dengue viruses. A recent estimate indicates 390 million dengue infections per year, of which 96 million manifest clinically with any severity of disease. The number of reported cases has increased from 2.2 million in 2010 to 3.2 million in 2015. Not only are the number of cases increasing as disease is spreading to new areas, but explosive outbreaks are occurring. The year 2016 was characterized by large dengue outbreaks worldwide. In 2015, Delhi recorded its worst outbreak since 2006 with over 15,000 cases.[2] Worldwide, annually about 500,000 people with DHF require hospitalization. Approximately 90 percent of them are children aged less than five years, and about 2.5 percent of those affected die. During epidemics, infection rate among those who have not been previously exposed to the virus are often 40 to 50 percent, but can also reach 80 to 90 percent.[3] Hepatic dysfunction and thrombocytopenia are common in dengue infection. Some of the patients have severe

[1,2]Associate Professor, [3]Post-graduate Trainee, Department of General Medicine; RKMSP, VIMS

vomiting and dehydration which can be present due to the hepatic involvement. Mechanism of liver injury in dengue may be due to direct effects of the virus or host immune response on the liver cells, circulatory compromise, metabolic acidosis and/or hypoxia caused by hypotension or localized vascular leakage inside the liver.[4,5]

The pathogenesis of thrombocytopenia in DF is not clearly understood. Increased peripheral destruction of antibody coated platelet is strongly suspected as the possible mechanism. Other modes include acute bone marrow suppression leading to a megakaryolytic condition and enhanced platelet destruction by the reticulo-endothelial system.[6] There are many cases of Dengue which are seen every year in Kolkata with hepatic involvement and thrombocytopenia. Hence we decided to analyse the data of patients admitted in our hospital to study the hepatic involvement, thrombocytopenia and hematocrit changes in patients of Dengue.

Materials and Methods :

The present retrospective study was conducted in Ramakrishna Mission Seva Pratishthan, Vivekananda Institute of Medical Sciences, Kolkata. All patients above 12 years of age admitted in Medicine wards from 1st January 2018 to 31st December 2018 with a positive Dengue IgM antibody report by ELISA method were enrolled in the study. Patients with incomplete indoor records, patients with hepatitis/thrombocytopenia due to any other cause like Malaria, Leptospirosis, acute/chronic liver disease and those who had co-infection of dengue with malaria/leptospirosis, were excluded from the study. Serum transaminase, platelet count and hematocrit on day 1, day 4 and day 7 or till complete recovery or death were analysed.

Hepatic involvement in our study was classified into 3 grades:

Grade A : elevated aminotransferase, with increased levels of at least one of the enzymes, but lesser than 3 times the normal value.

Grade B : elevated aminotransferase with the levels of at least one of the enzymes increased more than three times but less than ten times the reference values.

Grade C : elevated aminotransferase levels in one or both enzymes increased to at least ten times their normal values.

Thrombocytopenia was defined as platelet count less than 1,50,000/mm^3. Hematocrit >45 was considered to be hemoconcentration. Recovery was defined in the form of clinical/biochemical improvement. Clinical improvement was defined as relief from the presenting symptoms like fever, vomiting, arthralgia/myalgia, rash and hypotension. Biochemical improvement was defined as normalization of platelet count (above 1,50,000/mm^3), transaminases (<351IU/l) and hematocrit between 35 to 45. Platelet transfusion was given to those patients whose platelet counts were <10,000/ mm^3 and to those patients with signs of bleeding manifestations in the form of gum bleeding, epistaxis, hemoptysis, hematemesis, melena etc.

The numerical data was analysed by percentages, bar and pie diagrams. Paired t test was applied to find out the outcome of hepatic involvement on day 1, day 4, and day 7. Paired t test was also applied to find out the outcome of thrombocytopenia on day 1, day 4 and day 7. Paired t test was applied on hematocrit values also on day 1, day 4, day 7. Chi squared test was applied to find the trends in recovery time from thrombocytopenia, hepatic involvement and hematocrit.

Table 1: Age distribution of the study sample

Category	Number	Percentage(%)
12-19 years	30	27.02
20-29 years	40	36.03
30-39 years	20	18.01
40-49 years	10	9.00
50-59 years	4	3.60
60-69 years	4	3.60
>70 years	3	2.70
Total	**111**	**100**

Table 2: Gender distribution of study sample

Category	Number	Percentage(%)
Male	65	58.5
Female	46	41.5
Total	**100**	**100**

Table 3: Method of diagnosis of Dengue infection in the study sample

Methods of Diagnosis	Number	Percentage(%)
IgM ELISA	111	100

Table 4: Grade of Hepatic involvement and time taken to recovery (n=83)

Grade of Hepatic Involvement	Time to recovery			Total
	Within 4 days	Between 4 days days and a week	A week or more	
Grade A	16	16	21	53
Grade B	3	5	17	25
Grade C	0	2	3	5
Total	**19**	**23**	**41**	**83**

Table 5: Platelet count at presentation and time to recovery (n=111)

Level of platelet deficiency	Time to recovery			Total
	Within 4 days	Between 4 days & a week	A week or more	
<20000	2	0	0	2
20,000-99,999	3	17	30	50
1,00,000-1,49,999	10	10	8	28
=1,50,000	22	3	6	31
Total	**37**	**30**	**44**	**111**

Table 6: Distribution of patients with the parameter studied

Parameter	Number of patients	Percentage (%)
Only thrombocytopenia	16	14.41
Both thrombocytopenia and hepatic involvement	65	58.55
Only hepatic involvement	17	15.31
Neither thrombocytopenia nor hepatic involvement	13	11.71
Total	**111**	**100**

Table 7: Heamatocrit values at presentation and after a week

Hematocrit values	Number of patients			Total	Percentage (%)
	Within 4 days	4-7 days	More than 7 days		
35-45	**13**	**25**	**5**	**43**	**38.73**
46-55	**20**	**30**	**10**	**60**	**54.05**
>55	**0**	**6**	**2**	**8**	**7.20**
Total	**33**	**61**	**17**	**111**	**100**

Table 8: Distribution of patient with hepatitis with increased hematocrit

Parameter	Number of patients	Percentage (%)
Only increased hematocrit (>45)	30	27.02
Both increased hematocrit (>45) and hepatitis	15	13.51
Only hepatitis	36	32.43
Neither increased hematocrit (>45) nor hepatitis	30	27.02
Total	**111**	**100**

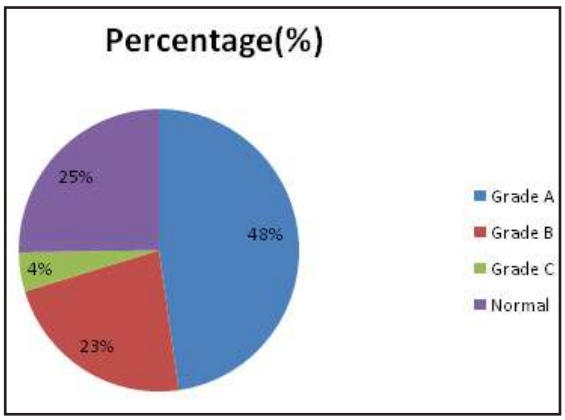


Fig. 1: Percentage distribution of grade of hepatitis

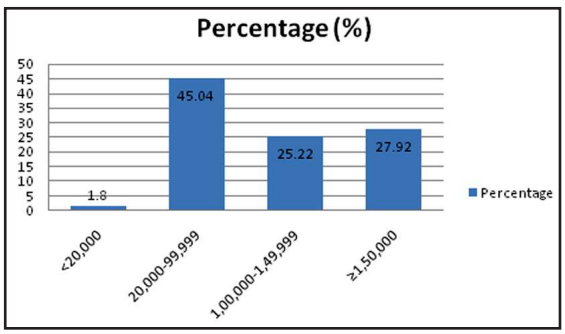


Fig. 2: Percentage distribution of patients according to platelet count

Results :

In our study 140 patients of dengue fever were admitted during the study period. But only 111 patients fulfilled the Inclusion and Exclusion criteria and hence only their records were analysed.

Table 1 shows the age distribution of the study participants and Table 2 shows gender distribution. Table 3 shows the method of detection of the Dengue infection. All the patients were diagnosed by IgM ELISA method.

Hepatic involvement :

28/111 (25.22%) had normal transaminase levels. 53/111 (47.74%) had Grade A, 25/111 (22.52%) had Grade B and 5/111 (4.50%) had Grade C hepatitis.

Thrombocytopenia :

Figure 2 shows the distribution of patient according to the platelet count. Table 4 shows the categorization of patients according to their time to recovery and also according to grade of hepatic involvement. The Chi- Squared test for trend for the above data yielded a p value of <0.05 which is statistically significant. This might be suggestive of a strong association between hepatic involvement and a longer time to recovery. The median values of SGOT were 62 (8-4340) and SGPT were 41 (7-2580). Three patients with grade C hepatic involvement succumbed to death. All of the patients with grade C had severe thrombocytopenia, hypotension and increased hematocrit.

Table 5 shows the trends of time to recovery of a patient from thrombocytopenia -an indicator of prognosis. The Chi-Squared test for trends for the above table yielded a p-value of <0.001

which is statistically very significant. This is in agreement with the previously known fact that severity of platelet deficiency at presentation is a poor prognostic indication of recovery as well as of poor outcomes.

