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ASSAM JOURNAL OF INTERNAL MEDICINE

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CONTENTS

CONTENTS

Editorial

SEPSIS in ICU

Brajendra Lahkar*

"Sepsis is a life threatening organ dysfunction caused by dysregulated host response to infection" which affect more than 30 million people worldwide and approximately 6 million deaths every year.[1] In a large international audit where data of 10069 patients from 730 ICUs from all over world were included, sepsis was present in 29.5% of patients including those 18% who had sepsis on admission. More importantly, 11.6% of those who did not have sepsis on admission to ICU developed sepsis during hospital stay.[2] Mortality rates in patient hospitalized with sepsis are in the range of 25 to 50%. Because of this high risk of death, it is important to detect sepsis accurately early enough to save lives. Once sepsis and septic shock is detected, it should be managed in intensive care unit equipped with dedicated team who are expert in managing them.

Detection of sepsis many a time becomes challenging. The Third International Consensus Definitions for Sepsis and Septic Shock guidelines (Sepsis-3) in 2016 has changed the focus from Systemic Inflammatory Response Syndrome (SIRS) to Sequential Organ Failure Assessment (SOFA) score. Emphasis has been given to organ failure. According to Sepsis-3 sepsis definition criteria, patients should have a suspected or documented infection and an acute increase of atleast 2 SOFA points from baseline. If patients meet the sepsis criteria and require vasopressor therapy to meet the mean arterial pressure (MAP) of atleast 65 mmHg and their lactate concentration is > 2 mmol/L, despite adequate fluid resuscitation, their condition is classified as septic shock.[3] To augment detection of sepsis in noncritical area such as ward it is suggested that we should use more simplified assessment score and "Quick SOFA" has been validated in these situations. Quick sequential Organ failure assessment score (qSOFA) has 3 components (4): Respiratory rate ≥22/minute, Altered mentation and Systolic blood pressure ≤100 mmHg. Presence of more than two components predicts bad outcome and should be managed in an ICU or in monitored area.

Once sepsis and septic shock has been detected in ICU, it is important to detect the source of sepsis and type of causative organism too. The most common source of sepsis is respiratory tract (67.4%) followed by abdomen (21.8%), blood stream infection, skin and soft tissue infection, urinary tract infection, catheter related infection and others.[2] If done correctly a good blood culture becomes positive in half of patients and can lead to targeted therapy and may help in deciding for de-escalation of therapy. Globally, Gram negative sepsis is more common than Gram positive sepsis but it depends upon the part of world where it occurs. Sepsis caused by some of most difficult to treat organisms such as *Acinetobacter* species, *Pseudomonus* species, *Klebsiella* species, *Enterobacter* species, *E.coli*, *Proteus*, *Staphylococcus* species including MRSA happens in ICU and most often they are multidrug resistant. Besides these

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organisms, sepsis caused by fungus and other organisms such as virus and protozoa are also increasing. It has also been observed that chance of acquiring sepsis with MDR pathogen is much higher if one develops sepsis inside ICU than in other areas. It is indeed very important to isolate organism as early as possible to start definitive therapy early and save lives. Newer development in this field is in the form of Polymerase Chain Reaction (PCR) based assay which can detect organisms in 6 to 8 hours as compared to conventional culture which take 2 to 3 days. Matrix-Assisted Laser desorption Ionization-time of flight(MULDI-TOF) is a mass spectrometry tool that allows rapid and accurate identification of genus and species for a wide range of Gram-negative and Gram positive bacteria as soon as an organism is available in a pure culture on solid media.

Treatment of sepsis in ICU is broadly focused on three aspects**: Hemodynamic stabilization, Infection control** and **modulation of the sepsis response and Supportive therapy** and well-organized teams are required to deliver this simultaneously in a planned manner.

Hemodynamic stabilization should be achieved using fluids and vasopressor agents early. Surviving Sepsis Guideline (SSC) 2016 recommends that after stabilizing airway and ventilation, fluid in the form of Crystalloid (Ringer's lactate or Normal saline) should be started at 30 ml/kg body weight if hypotension and or hypo perfusion is evident.[5] Among the crystalloids, newer evidences are suggesting that balanced crystalloid causes less Acute kidney injury than with normal saline when used as resuscitative fluid in patients without relative contraindications such as traumatic brain injury and hyperkalemia.[6] The debate over which one of crystalloid is better is not over yet. Hopefully the ongoing study "Plus" will give some concrete evidence whether balanced crystalloid Plasma-Lyte A is better than normal saline in reducing 90-day mortality in critically ill patients.