Table 6 shows the distribution of patient with the parameter studied (only thrombocytopenia, only hepatic involvement, both thrombocytopenia and hepatic involvement; and neither thrombocytopenia nor hepatic involvement). Percentage of only thrombocytopenia (platelet count <1,50,000/cu. mm.) (no hepatic involvement) among diagnosed dengue fever cases = 16/111 i.e. 14.41%. Percentage of only hepatic involvement (SGOT and/or SGPT >35 IU/L) (no thrombocytopenia) among diagnosed dengue fever cases = 17/111 i.e. 15.31%. Percentage of both thrombocytopenia and hepatic involvement among diagnosed dengue fever cases = 65/111 i.e. 58.55%. Percentage of neither thrombocytopenia nor hepatic involvement among diagnosed dengue fever cases = 13/111 i.e. 11.71%. Apart from thrombocytopenia and hepatic involvement in our study, Hypotension was present in 32 (28.8%) of patients on admission. Serositis was present in 14 (12.6%) patients.

Hematocrit values :

Table 7 shows hematocrit values of patients at the time of admission and after one week. Out of 111 patients 43 patients (38.73%) had normal hematocrit throughout the hospital stay. 60 patients (54.05%) had hematocrit values in between 46-55 with maximum patient i.e. 30 (50%) in between 4-7 days and 10 patients (16.6%) after 7 days. Only 8 patients (7.20%) had hematocrit value above 55. Out of the 8 patients, 6 patients (75%) had such hematocrit value in between 4-7 days.

Table 8 shows changes of hematocrit values with hepatitis. Percentage of patients with only elevated hematocrit (>45) is 27.02%. 13.51% patients had both increased hematocrit (>45) with hepatitis. Only hepatitis was seen in 32.43% patients. 27.02% patients had Neither increased hematocrit nor hepatitis.

Death occurred in 3 patients who had Grade C hepatitis with platelet count <2500 and hematocrit >45 due to dengue shock syndrome which is resistant to therapy.

Discussion :

There is abundance of clinical cases of dengue but scanty published data on information about hepatic involvement, thrombocytopenia and hematocrit changes occurring simultaneously in dengue patients in India, majority of the reported studies are from the Asian countries outside India.

This was a retrospective observational study done at a tertiary care centre. In our study out of 111 patients, 65 patients were males (58.5%) and 46 patients (41.5%) were females, which was similar to a study done by Om Prakash et al, out of 699 patients, 65% were males and 35% were females.[7] In another study done by Souza et al of 1585 patients there was a female preponderance of 58.3%.[8] Francisca from Brazil reported 53.25% males and 46.75% females. Jehangir and Asar Khan studied the incidence of Dengue and found 68.6% were males and 31.3% were females. The gender distribution varies from place to place, and country to country. It depends on the health care seeking tendancies and available outreach facilities and awareness about the illness amongst the patients themselves and their primary care givers.

In our study, majority of the study population (36.03%) were in the age group of 20-29 years with a mean age of 24.5 years, which was comparable to a study reported by Trung et al, where the mean age ranged between 15 to 35 years.[9] Lifestyle habits of youngsters like improperly covered extremities with clothes, sleeping in open air without mosquito nets or mosquito repellents may be the reason for higher study population in the age group of 20-29 years.

In our study hepatic involvement was studied on the basis of aminotransferase elevation. Total 74.77% (83/111) of patients had elevated aminotransferase. Grade A in 47.74%, Grade B in 22.52%, Grade C in 4.50% of patients. Transaminase levels started improving within first week of illness but recovery occurred in majority of the patients by the end of 7 days or more. There were 3 deaths in patients who had severe hepatitis (Grade C) along with thrombocytopenia and hypotension and hematocrit >45. The postulated pathogenetic mechanisms of hepatic involvement in dengue are direct hepatotoxic effects of the virus, immune response of the host on the hepatocytes, ischaemic hepatitis, hypoxia mediated hepatic injury, tissue tropism of the dengue viral serotypes.

In a study by Wong et al 91% had AST elevation and 72% had ALT elevation. Kuo et al reported 90% had abnormal AST and 80% had abnormal ALT. In our study 77% had AST elevation and 59.7% had ALT elevation. These studies showed that hepatic involvement in Dengue fever is not uncommon as it was thought to be. Although Dengue Virus is not hepatotropic virus, the above postulated mechanisms are responsible for the pathogenic effects. In a study by Parkash in Karachi, AST was reported as high as 95% and ALT 86%. This study included only DHF patients so the hepatic involvement was high in the study.[7] There were 3 deaths in patients who had severe hepatitis grade C along with thrombocytopenia and hypotension and hematocrit >45.

Thrombocytopenia is a common manifestation of Dengue fever. It may remain asymptomatic or cause clinical manifestations ranging from petechial rash to bleeding from mucosal sites to frank dengue hemorrhagic fever or dengue shock syndrome. Studies suggest that the cause for thrombocytopenia is multifactorial which includes decreased formation due to suppression of megakaryocytopoiesis; as well as increased destruction of platelets due to clearance by DENV-induced apoptosis and antiplatelet antibodies.[10] In our study thrombocytopenia was based on platelet count at the time of admission. Total 80/111 i.e. 72.07% had thrombocytopenia during presentation. According to study done by Nandini Chatterjee et al, 55% of patients had thrombocytopenia.[11] Study done by Rachel Daniel et al also demonstrated thrombocytopenia was present in (225/250) 90% cases.[12]

Majority of the patients in our study (45.04%) had a platelet count ranging from 20,000-99,999, which was similar to other studies where the median platelet counts were 48,000. Platelet count less than 20,000 in 1.80% cases, 20,000-99,999 in 45.04% cases, 1,00,000-1,49,999 in 25.22% cases.

In a study done by Amitava Acharyya, total 36.9% (141) cases had platelet count between 36,000 and 1,00,000; while 10.5% (40) patients platelet count below 35,000 which was similar to the findings in our study.[13]

The length of hospital stay in our study ranged from 4 to 7 days with an average of 5 days. In

a study by Lye et al the length of stay was 3 days and in a study by Khan et al the length of stay was 4 days. The length of stay depends on the severity of thrombocytopenia, hepatic involvement, correction of hypotension, symptomatic improvement from fever, bodyache, arthralgias, nausea, vomiting and abdominal pain. Patients of Dengue hemorrhagic fever and dengue shock syndrome require a prolonged stay in the hospital.

A Brazilian study done by Francisca Raimunda et al (2012) showed that transaminitis occurred in patients developing thrombocytopenia with raising hematocrit in Dengue fever (mainly DHS). The abnormalities started on 3rd day and normalized by day 11th. Limitation of our study was inability to study the serotype of Dengue Virus.

Conclusion :

This study shows significant association between hepatic involvement, severe thrombocytopenia and hematocrit >45 in predicting the morbidity and mortality of dengue fever. Therefore more studies from the Indian subcontinent should be carried out to correlate the serotype of Dengue Virus and the hepatic involvement, thrombocytopenia and hematocrit changes in dengue fever.

Conflict of Interest : None

References :

1. World Health Organization, Special Programme for Research, Training in Tropical Diseases, World Health Organization. Department of Control of Neglected Tropical Diseases, World Health Organization. Epidemic, Pandemic Alert. Dengue: guidelines for diagnosis, treatment, prevention and control. World Health Organization; 2009.
2. WHO (2018), Fact Sheet, 2nd Feb. 2018.
3. WHO (2011), Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever, Revised and expanded edition, Regional office of SEAR.
4. Itha S, Kashyap R, Krishnani N, Saraswat VA, Choudhuri G, Aggarwal R. Profile of liver involvement in dengue virus infection. National Medical Journal of India. 2005 May 1; 18(3):127.
5. Fernando S, Wijewickrama A, Gomes L, Punchihewa CT, Madusanka SD, Dissanayake H, Jeewandara C, Peiris H, Ogg GS, Malavige GN. Patterns and causes of liver involvement in acute dengue infection. BMC infectious diseases. 2016 Dec 1; 16(1):319.
6. Chikkaveeraiahan SK, Srinath KM, Kumar SK, Reddy PK. Hepatic profile and platelet count as a prognostic indicator in Dengue fever, from a tertiary care hospital in south India. Int Journal Appl Basic Med Res 2016; 5:54-31.
7. Parkash O, Almas A, Jafri SW, Hamid S, Akhtar J, Alishah H. Severity of acute hepatitis and its outcome in patients with dengue fever in a tertiary care hospital Karachi, Pakistan (South Asia). SMC gastroenterol 2010;10:43-47.
8. Souza LJ, Alves JG, Nogueira RM, Gicovate Neto C, Bastos DA, Siqueira EW, Souto Filho JT, Cezário TD, Soares CE, Carneiro RD. Aminotransferase changes and acute hepatitis in patients with dengue fever: analysis of 1,585 cases. Brazilian journal of infectious diseases. 2004 Apr; 8(2):156-63.
9. Thu TL, Minh DN, Van NT, Tinh HT, Van Vinh CN, Wolbers M, Hoai TD, Farrar J, Simmons C, Wills B. Clinical features of dengue in a large Vietnamese cohort: intrinsically lower platelet counts and greater risk for bleeding in adults than children. PLoSNegl Trop Dis. 2012 Jun 26; 6(6):e1679.
10. Schexneider KI, Reedy EA. Thrombocytopenia in dengue fever. Current hematology reports. 2005 Mar; 4(2):145.
11. Chatterjee N, Mukhopadhyay M, Ghosh S, Mondol M, Das C, Patar K. An observational study of dengue fever in a tertiary care hospital of eastern India. J Assoc Physicians India. 2014 Mar; 62(3):224-7.
12. Daniel R, Philip AZ. A study of clinical profile of dengue fever in Kollam, Kerala, India.
13. Acharyya A, Ghosh K, Bhattacharyya A, Ghosh M, Chakraborty S, Ghosh S, Pal M. The dengue fever and its complication: A scenario in a tertiary-level hospital of greater Kolkata. Annals of Tropical Medicine and Public Health. 2016 Mar 1; 9(2):92-96.

Original Article

A Prospective Study to Ascertain The Incidence of Pruritus in Pregnancy with Intrahepatic Cholestasis of Pregnancy (ICP) and Its Maternal and Perinatal Outcome

Dr. Arunabha Das[1], Dr. Sanam Islam[2], Prof. Krishnendu Gupta[3]

Abstract :

Background :

Pruritus is common in pregnancy, usually seen in 3-14% patients. It is thought to becaused by raised levels of certain chemicals in blood such as hormones. With progression of the pregnancy, the skin of the abdomen is stretched which often leads to more pruritus. Intrahepatic cholestasis of pregnancy (ICP) is a liver disease unique to pregnancy characterised by pruritus in the absence of skin rash with abnormal liver function tests (LFTs) occurring in the 2nd and 3rd trimester of pregnancy which disappears spontaneously after delivery. The clinical importance lies in the potential foetal risks like preterm birth, foetal distress, meconium-stained liquor, intrauterine foetal death (IUFD) and maternal risks like post-partum hemorrhage (PPH), sleep deprivation and malabsorption.

Methodology :

A prospective observational study was carried out over a period of one year. A total of 150 pregnant women who complained of pruritus at or after 20 weeks of gestation were selected after giving due consideration to the inclusion and exclusion criteria. This determined the prevalence of ICP in the study population and acomparison of the maternal and perinatal outcomes with those not developing cholestasis was also determined.

Outcome :

The incidence of ICP in our study population was 21.6%. The mean age of women affected with obstetric cholestasis was 28 years +5.19 years. Most of the patients responded well to treatment (75.8%). Foetal distress was found in 8.33% of the mothers without ICP but 27.27% of mothers with ICP had foetal distress. The mothers presenting with pruritus without ICP had 4.17% abnormal CTG but mothers with ICP had 18.18% abnormal CTG. The meconium-stained liquor was found in 42.42% of the mothers with ICP, but it was seen only 3.33% in mothers without ICP.

Keywords :

Pruritus Gestationis, Intrahepatic Cholestasis of Pregnancy, Maternal outcome, Perinatal outcome

Introduction :

During pregnancy, pre-formed immunological, metabolic, endocrine and vascular changes occur which make pregnant women susceptible to skin changes which are physiological and pathological leading to the development of pruritus. It can be a source of significant discomfort. The cause may range from normal cutaneous changes common to all pregnancies, dermatoses unique to pregnancy and flares of pre-existing dermatoses[1]. Rasheed S et al[2] reported ICP increased the need for special neonatal care.

[1]Assistant Professor; [2]Postgraduate Trainee; [3]Professor, Dept of Obstetrics &Gynaecology, RKMSP, VIMS

Sosa SY et al[3] reported mean age of obstetric cholestasis cases was 29.2+6.8 years. Keynon AP et al[4] in 6532 pregnant women found that pruritus in pregnancy affected 23% of pregnancies of whom 16% developed obstetric cholestasis and itching was most severe in palms and soles in such cases.

Aims and Objectives :

General Objectives :

To compare the maternal and perinatal outcomes of the patients diagnosed with ICP in comparison with those with pruritus in absence of ICP.

Specific Objectives :

1. To detect maternal symptoms like coagulation defects due to vitamin K deficiency that may predispose to PPH and chance of increased operative delivery.
2. To detect foetal and neonatal risks such as preterm delivery (both iatrogenic and spontaneous), foetal distress due to foetal hypoxia, abnormal CTG, meconium staining of amniotic fluid and rarely, IUFD (intrauterine foetal death).

Materials & Methods :

Study Design :

Hospital based prospective observational study.

Study Setting and Duration :

The present study was undertaken at the Department of Obstetrics & Gynaecology, Ramakrishna Mission Seva Prathishthan, Vivekananda Institute of Medical Sciences, a tertiary multi-specialty hospital, over a period of one year (2017-18)

Study Population :

150 pregnant women with pruritus, at or beyond 20 weeks of gestation, who fulfilled the eligibility criteria during the study period in the above referral centre were selected as the study group after proper and detailed history taking.

Exclusion Criteria :

* Patients with established liver disease like cholelithiasis, auto-immune liver disease etc.
* Patients with preeclampsia and eclampsia
* Patients with positive hepatitis markers
* Patients with diagnosed skin disease causing pruritus prior to pregnancy.

Statistical Analysis :

Categorical variables were expressed as Number of patients and percentage of patients and compared across the groups using Pearson's "Chi Square Test" for Independence of Attributes/ Fisher's "Exact Test" as appropriate.

Continuous variables were expressed as Mean, Median and Standard Deviation and compared across the 2 groups using Mann-Whitney "U Test".

The statistical software SPSS version 20 was used for the analysis.

An alpha level of 5% was taken, i.e. If any p value was less than 0.05, it was considered significant.

Results and Analyses :

Table I

ICP	Frequency	%
Absent	120	78.4
Present	33	21.6
Total	**153**	**100.0**

Table II

		ICP		Total	P value	Significance
		Absent (%)	**Present (%)**			
Site of Pruritus	Abdomen Thigh	98(81.67)	0	98(64.05)	<0.001	Significant
	General	20 (16.67)	5 (15.15)	25 (6.34)		
	Palm Sole	2 (1.67)	28 (84.85)	30 (19.61)		
Total		**120 (100)**	**33 (100)**	**153 (100)**		

Table III

		ICP		Total	P value	Significance
		Absent (%)	**Present (%)**			
PPH	No	107 (89.17)	30 (90.91)	137 (89.54)	0.532	NOT Significant
	Yes	13 (10.83)	3 (9.09)	16 (10.46)		
Total		**120 (100)**	**33 (100)**	**153 (100)**		

Table IV

		ICP		Total	P value	Significance
		Absent (%)	**Present (%)**			
Mode of Delivery	EL LSCS	25 (20.83)	10 (30.3)	35 (22.88)	0.331	Not Significant
	EM LSCS	47 (39.17)	14 (42.42)	61 (39.87)		
	VD	48 (40)	9 (27.27)	57 (37.25)		
Total		**120 (100)**	**33 (100)**	**153 (100)**		

Table V

		ICP		Total	P value	Significance
		Absent (%)	**Present (%)**			
Fetal Distress	No	110 (91.67)	24 (72.73)	134 (87.58)	0.532	NOT Significant
	Yes	10 (8.33)	9 (27.27)	19 (2.42)		
Total		**120 (100)**	**33 (100)**	**153 (100)**		

Table VI

		ICP		Total	P value	Significance
		Absent (%)	**Present (%)**			
IUFD or still Born	No	120 (100)	32 (96.97)	152 (99.95)	0.216	Significant
	Yes	0	1 (3.03)	1 (0.65)		
Total		**120 (100)**	**33 (100)**	**153 (100)**		

Table VII

		ICP		Total	P value	Significance
		Absent (%)	**Present (%)**			
NICU Admission	No	96 (80)	20 (60.61)	116 (75.82)	0.021	Significant
	Yes	24 (20)	13 (39.39)	37 (24.18)		
Total		**120 (100)**	**33 (100)**	**153 (100)**		

Table VIII

	AST at detection	**AST after 4 weeks of UDCA**	**AST at 6 weeks post-partum**
Mean	184.39	108 12	33.75
Median	160.00	92.00	34.00
Std. Deviation	112.67	79.87	4.71

Table IX

	ALT at detection	**ALT after 4 weeks of UDCA**	**ALT at 6 weeks post-partum**
Mean	178.94	114.12	32.25
Median	169.00	88.00	32.50
Std. Deviation	111.47	90.59	5.52

Discussion :

Incidence of ICP in study population.

Table 1 shows that, the incidence of ICP in our study population was 21.6%. In our study the total number of the mothers presenting with pruritus was 153 and out of this, 33 mothers had ICP.

Distribution according to maternal age.

Most of the patients (51.63%) were with age between 26 – 30 years which was significantly higher than that of other groups like age between 20 – 25 years and 31 – 35 years. 45.45% of patients with ICP were 26 – 30 years of age, 21.21% in 20 – 25 years of age and 33.33% in 31 – 35 years of age. Whereas 53.33% of patients without ICP were 26 – 30 years of age, 24.17% in 20 – 25 years of age and 22.5% in 31 – 35 years of age. Rasheed S et al[2] reported that mean age of women affected with obstetric cholestasis was 28 years +5.19 years.

Incidence of pruritus with and without ICP according to number of pregnancies.

In our study population 98.04% had singleton pregnancies and 1.96% had multiple pregnancies. Patients with ICP had 3.03% multiple pregnancies and patients without ICP had 1.67% multiple pregnancies. But Sczech et al[5] showed that 78% had a singleton gestation and 22% had a multiple gestation.

Distribution according to the site of pruritus.

In our study population, 81.76% pruritic mothers without ICP had itching on the abdomen and thighs, followed by generalized itching (16.67%), and palms and soles (1.67%) as shown in Table II, but the mothers with ICP had itching most commonly on palms and soles (84.85%) which was highly significant (p=0.001). Keynon et al[4] mentioned that the most common location of itching during pregnancy was on the abdomen. Szczech[5] et al showed that the most common location of itch was on the abdomen (90%). Glantz et al[6] reported generalized itch of greater severity commonly affecting hands and feet with deterioration during night is frequently connected with ICP.

Distribution of deranged coagulation profile.

3.03% of the patients with ICP had deranged coagulation profile. Mostly they had increased PT. But no one had deranged coagulation profile in our study population without ICP. So it was not significant (p=0.216).

Symptomatic response to UDCA (ursodeoxycholic acid).

Most of the patients responded well to UDCA treatment (75.8%). Laifer SA et al[7] found that UDCA is associated with significant decrease in serum transaminases and relief of pruritus. Roncaglia et al[8] reported that UDCA is considered to be a safe treatment option in later half of pregnancy and this treatment can reduce itchiness, improve the function of the liver and reduce the risk to the foetus.