In patients with septic shock requiring vasopressors, a targeted MAP of 65 mm Hg within the first hour is recommended.[7] Norepinephrine is the recommended first-choice vasopressor in septic shock. If MAP is not maintained at 65 mm Hg or greater with norepinephrine alone or if the norepinephrine dose needs to be decreased, either vasopressin (up to 0.03 unit/minute) or epinephrine can be added to norepinephrine.[5] Dopamine can be considered as an alternative vasopressor agent to norepinephrine only in highly selected patients (e.g. patients with low risk of tachyarrhythmias and absolute or relative bradycardia). **Angiotensin II** has sparked interest as vasoactive agent in distributive or septic shock. Studies have suggested that patients who develop AKI requiring Renal Replacement Therapy in the setting of vasodilatory shock will benefit from angiotensin II.[8] ***Intravenous hydrocortisone*** (200 mg/day) can be considered in patients who have not achieved hemodynamic stability with fluid resuscitation plus vasopressors.[5]

Hemodynamic stability should be assessed during resuscitation and during fluid challenge. Dynamic parameters such as Passive leg raising (PLR) and Stroke volume variation are better indicators than Static parameters such as Central venous pressure monitoring. Lung ultrasonography, Inferior vana cava collapsibility assessment by USG and echocardiography also are useful tools to assess volume status. The current SSC guidelines recommend normalizing lactate as a resuscitation goal and parameters such as central venous pressure (CVP) and Scvo2 guide therapy are no longer recommended. Now Microcirculation-targeted therapies, where changes in microcirculation during shock state and during resuscitation have been monitored, are explored to make it a tool to guide therapy during resuscitation.

Infection control is the most definitive therapy for sepsis and every hour delay in delivering appropriate antibiotic is associated with

increasing mortality by 7.6%.[9] For optimal antimicrobial dosing strategies, pharmacokinetic and pharmacodynamic principles and specific drug properties should be considered. Empiric therapy with one or more broad spectrum antibiotic to cover all likely pathogen is recommended. In selecting a drug it's always preferable to follow one's own antibiotic policy which is again based on own drug sensitivity pattern data. In situations where multi drug resistant organisms are possible, combinations of antibiotics are justified. Before starting antibiotic it is important, to send blood samples for culture if possible. This will give an excellent opportunity to confirm the organism and to deescalate antibiotic therapy when reports are back. Though diagnostic value of **Procalcitonin** in sepsis is doubtful, its use to deescalate therapy has been well established. One should always look for source of sepsis and must plan for source control early in the course of sepsis. Any infectious source such as infected line and intra-abdominal abscess ets should be removed urgently.

Supportive therapy in sepsis and septic shock includes **sedation and analgesia** and non-benzodiazepines are preferred agents as sedatives in sepsis. Dexmeditomidine is one such agent which is being used more and more due to its ability to induce controlled sedation. **Enteral nutrition** should be considered early as soon as patient is hemodynamically stable. ASPEN guideline recommends enteral feeding early within 24 to 48 hours. Parenteral nutrition is only considered if enteral feeding is not feasible within 7 days. **Venous thromboembolism (VTE) prophylaxis** should be considered in all septic and septic shock patients unless contraindicated.[5] Low molecular weight heparin (LMWH) is preferred over unfractionated heparin unless it is contraindicated. To prevent stress ulcer in septic and septic shock patients **stress ulcer prophylaxis** should be offered to these patients. Pantoprazole has been shown to marginally reduce bleeding episodes but incidence of ventilator associated pneumonia increased in the group treated with pantoprazole.[10] In patients with shock and or ARDS **Ventilatory support** should be initiated as per ARDSnet guideline where lung protective ventilation strategy with low tidal volume, setting a target to keep driving pressure below 15mmHg and actively considering prone ventilation early in refractory hypoxaemia are hallmarks. **Glucose control** to keep blood sugar level around 110 to 180 is achieved by using appropriate insulin therapy whenever needed. In patients with acute kidney injury needing **renal replacement therapy** both continuous renal replacement therapy (CRRT) and intermittent hemodialysis (IHD) including sustained low efficiency dialysis (SLED) in continuous mode are effective. CRRT may be preferred in hemodynamically unstable patients. There are no effective drugs currently available with possible exception of corticosteroids in septic shock **to modulate sepsis response**. But there are few promising therapies which may help in sepsis response. One of the novel therapy which include **Vitamin C** (1.6gm 6 hours for 4 days), **Hydrocortisone** (50mg 6 hours for 7 days and then tapered over 3 days) and **Thiamine** (200mg twice daily for 4 days) has shown to reduce mortality (8.5% in intervention group as compared to 40.4% in control group).[11] Another molecule which has generated lots of discussion is beta-blocker. May consider using **â-blockers** in patients with septic shock with tachycardia and high cardiac output. It is yet to be an acceptable therapy in sepsis. Blood purification in septic shock includes **High volume hemofiltration** adsorption technique like **Cytosorb cartridge**s. These methods are still not proven or recommended to be used generally. **Transfusion** of packed RBC is considered if Hb% is <7gm%. Erythropoietin is not recommended. FFP is not indicated unless there is bleeding episodes along with coagulation abnormalities in septic shock. In septic shock associated with lactic acidosis, **bicarbonate therapy** is not indicated unless pH is <7.15.[5]