Distribution according to PPH.

In our study 9.09% of ICP mothers and 10.83% of mothers without ICP had PPH in our study (Table III). Dang et al[9] reported significantly increased incidence of PPH (29.78%). Ray et al[10] also found 25% incidence of PPH among cholestasis patients.

Distribution according to PPROM.

9.09% of ICP mothers and 6.67% of the mothers without ICP had PPROM in our study. Padmaja et al[11] reported a significant increase in incidence of PPROM in OC group, about 8.9%.

Distribution according to the mode of delivery.

Most of the patients underwent caesarean section, out of which 22.88% had elective LSCS and 39.87% had emergency LSCS. The number of cases of operative delivery were higher than the vaginal delivery (VD). For ICP mothers, EL LSCS was 30.3%, EM LSCS was 42.42% and VD 27.27%. For the mothers without ICP, 20.83% had EL LSCS, 39.17% had EM LSCS and 40% had VD (Table IV). According to Keynon et al[4] women with OC delivered by caesarean section significantly more often (36.0%) than in general obstetric population. Rasheed et al[2] reported spontaneous delivery rate of 80% with emergency LSCS rate of 16.7% and elective LSCS rate of 3.3%. Caesarean section rate was rather high in our study. It was 72.73 % in mothers with ICP, as like many UK hospitals, our tertiary private hospital also adopts a policy incorporating antenatal surveillance of some form with elective delivery by 37 – 38 weeks.

Distribution according to foetal distress.

Foetal distress (Table V) was found in 8.33% of the mothers without ICP but 27.27% of mothers with ICP had foetal distress which was significant (p=0.007). Sultana et al[12] also found 33.3% babies complicated with foetal distress in obstetric cholestasis patients.

Distribution according to abnormal CTG (cardiotocography).

In our study mothers presenting with pruritus without ICP had 4.17% abnormal CTG but mothers with ICP had 18.18% abnormal CTG which was significant (p-0.013). Ray et al[10] reported intrapartum CTG in 29.03% cases of OC. Gupta et al[13] noted abnormal CTG in 7.2% cases.

Distribution according to meconium stained liquor.

In our study, meconium stained liquor was found in 42.42% of the mothers with ICP, which was found to be (11) reported higher incidence of meconium passage (17%) at delivery. According to Gupta et al[13] cholestasis patients had higher incidence of thick meconium passage during labor (12.9%), but it was seen only 3.33% in mothers without ICP. Padmaja et al[11] reported higher incidence of meconium passage (17%) at delivery.

Distribution according to birth weight (LBW).

The mothers presenting with pruritus without ICP the mean birth weight of babies was 2.8+0.41 kg with range 1.83 – 3.82 kg, and median of birth weight was 2.91 kg. The table shows that mean birth weight of the babies of the patients with OC was 2.60+0.42 kg with range 1.66 – 3.21 kg and median was 2.65 kg which was highly significant (p=0.013). Sosa et al[3] reported that neonates of OC mothers has an average weight of 2381+533 gm, while babies of mothers in the control cohort had an average weight of 3118+470 gm (p>0.001).

Distribution according to IUFD (Intrauterine foetal death)/still born.

IUFD or still born was found only in 1 mother out of 33 mothers with ICP but none was found in the mothers without ICP in our study (Table VI).

Distribution according to NICU admission.

39.39% babies of the mothers with ICP required NICU admission which was significant (p=0.021) in our study. Severely unstable neonates were kept in NICU for monitoring and treatment (Table VII). The causes of their morbidity were many

like foetal distress, thick meconium staining, prematurity or very low birth weight. Keynonet al[4] reported 14% infants required admission to special care baby unit. They also found no perinatal death among cholestasis patients. There was no perinatal mortality among cases in our study. Gupta et al[13] also reported no perinatal mortality in patients with OC.

Changes of bilirubin at detection, after 4 weeks of UDCA (ursodeoxycholic acid) treatment and 6 weeks postpartum.

In our study, at detection the mean bilirubin of the mothers with ICP was (0.87+0.22) with range 0.40 – 1.20 mg/dl and median 0.90. After 4 weeks of UDCA treatment the mean bilirubin was (0.64+0.14) with range 0.40 – 0.90 mg/dl and median 0.60. At 6 weeks post-partum period mean bilirubin was (0.59+0.15) with range 0.30 – 0.80 mg/dl and median 0.60.

Changes of AST (aspartate transaminase) at detection, after 4 weeks of UDCA (ursodeoxycholic acid) treatment, at 6 weeks postpartum.

In our study, at detection the mean AST of the mothers with ICP was (184.39+0.112.67) with range 67.00 – 536.00 mg/dl and median was 160.00 (Table VIII). After 4 weeks of UDCA treatment the mean AST was (108.12+79.87) with range 28.00 – 416.00 mg/dl and median was 92.00. At 6 weeks post-partum period mean AST was (33.75+4.71) with range 22.00 – 40.00 mg/dl and median was 34.00. Laifer et al[7] concluded in their study that ursodeoxycholic acid treatment in obstetric cholestasis is an effective therapy for relief of pruritus and improvement of liver dysfunction that occurs with intrahepatic cholestasis of pregnancy.

Changes of ALT (alanine transaminase) at detection, after 4 weeks of UDCA (ursodeoxycholic acid) treatment and at 6 weeks postpartum.

In our study, at detection the mean ALT of the mothers with ICP was (178.94+111.47) with range 65.00 – 582.00 mg/dl and median was 169.00 (Table IX). After 4 weeks of UDCA treatment the mean ALT was (114.12+90.59) with range 32.00 – 424.00 mg/dl and median was 88.00. At 6 weeks post-partum period mean ALT was (32.25+5.52) with range 21.00 – 44.00 mg/dl and median was 32.50.

Wang et al[11] published a study on perinatal outcome of intrahepatic cholestasis of pregnancy. They retrospectively analysed 1210 cases of OC in the last 10 years and concluded that the important measures to decrease perinatal mortality include paying attention to foetal monitoring in the presence of threatened premature labour, occasional uterine contractions and prenatal meconium and take timely intervention of pregnancy.

Riosecoet al[13] reported a study of perinatal outcome of 320 consecutive patients with intrahepatic cholestasis of pregnancy and found a higher incidence of meconium staining in the amniotic fluid at delivery of 25% vs. 16% in the control group.

The pathogenesis of foetal complications is still poorly understood, although a role of bile acids or toxic metabolites of bile acids has been suggested[7]. Bile acids were shown to induce contraction of the chorionic veins of the placenta, and the myometrial sensitivity of healthy women to oxytocin was increased after incubation with cholic acids[14,15]. Bile acids are also known to cause an increase in colonic motility and subsequent meconium passage[16].

Despite many studies of foetal assessment and maternal medications, the Royal College of Obstetrics and Gynaecology (2006) advise thatthere is no evidence that any specific treatment improves maternal symptoms or foetal outcomes. Lack of possible evidence about specific treatment is the reason why active management by induction of labour or/ and caesarean section at 37–38 weeks is advised in order to avoid the risks of late stillbirth[19].

As we have seen that pruritus was common in pregnancy and many among them had obstetric cholestasis, incidence rate was a little high in our hospital. Larger studies are needed to assess the correct incidence of OC among the mothers presenting with pruritus. We have seen that both the maternal and foetal complications are higher among the mothers with ICP than the mothers without ICP. So it is very important to diagnose obstetric cholestasis early and further trials needed to conclude whether policies of active management like antenatal foetal surveillance and elective early delivery, could improve obstetric outcomes or only increase early intervention rate resulting in caesarean section, iatrogenic prematurity, PPH etc. Current treatment strategies have questionable benefit of reducing perinatal morbidities particularly intrauterine foetal demise near term or improving maternal and perinatal morbidities very effectively, but may be effective in controlling pruritus and improving biochemical response to some extent. A randomized control trial of elective versus anticipated delivery is needed and we need to establish whether the severity of clinical symptoms, biochemical abnormality and their treatment response are related to obstetric outcome.

Moreover, as our study period was limited and sample size was small, the result may not reflect the true picture obtained from previous studies. For better results, further extensive and long-term studies are needed.

Summary and Conclusion :

In this study we came to appreciate that the incidence of obstetric cholestasis (OC) in mothers presenting with pruritus is high in our hospital, as it is a tertiary care hospital. Incidence of pruritus with and without ICP is almost equal in primigravida and multigravida patients, but significant numbers of multipara patient have history of previous pregnancy affected with OC. A large number of the patients presented with characteristic pruritus especially in palms and soles followed by deranged liver function tests. Majority of cases are diagnosed in late gestational age, mostly during 28 – 36 weeks period of gestation. So, obstetric cholestasis is a disease of late pregnancy. In obstetric cholestasis, maternal and neonatal morbidities are more than the mothers without ICP. Maternal morbidities are due to sleep disturbances, coagulation abnormality and PPH and caesarean section rates are raised in OC. In OC, maximum numbers of patients are delivered at 37 to 38 weeks, due to active maternal and foetal surveillance and early intervention. Neonatal morbidities are due to foetal distress, prematurity, low birth weight and meconium staining of amniotic fluid. Foetal outcomes are improved with a variety of strategies of active management; the most effective intervention has not currently been established. Ursodeoxycholic acid (UDCA) treatment is associated with marked improvement of symptoms and biochemical abnormalities. Almost all patients have postnatal resolution within 6 weeks of delivery. However, large therapeutic trials are required to establish which

specific drug treatments or management strategies are effective at reducing the rates of adverse maternal and foetal outcomes. In this study, both the sample size and the time period being limited, it therefore may not reflect the true magnitude of the problem; however the take home message clearly is that early diagnosis and active maternal and foetal surveillance is of utmost importance to avoid adverse outcomes.

Conflict of Interest : None

Ethical Clearance : Institutional Ethics Committee.

References :

1. Bechtel MA. Pruritus in Pregnancy and Its Management. Dermatol Clin. 2018;36(3):259–265.
2. Rasheed S, Afghan S, Mazhar SB. Fetomaternal outcome in patients with obstetric cholestasis. Ann Pak Inst Med Sci. 2009;5(4):211–215.
3. Sosa SY, Valenzuela A, Pacheco J et al. Intrahepatic Cholestasis of Pregnancy: Evaluation of Risk Factors and Predictive Factors. The Internet Journal of Gynecology and Obstetrics. 2010;12(2):465–474.
4. Kenyon AP, Tribe RM, Piercy CN et al. Pruritus in pregnancy: a study of anatomical distribution and prevalence in relation to the development of obstetric cholestasis. Obstet Med. 2010;3(1):25–29.
5. Szczech J, Wiatrowski A, Hirnle L et al. Prevalence and Relevance of Pruritus in Pregnancy. BioMed research international, 2017.
6. Glantz A, Marschall HU, Lammert F et al. Intrahepatic cholestasis of pregnancy: a randomized controlled trial comparing dexamethasone and ursodeoxycholic acid. Hepatology. 2005;42(6):1399–1405.
7. Laifer SA, Stiller RJ, Siddiqui DS et al. Ursodeoxycholic acid for the treatment of intrahepatic cholestasis of pregnancy. J Matern Fetal Med. 2001;10(2):131–135.
8. Roncaglia N, Arreghini A, Locatelli A et al. Obstetric cholestasis: outcome with active management. Eur J Obstet Gynecol Reprod Biol. 2002;100(2):167–170.
9. Dang A, Agarwal N, Bathla S et al. Prevalence of liver disease in pregnancy and its outcome with emphasis on obstetric cholestasis : An Indian scenario. J ObstetGynecol India. 2010;60(5):413–418.
10. Ray A, Tata RJ, Balsara R et al. Cholestasis of pregnancy. J Obstet Gynecol India. 2005;55(3):247–250.
11. Padmaja M, Pal B, Gupta JK et al. A study of obstetric cholestasis. J ObstetGynaecol India. 2010;60(3): 225–231.
12. Sultana R, Sarwar I, Fawad A et al. Neonatal outcome in obstetric cholestasis patients at Ayub Teaching Hospital Abbottabad. J Ayub Med Coll Abbottabad. 2009;21(4):76–78.
13. Gupta A, Kakkar T, Gupta Y et al. Cholestasis of pregnancy. J Obstet Gynecol India. 2009;59(4):320–323.
14. Laifer SA, Stiller RJ, Siddiqui DS et al. Ursodeoxycholic acid for the treatment of intrahepatic cholestasis of pregnancy. J MaternFetal Med. 2001;10(2):131–135.
15. Royal College of Obstetricians and Gynaecologists. Obstetric cholestasis. Green-Top Guideline No. 43, 2006.
16. Ropponen A, Sund R, Riikonen S et al. Intrahepatic cholestasis of pregnancy as an indicator of liver and billliary diseases: a population-based study. Hepatology. 2006;43(4):723–728.
17. Szczech J, Wiatrowski A, Hirnle L et al. Prevalence and Relevance of Pruritus in Pregnancy. BioMed research international. 2017.
18. Sosa SY, Valenzuela A, Pacheco J et al. Intrahepatic Cholestasis of Pregnancy: Evaluation of Risk Factors and Predictive Factors. The Internet Journal of Gynecology and Obstetrics. 2010;12(2):465–474.
19. Roncaglia N, Arreghini A, Locatelli A et al. Obstetric cholestasis: outcome with active management. Eur J Obstet Gynecol Reprod Biol. 2002;100(2):167–170.

Case Report

Gastro-Intestinal Non-Hodgkin's Lymphoma

Dr. Ishita Laha[1], Dr. Achintya Kumar Das[2], Dr. Shivaji Mandal[3]

Abstract :

The gastrointestinal tract is the most frequent site of Non-Hodgkin's Lymphoma (NHL) outside of the lymph nodes themselves. This tract is much more frequently compromised by tumours secondary to primary disease elsewhere in the body than by primary lymphomas of the gastrointestinal tract itself which are rare. Their development and prognosis are quite different from those of adenocarcinomas. It is important to keep them in mind in differential diagnosis in daily clinical practice, although rare. We review the literature and report the case of a 21-year-old boy with primary small bowel lymphoma that was diagnosed only after excision of the swelling.

Keywords :

Non-Hodgkin Lymphoma, Primary Gastro-intestinal Lymphoma, Diffuse Large B Cell Lymphoma, Small intestine.

Introduction :

The incidence of Non-Hodgkin lymphoma (NHL) increases with age and peaks in individual aged 80-90 years[1,2]. The gastrointestinal tract is the most frequent site of extra nodal lymphoma. Gastrointestinal tract extra nodal lymphoma accounts for 4% to 20% of all NHL, most of which are of B cell lineage that develop in Mucosa Associated Lymphoid Tissue (MALT)[3]. The involvement of T-cell lymphomas is less frequent and has a heterogeneous presentation[4,5]. This type of lymphoma is generally associated with a history of celiac disease and reveals tumour cells that are Cluster of Differentiation CD 3, CD 7 and CD 103 a positive; CD 5 and CD 4 negative and CD 8 positive or negative[6]. Risk factors for the development of primary intestinal lymphoma include *H. pylori* infections, celiac disease, inflammatory bowel disease, and immunosuppressive states associated with Human Immunodeficiency Virus (HIV) infections and solid organ Transplantation[7]. Here we report a case of Diffuse Large B Cell Lymphoma (DLBCL) who attended our outpatient department with abdominal swelling and pain of a week's duration with no co morbidities.

Case Presentation :

A 21-year-old male attended with right lower abdominal pain and swelling in the right lower quadrant for one week. He had a history of a single episode of severe colicky pain one week before which was relieved on administration of intra-venous analgesics. The patient denied change in bowel habit, gastrointestinal (GI) bleeding, weight loss, anorexia, fever, night sweats or pruritus. General survey was essentially normal apart from the swelling in his right lower quadrant. The swelling was 15 x 10 cm in size in the right lower quadrant extending beyond the midline, oval shaped with smooth margins and hard consistency. (Figures 1,2) The swelling was tender to touch, fixed, not moving with respiration and all borders could be delineated. It was not compressible and the leg rising test

[1]Junior Resident, [2,3]Professor, Department of General Surgery, RKMSP, VIMS

confirmed it to be an intra-abdominal swelling. No other distant lymphadenopathy was noted. Examination of the scrotum and testis was normal.

Liver profile and peripheral full blood count were normal but the C reactive protein (CRP) level was raised. HIV and hepatitis screen were negative. Ultrasound imaging performed on the first day on the day of severe abdominal pain suggested a 14 x 10 x 8 cm mass in the right iliac fossa possibly arising from the appendix with hypoechoic areas noted within the mass. There was free fluid noted in the right iliac fossa suggestive of appendicular abscess. A Contrast enhanced CT scan of the abdomen was obtained which showed a mass of soft tissue density arising from the small intestine and raised the possibility of gastro-intestinal stromal tumour. The lumen was clear and no additional lymph nodes seen (Figure 3,4). Other organs were normal.

Emergency exploration of the abdomen was performed. The mass was seen to arise from the mesenteric border of the small intestine and there was a small swelling noted in the ascending colon (Figure 5,6). A Right hemicolectomy was performed with ileo-transverse side to side anastomosis. The patient had an uneventful post-operative period.

The histopathological report was suggestive of high grade, Non-Hodgkin lymphoma, diffuse, large cell type, involving the small intestine, mesenteric lymph nodes and perinodal tissue. The surgical margins were free of lesion. On immunohistochemical stain, cells expressed CD20, CD10, bcl2, bcl 6, MUMI and were negative for CD5. About 15% of the cells expressed c-myc, ki67 index was about 98%. The inference was Diffuse Large B cell lymphoma.

Multidisciplinary Tumour Board was arranged to discuss the further line of management for this patient. The recommended chemotherapy based on the CHOP scheme : combination of cyclophosphamide, doxorubicin, vincristine and prednisone[16,17] for 21 days with 8 such cycles.

Discussion :

The GI tract is the predominant site for extra nodal non-Hodgkin lymphomas. DLBCL is the most common histological subtype[8] with approximately 25% of non-Hodgkin's lymphoma (NHL) cases in the developed world[9]. Secondary GI involvement is commoner than primary GI lymphoma, the latter accounting for about 15% to 20% of GI lymphomas. The stomach is most commonly involved (75%), followed by small bowel (9%) and ileo-caecal region (7%). Furthermore, 6% have more than one GI site involved, and diffuse colonic involvement is seen in 1% of cases[10]. Studies have shown that the most common symptoms include abdominal pain, anorexia and weight loss[11], as well as nausea and vomiting, change in bowel habit, GI bleeding, intussusception and intestinal perforation[12].

The Dawson criteria are the classic tests for diagnosis of gastrointestinal Lymphoma[13]. They include:

- Absence of palpable adenopathy in clinical examination
- Absence of mediastinal lymphadenopathy in a chest x-ray
- Normal WBC differential count
- Disease confined to the intestine and adjacent nodes, without involvement of liver or spleen.

With the above non-specific picture, it proposes a diagnostic challenge. An accurate diagnosis is often only made after surgical exploration[14].

Treatment of gastrointestinal tract lymphomas is related to each patient's particular characteristics, tumour type and stage. Surgical resection and chemotherapy have been and remain the mainstays of treatment.