Sepsis is a heterogeneous syndrome and identification of distinct clinical phenotypes may allow more specific therapy and improve outcome. Four distinct phenotypes have been identified in a recently published study[12] : **Alpha** phenotype is the most common and included patients with need for lowest doses of vasopressors. Mortality was 5%. **Beta** phenotype patients are older, with more chronic illness and renal dysfunctions. Mortality was 13%. **Gamma** phenotype patients had more pulmonary involvement. Mortality was 24%. **Delta** phenotype patients had more Liver dysfunctions and septic shock. Mortality was 40%. This phenotyping will help in planning targeted therapy for each group.

Managing Sepsis in ICU is a challenging task for all intensivist and as there is lot of heterogeneous factors including host defense mechanism, every individual patient with sepsis and septic shock demands detailed examination and custom made therapy which may be unique for that particular patient. It is also important to know that in resource poor situations where sepsis is believed to be more prevalent recommendations and guidelines are slightly different to adapt to such situation so that septic patient gets adequate treatment even in most challenging situations.[13]

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Original Article

Microbial pofile of catheter related sepsis in ICU

A Tarat*, R Bhattacharyya**, S Dey***, R Kumar****

ABSTRACT

45patients admitted in central ICU Assam Medical College, on ventilation with central line catheter and urinary catheter were analysed. Blood culture and tracheal culture were sent for microbiological profile study. The sample collection was done taking strict antiseptic precaution. Daily monitoring was done for any changes in vital, local erythema, fever and any change in routine blood study. Tracheal aspirate was sent when the colour was purulent and urinary sample was also sent routinely after 72 hours. Patient received antibiotic as per protocol in ICU. *Acinetobacter baumannii, Klebsiella pneumoniae*, MRSA and few cases of *Pseudomonas aeruginosa* predominated in all type of infection.

Key words : *Catheter , central line- urinary, tracheal aspirate, blood culture- microbiological study.*

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INTRODUCTION :

Sepsis is the most frequent cause of admission to an intensive care unit (ICU) as well as the most common cause of death in ICU.[1] The Global Burden of Disease described infection as the cause of death of more than 10 million people per year worldwide.[2] The purpose of this study is to elucidate the pattern of organism colonising some of the established routes of infection, their microbiological profile and drug culture and sensitivity. For the purpose of standardisation the following CDC guidelines were adhered amongst all patients admitted in CICU: Guidelines for prevention of catheter – associated urinary tract infections 2009[3] and Guidelines for the prevention of intravascular catheter- related infections, 2011.[4]

MATERIAL AND METHOD :

45 cases of different ages and sexes were included for the study. All patients were intubated and mechanically ventilated more than 96 hours to 30 days. Samples of urine, central catheter line tip, tracheal aspirate and blood for culture was taken for study. All central line was inserted in Central ICU. No patients in the study had any catheter or any indwelling line given outside at the time of admission in Central ICU. Central line catheter site was covered with transparent antiseptic dressing (tegaderm). Daily monitoring was done for any change in vitals (BP, pulse rate, temperature, respiratory rate), local erythema and recorded. Urinary catheter routine culture was sent at minimum 3 days duration or earlier if the colour of urine was hazy. Tracheal cultures were taken after minimum 48 hrs of ventilation or when the colour of the sputum was purulent. Blood cultures were sent routinely to the Microbiology Department for routine culture and sensitivity. All culture were taken and sent aseptically. Microbiology Department had closed monitoring of sample collected with detailed history, antibiotic already patient was getting noted in the sample list copy to Microbiology Department. Microbiological reports coming after 72 to 96 hours were analysed. Statistical plotting was done

All patients were started antibiotic as per protocol in the Central ICU.

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RESULTS:

The pattern of organism in all 45 cases was compared and statistical analysis was done.

Detailed underneath are the results of the study in our Central ICU.

1. Blood C/S Routine:

32 out of 45 cases showed blood culture positivity. Highest number of patients was infected with *Klebsiella pneumoniae* (27%), followed by Methicillin resistant CONS (16%), MRSA (11%), Citrobacter (9%), Yeast(4%) and *Spingomonas paucimobilis* (4%).

The Gram stain pattern in 29 bacterial infections was 41% Gram positive and 59% Gram negative.