Radiation therapy historically had some role for local lesions of significant volume and for lesions which cannot be resected, but, particularly in the case of the small intestine, it has been abandoned due to frequent involvement of several segments and the risks of post-radiation enteritis. Biological management with rituximab has shown benefits, especially for diffuse B-cell lymphoma[15]. For DLBC, as in this case, chemotherapy is most frequently based on the CHOP scheme combination of cyclophosphamide, doxorubicin, vincristine and prednisone. When rituximab is added, this becomes the R-CHOP regimen. Rituximab is a genetically engineered chimeric monoclonal antibody that binds specifically to CD20 antigen, a phosphoprotein that is expressed in B lymphocytes[16,17].

Patient prognosis is related to factors that include age, histological subtype, stage at diagnosis and the presence or absence of systemic symptoms. Although the literature reports that the disease stage is the most important prognostic factor for survival, it has been observed that perforation at the onset of the disease is a deleterious factor which is clearly associated with early mortality during the course of treatment[18,19,20].

In this case report we did a surgical resection, which is to be followed by chemotherapy. In conclusion an accurate diagnosis, the evaluation of the extension of the disease in addition to presence /absence of co morbidities should be taken into consideration to decide the therapeutic protocol.

Conclusion :

This case highlights the fact that very advanced disease may present with non-specific and insidious symptoms which requires thorough investigations, if not explained by the commoner pathology. Our patient lacked the typical B-symptoms and GI red flag symptoms with a normal blood count and other blood investigations that do not preclude extensive lymphomatous gastrointestinal involvement despite the high disease burden.

Disclosure & Ethics Statement :

No conflict of interest disclosed by any author. Informed consent was obtained from the patient prior to inclusion of the photographs used.

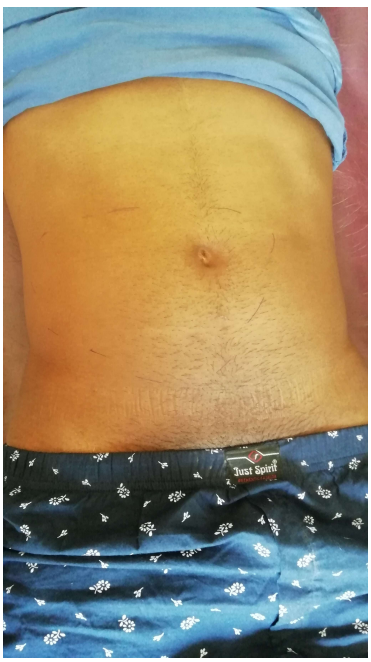


Figure 1 : Swelling on inspection (top view)

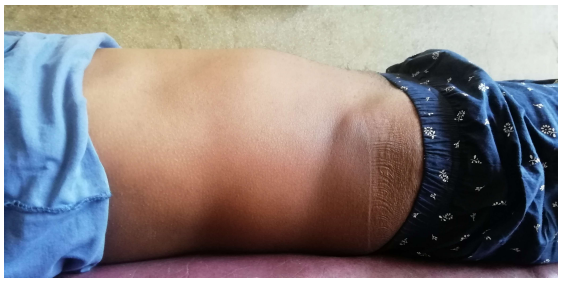


Figure 2 : Swelling on inspection (lateral view)

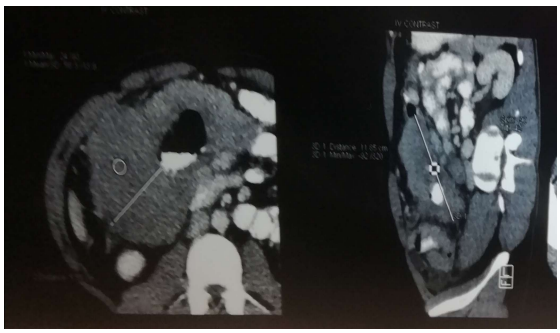


Figure 3 : CECT image of the homogenous mass of soft tissue density arising from small intestine

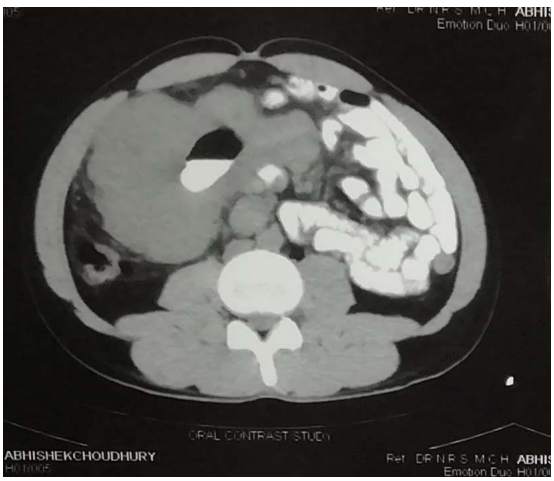


Figure 4 : CECT image showing a solitary mass with no intraluminal obstruction.

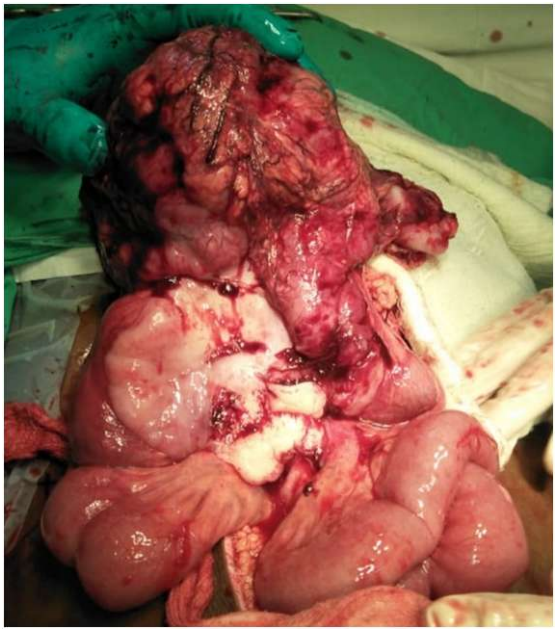


Figure 5 : Intraoperative image of the mass adherent to small gut

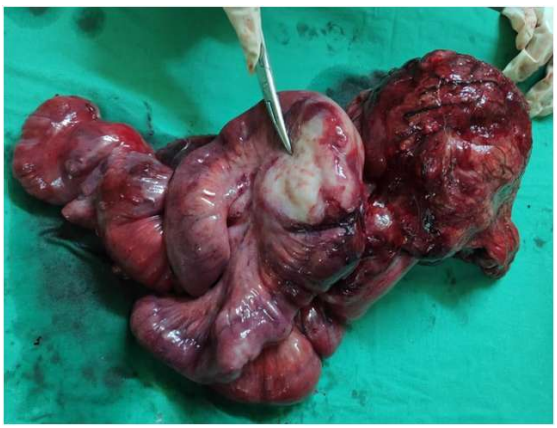


Figure 6 : Image of the specimen

References :

1. Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer statistics, 2000. CA Cancer J Clin 2000; 50: 7-33.
2. Rabkin CS, Devesa SS, Zahm SH, Gail MH. Increasing incidence of non-Hodgkin's lymphoma. Semin Hematol 1993; 30: 286-296.
3. Damore F, Brincker H, Grønbaek K, et al. Non-Hodgkins lymphoma of the gastrointestinal tract: a population-based analysis of incidence, geographic distribution, clinicopathologic presentation features, and prognosis. Danish Lymphoma Study Group. J Clin Oncol 1994; 12(8):1673-84.
4. Molina R, Jiménez A, López JL, et al. Linfoma T primario intestinal: a propósito de dos casos con revisión de la literatura. An Med Int (Madrid). 2002;19:457-9.
5. Vaquero L, Alvarado M, Arias L, et al. Linfoma intestinal de células T asociado a enteropatía y sin relación con enfermedadcelíaca. Gastroenterol Hepatol. 2012;35(1):17-21.
6. Egan LJ, Walsh SV, Stevens FM, Connolly CE, Egan EL, Mc carthy CF. Celiac-associated lymphoma. A single institution experience of 30 cases in the combination chemotherapy era. J Clin Gastroenterol 1995; 21: 123-129.
7. Pellisé M, Castells A. Tumores del intestinodelgado. En: Montoro M, Garcia JC. Gastroenterología y hepatología. Asociación Española de Gastroenterología. Madrid: Jarpyo Editores; 2012. p. 435-42.
8. Fleming JP, Smith K, Bennett R, et al. A case of primary gastrointestinal lymphoma presenting as colonic perforation. J Case Rep Images Surg 2017;3:29–34.
9. Morton LM, Wang SS, Devesa SS, Hartge P, Weisenburger DD, Linet MS. Lymphoma incidence patterns by WHO sub type in the United States, 1992-2001. Blood. 2006 Jan;107(1):265–76.
10. Koch P, del Valle F, Berdel WE, et al. Primary gastrointestinal non-Hodgkin's lymphoma: II. Combined surgical and conservative or conservative management only in localized gastric lymphoma--results of the prospective German Multicenter Study GIT NHL 01/92. J Clin Oncol 2001;19:3874–83.
11. Suresh B, Asati V, Lakshmaiah KC, et al. Primary gastrointestinal diffuse large B-cell lymphoma: A prospective study from South India. South Asian J Cancer 2019;8:57.
12. Tauro LF, Furtado HW, Aithala PS, et al. Primary lymphoma of the colon. Saudi J Gastroenterol 2009;15:279.
13. Dawson MP, Cornes JS, Morson BC. Primary malignant lymphoid tumours of the intestinal tract. Report of 37 cases with a study of factors influencing prognosis. Br J Surg. 1961;49:80-9.
14. Ramia JM, Sancho E, Lozano Ó, et al. Linfomaprimario de intestino delgado. Cir Esp. 2007;81(1):46-8.
15. Ghimire P, Wu GY, Zhu L. Primary gastrointestinal lymphoma. World J Gastroenterol. 2011;17(6):697-707.
16. Paz R, Herrera R. Linfoma intestinal. Caso clínico. Rev DiagImagem. 2008;3(1):52-4.
17. Grande C. Actualización del tratamiento del linfomadifuso de células grandes B. Cuadernos de Hematología. Hospital Universitario Doce de Octubre [internet]. 2011.
17. Campos Rojas A, Monterroso V, Regocez Z, et al. Linfomas del tracto gastrointestinal: reporte de 19 casos. Rev Costarricense Cien Med. 1994;15(1/2):3-14.
18. Albújar B, Diaz P, Tantaleán R. Linfomasgastrointestinalesprimarios:cuadroclínicopatológico y sobrevida. Rev Gastroenterol Perú. 1995;15(2):141-51.
20. Vaidya R, Habermann TM, Donohue JH, et al. Bowel perforation in intestinal lymphoma: incidence and clinical features. Ann Oncol. 2013;24:2439-43.

Review Article

Transoral Ultrasonic Surgery (TOUSS) : A New Field in Otolaryngology - Head & Neck Surgery

Dr. Shaoni Sanyal[1], Dr. Ranjan Raychowdhury[2]

Abstract :

Transoral ultrasonic surgery (TOUSS) is an endoscopic alternative to transoral robotic surgery (TORS). It was first described by Fernandez et al in 2014. TORS promised to revolutionize transoral surgery promising better visualisation, minimally invasive, precise, surgery. The limiting factor, however, is the cost of surgery using robotics.

TOUSS provides a more economically viable alternative to robotic surgery.

One drawback of TOUSS at present is the fact that the instrumentation is still designed for laparoscopic and thoracoscopic surgery and is therefore less ergonomic for transoral endoscopic surgery.

Keywords :

Ultrasonic Surgical Procedures, Robotics, Laser therapy, Ergonomics

Background :

Transoral ultrasonic surgery (TOUSS) is a new endoscopic alternative to transoral robotic surgery (TORS) for approaching pharyngeal and laryngeal pathology based on the ultrasonic scalpel as a resection tool.

Ultrasonic instruments consist of a piezoelectric transducer which transforms electrical pulses into mechanical energy. This is then transferred to the active component of the device in the form of longitudinal vibrations with a frequency of 22-55 kHz. The application of this mechanical energy to biological tissue causes protein denaturation due to the rupture of hydrogen bonds, thus causing low-temperature vascular dissection and coagulation. Due to these characteristics, ultrasonic technology is widely used both in open and endoscopic surgery[1]. It is commonly marketed under the brand names Harmonic (Ethicon), Thunderbeat (Olympus) and Ligasure (Covidien).

The ultrasonic scalpel is widely used in head and neck surgery, particularly in the oral cavity, oropharynx, and the neck[2,3]. However, the CO_2 laser is still the preferred instrument for benign and malignant lesions of the larynx and hypopharynx when approached transorally (Transoral Laser surgery or TOLS).

Over the last 15 years transoral robotic surgery (TORS) has demonstrated its feasibility, high rates of local control and good functional outcomes for lesions of oral cavity, oropharynx and laryngopharynx. The high costs of robotic surgery limit its widespread use, which is a particular drawback in our country.

TOUSS in the Literature :

Many papers have been published about the safety, utility and advantages of the ultrasonic scalpel. It has been used routinely in surgical settings such as laparoscopic surgery and open abdominal and thoracic procedures in the last two decades[1]. In head and neck surgery it has been widely used in openand minimally invasive thyroidectomy, glossectomy, tonsillectomy, laryngectomy and neck dissection[2].

[1]Senior Resident, [2]Professor, Department of ENT Head & Neck Surgery, RKMSP, VIMS, Kolkata

TOUSS was first described by Fernandez et al, who treated 11 consecutive patients with pharyngeal and supraglottic carcinomas between December 2013 and August 2014 in a tertiary centre in Spain. All tumours were resected transorally with a 35cm Thunderbeat TM (Ultrasonic scalpel). Exposure was achieved using GyrusTM FK-retractor and Olympus ENDOEYE Flex 5 mm 2D/10 mm 3D deflecting tip video laparoscopes. The mean setup time was 16 minutes (range 5–32 minutes). The average resection time was 70.9 minutes (range 8–150 minutes). The surgical margin was negative in ten patients (90.9 %)[4].

In a second paper, published in 2015 Fernandez et al documented the use of TOUSS for total laryngectomy (TL). Two patients, one with subglottic carcinoma and one salvage TL with partial pharyngectomy for a local relapse after chemoradiotherapy of a glottic carcinoma, underwent TOUSS assisted TL. Thetumours were completely removed with free surgical marginin both patients. The functional recovery was satisfactory interms of swallowing and speech[5].

In an earlier study, Shiotani et al used distending laryngoscope along with standard laparoscopic instruments for transoral resection of supraglottic and hypopharyngeal tumours in 30 patients. In 21 cases the 3-year disease-specific survival rate and the laryngeal preservation rate were each 95%. Normal food intake was possible in all patients[6].

Discussion :

Transoral approaches to the larynx and pharynx are, in general, less morbid than traditional open surgical procedures, with quicker recovery times and shorter hospital stay.

Traditional transoral surgery (eg tonsillectomy) is limited by anatomical hindrances to the surgeon's line of sight, such as the base of the tongue, the curvature of the oropharynx and the orientation of the hypopharynx and larynx with respect to the oral cavity. To overcome this problem various instruments, e.g. the Zeitel's distending laryngoscope and the Feyh-Kastenbauer retractor, have been designed. These allow access for a CO_2 laser mounted on an operating microscope, still limited by the physical necessity of the LASER working in a straight line.

TORS promised to revolutionize transoral surgery as the robotic systems allowed the use of an angled endoscopic camera; providing the surgeon with a magnified,"round the corner" view, along with a combined 570 degree movement of the robotic arms. The major advantages of transoral robotic surgery include minimally invasive, precise, surgery with oncological results which are comparable to open procedures in carefully selected cases[7]. The limiting factor, however, is the cost of surgery using robotics. The da Vinci system costs $ 1.4 million (Rs. 7 crores) with annual maintenance costs of around $ 100,000[8]. Although India is emerging as a hub for low-cost robotic surgery, procedures using the robot cost anywhere between Rs 4 to 5 lakhs. A traditional laparoscopic set, in comparison, costs Rs 9 lakhs to set up and the average cost of a laparoscopic procedure is much more affordable for the average Indian patient. It is true that Indian health insurance policies are beginning to cover robotic surgery, but, at the cost of higher premiums.

TOUSS provides a more economically viable alternative to robotic surgery. Training facilities for laparoscopic procedures and expertise are

already widely available across the country. This contrasts with robotic head and neck surgery where initial training is usually obtained abroad (notably in South Korea) followed by a mentorship period involving a foreign expert visiting the Indian centre. A search of the internet brings up details of around 20 Indian centres (both Government and Private) providing TORS. A similar search reveals that as of 21st May 2020 there are 542 medical colleges and 64 stand-alone post-graduate institutes in India recognised by the National Medical Commission, all equipped with laparoscopic surgical facilities.

One drawback of TOUSS at present is the fact that the instrumentation is still designed for laparoscopic and thoracoscopic surgery and is therefore less ergonomic for transoral endoscopic surgery.

Our experience :

So far two patients have undergone transoral surgery using the laparoscopic set in our Department : the first with a vallecular cyst and the second with a pedunculated tumour of the laryngopharynx. In both cases, the visualisation was far superior to the alternative traditional procedure, with a better outcome and shorter operative time.

Conclusion :

TOUSS is an exciting new approach to transoral surgery of the pharynx and larynx which is significantly cheaper than robotic transoral surgery. Well designed comparative studies are required to establish whether it provides equivalent surgical outcomes to both traditional and robotic surgery.

References :

1. Seehofer D, Mogl M, Boas-Knoop S, Unger J, Schirmeier A, Chopra S, Eurich D. Safety and efficacy of new integrated bipolar and ultrasonic scissors compared to conventional laparoscopic 5-mm sealing and cutting instruments. Surgical endoscopy. 2012 Sep;26(9):2541-9.
2. Metternich FU, Wenzel S, Sagowski C, Ja¨kel T, Koch U (2002) The ''Ultracision Harmonic Scalpel'' ultrasound activated scalpel. Initial results in surgery of the tongue and soft palate. HNO 50(8):733–738.
3. Salami A, Bavazzano M, Mora R, Dellepiane M. Harmonic scalpel in pharyngolaryngectomy with radical neck dissection. Journal of Otolaryngology--Head & Neck Surgery. 2008 Oct 1;37(5).
4. Fernández-Fernández MM, Montes-Jovellar L, Arias PL, Del Alamo PO. TransOral endoscopic UltraSonic Surgery (TOUSS): a preliminary report of a novel robotless alternative to TORS. European Archives of Oto-Rhino-Laryngology. 2015 Dec;272(12):3785-91
5. Fernández-Fernández MM, González LM, Calvo CR, Arias PP, Cabré FC, Del Álamo PO. Transoral ultrasonic total laryngectomy (TOUSS-TL) : description of a new endoscopic approach and report of two cases. European Archives of Oto-Rhino-Laryngology. 2016 Sep; 273(9):2689-96.
6. Shiotani A, Tomifuji M, Araki K, Yamashita T, Saito K. Videolaryngoscopic transoral en bloc resection of supraglottic and hypopharyngeal cancers using laparoscopic surgical instruments. Annals of Otology, Rhinology & Laryngology. 2010 Apr;119(4):225-32.
7. Roselló À, Albuquerque R, Roselló-Llabrés X, Marí-Roig A, Estrugo-Devesa A, López-López J. Transoral robotic surgery vs open surgery in head and neck cancer. A systematic review of the literature. Medicina Oral, Patología Oral y CirugíaBucal. 2020 Sep;25(5):e599.
8. Morgan JA, Thornton BA, Peacock JC, Hollingsworth KW, Smith CR, Oz MC, Argenziano M. Does robotic technology make minimally invasive cardiac surgery too expensive? A hospital cost analysis of robotic and conventional techniques. Journal of cardiac surgery. 2005 May;20(3):246-51.

Short Communication

An Evidence Based Summary of Pre-Hospital Care for Symptomatic COVID 19 Patients

Dr. Sumit Sengupta

Editor's note : *Given the severity of the second wave we are currently experiencing I am reproducing, with permission of the author, these helpful guidelines which may be of benefit to us all. As Dr. Sengupta rightly says, these are extraordinary time.*

This is a personal summary of the COVID situation (without going into nuances or details) with some references meant for non-specialists and some recommendations for various situations. They are based on ballpark figures, approximations and estimates and are therefore not written in stone and will change with time. Ordinarily these discussions are meant to be face to face with a specialist and tailored to specific situations in each patient, but these are extraordinary times.

If 100 patients get COVID-19 : 85 will settle with no treatment at all. 15 of these 100 will develop SpO2 (oxygen saturation) levels of 93 and below[1] (usually between days 8 to 12)[2] and should be hospitalized.

10 of these 15 will settle with nasal oxygen up to 6 litres/minute, steroids, prophylactic anticoagulants and occasionally Tocilizumab. Remdesivir may be given at this stage but it does not decrease deaths. Convalescent plasma has not been found to be beneficia [3,4,5,6,7].

The other 5 will require critical care and escalation of respiratory support with non-invasive ventilation /CPAP or HFNC (High flow nasal cannula) oxygen. 3 out of 5 will settle down and be discharged. 2 will need to be intubated and invasively ventilated. 1 of these 2 will survive.

Even under ideal conditions 1 of 100 symptomatic covid patients may die[8]. If hospital beds are not available all 5 who get critically ill and perhaps half of those who become hypoxic will die – increasing deaths to about 10 in 100.

Asymptomatic patients in general do not get hypoxic or die. The infection fatality rate (including both symptomatic and asymptomatic patients) is estimated at 0.3% retrospectively looking at positive serology[9,10].

Prehospital Care :

There is no proven treatment for non-hospitalized patients and in particular HCQS[11,12,13], Azithromycin[14], Doxycycline[15], Vitamin C[16], Vitamin D[17], Zinc[16] and Favipiravir[18,19] do not work and is not recommended. Ivermectin is not recommended because of poor quality data[3,6] and trials showing lack of efficacy[20].

Colchicine[21] and inhaled Budesonide[22,23] have some data as prehospital treatment, but their efficacy is still debated. If used Colchicine is given 0.5mg twice daily for 3 days, then once daily up to 14 days (Colchicine cannot be used in kidney or liver disease and pregnancy). Budesonide has been used via inhaler 800 mcg twice daily. There is a signal of reduced hospital admissions with these medications which need to be confirmed by more robust trials.

Consultant Pulmonologist, AMRI Salt Lake, Kolkata

Prehospital Care in Patients Who Should be Hospitalized :

With the onset of hypoxia (defined as SpO2 <94) the patient should be in hospital but may not find a bed. In these extenuating circumstances it is reasonable to start treatment with Dexamethasone 6 mg (OR Methylprednisolone 32 mg OR Prednisolone 40 mg) once daily after breakfast for 10 days along with prophylactic anticoagulation (Either Rivaroxaban 10 mg once daily OR Apixaban 2.5 mg twice daily orally). The patient and their carers must be warned that a substantial proportion of such patients will deteriorate and likely die if not treated in hospital. Please note that starting steroids before the patient becomes hypoxic is likely to HARM the patient.

References :

1. Guan W, Ni Z, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med.* 2020;382(18):1708-1720. doi:10.1056/NEJMoa2002032.
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet.* 2020;395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5.
3. WHO. Therapeutics and COVID-19: living guideline. Published 2021. Accessed April 14, 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.1
4. NIH. Therapeutic Management. COVID-19 Treatment Guidelines. Published 2021. Accessed April 25, 2021. https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/
5. NICE. Overview | COVID-19 rapid guideline: managing COVID-19|Guidance|NICE. Published 2021. Accessed April 18, 2021. https://www.nice.org.uk/guidance/NG191.
6. Adarsh Bhimraj A, Morgan RL, Hirsch Shumaker A, et al. *Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19.;* 2021. Accessed April 14, 2021. www.idsociety.org/COVID19guidelines.
7. Chalmers JD, Crichton ML, Goeminne PC, et al. Management of hospitalised adults with coronavirus disease 2019 (COVID-19): a European Respiratory Society living guideline. *Eur Respir J.* 2021;57(4). doi:10.1183/13993003.00048-2021
8. Wilson N, Kvalsvig A, Barnard LT, Baker MG. Case-Fatality Risk Estimates for COVID-19 Calculated by Using a Lag Time for Fatality. Emerg Infect Dis J - CDC. 2020;Volume 26 (Number 6). doi:10.3201/eid2606.200320.
9. Levin AT, Hanage WP, Owusu-Boaitey N, Cochran KB, Walsh SP, Meyerowitz-Katz G. Assessing the age specificity of infection fatality rates for COVID-19: systematic review, meta-analysis, and public policy implications. *Eur J Epidemiol.* 2020;35(12):1123-1138. doi:10.1007/s10654-020-00698-1.
10. Ioannidis JPA. Infection fatality rate of COVID-19 inferred from seroprevalence data. *Bull World Health Organ.* 2021;99(1):19-33F. doi:10.2471/BLT.20.265892.
11. Skipper CP, Pastick KA, Engen NW, et al. Hydroxychloroquine in Nonhospitalized Adults With Early COVID-19. *Ann Intern Med.* 2020;173(8):623-631. doi:10.7326/M20-4207.
12. Omrani AS, Pathan SA, Thomas SA, et al. Randomized double-blinded placebo-controlled trial of hydroxychloroquine with or without azithromycin for virologic cure of non-severe Covid-19. *EClinicalMedicine.* 2020;29. doi:10.1016/j.eclinm.2020.100645.
13. Mitjà O, Corbacho-Monné M, Ubals M, et al. Hydroxychloroquine for Early Treatment of Adults With Mild Coronavirus Disease 2019: A Randomized, Controlled Trial. *Clin Infect Dis.* 2020;(ciaa1009). doi:10.1093/cid/ciaa1009.
14. Butler CC, Dorward J, Yu L-M, et al. Azithromycin for community treatment of suspected COVID-19 in people at increased risk of an adverse clinical course in the UK (PRINCIPLE): a randomised, controlled,

open-label, adaptive platform trial. The Lancet. 2021;397(10279):1063-1074. doi:10.1016/S0140-6736(21)00461-X.

15. Study finds azithromycin and doxycycline ineffective for Covid-19. Accessed April 25, 2021. https://www.clinicaltrialsarena. com/news/uk-study-azithromycin-doxycycline.
16. Thomas S, Patel D, Bittel B, et al. Effect of High-Dose Zinc and Ascorbic Acid Supplementation vs Usual Care on Symptom Length and Reduction Among Ambulatory Patients With SARS-CoV-2 Infection: The COVID A to Z Randomized Clinical Trial. JAMA Netw Open. 2021;4(2):e210369. doi:10.1001/jamanetworkopen.2021.0369.
17. Murai IH, Fernandes AL, Sales LP, et al. Effect of a Single High Dose of Vitamin D3 on Hospital Length of Stay in Patients With Moderate to Severe COVID-19: A Randomized Clinical Trial. *JAMA.* 2021;325(11):1053-1060. doi:10.1001/jama.2020.26848.
18. Dabbous HM, El-Sayed MH, El Assal G, et al. Safety and efficacy of favipiravir versus hydroxychloroquine in management of COVID-19: A randomised controlled trial. *Sci Rep.* 2021;11(1):7282. doi:10.1038/s41598-021-85227-0.
19. Ueda M, Tanimoto T, Murayama A, Ozaki A, Kami M. Japan's Drug Regulation During the COVID-19 Pandemic: Lessons From a Case Study of Favipiravir. *Clin Pharmacol* Ther. Published online April 21, 2021. doi:10.1002/cpt.2251.
20. López-Medina E, López P, Hurtado IC, et al. Effect of Ivermectin on Time to Resolution of Symptoms Among Adults With Mild COVID-19: A Randomized Clinical Trial. *JAMA.* 2021;325(14):1426-1435. doi:10.1001/jama.2021.3071.
21. Tardif J-C, Bouabdallaoui N, L'Allier PL, et al. Efficacy of Colchicine in Non-Hospitalized Patients with COVID-19. *medRxiv.* Published online January 27, 2021:2021.01.26.21250494. doi:10.1101/2021.01.26.21250494.
22. Group PC, Yu L-M, Bafadhel M, et al. Inhaled budesonide for COVID-19 in people at higher risk of adverse outcomes in the community: interim analyses from the PRINCIPLE trial. *medRxiv.* Published online April 12, 2021:2021.04.10.21254672. doi:10.1101/2021.04.10.21254672.
23. Ramakrishnan S, Nicolau DV, Langford B, et al. Inhaled budesonide in the treatment of early COVID-19 (STOIC): a phase 2, open-label, randomised controlled trial. *Lancet Respir Med.* 2021;0(0). doi:10.1016/S2213-2600(21)00160-0.