Figure 1

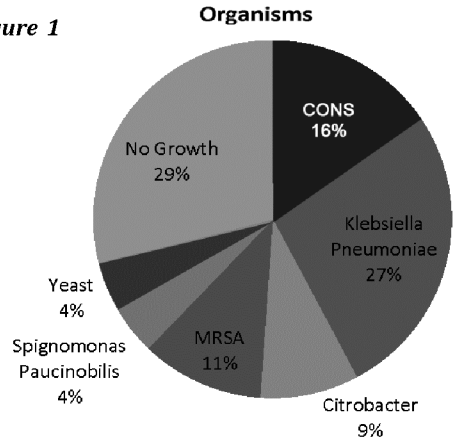
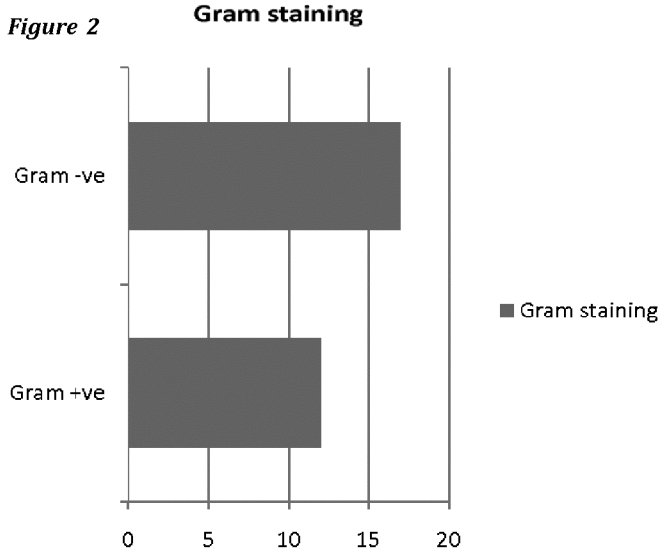


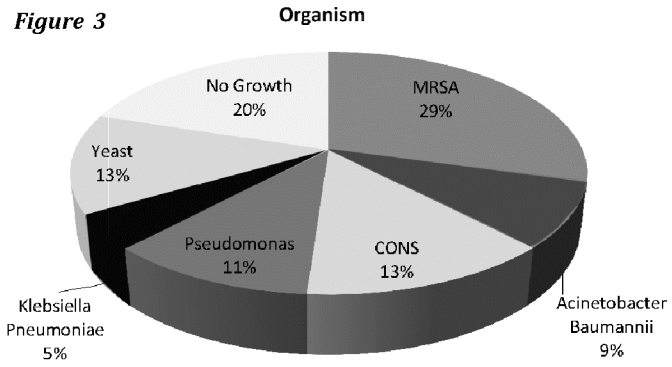
Figure 2



2. Central line tip C/S:

Catheter tip infection was positive earliest from 4th day on onwards. 32 out of 45 patients had growth on culture of central line tip. Highest number of patients were infected with MRSA (27%) followed by CONS and Yeast 12 % each, *Pseudomonas* 10% , *Acinetobacter baumannii* 8% and *Klebsiella pneumonia* 4%. Gram staining was done in 30 bacterial causes of colonisation and the results were: Gram positive 64% and Gram negative 36%. It is interesting to note that in 4 cases tip culture showed growth of more than one microbial flora, yeast being common in all.

Figure 3



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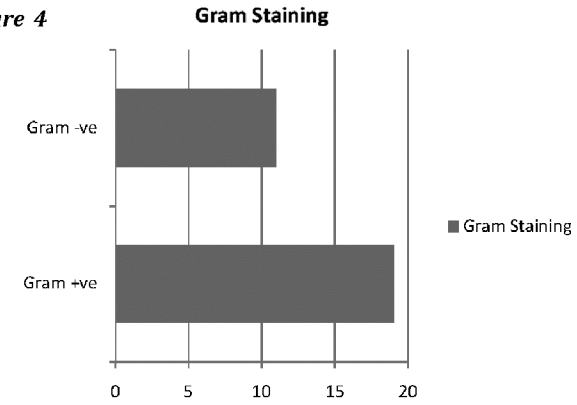


3. Tracheal aspirate C/S:

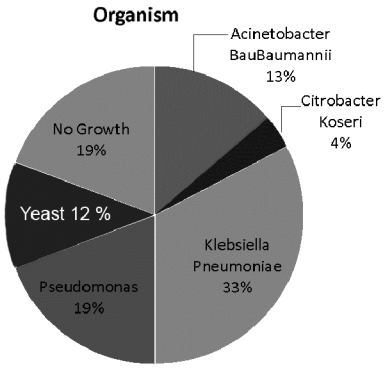
In case of tracheal aspirate culture 10 cases showed double infection, with yeast being common in 3 of the cases. [Figure 5] [Figure 6]

4. Urine C/S:

The growth in urine culture was predominated by gram negative organism (59%) followed by fungus (21%). Rest of the cases were sterile.

[Figure 7] [Figure 8]

Figure 5



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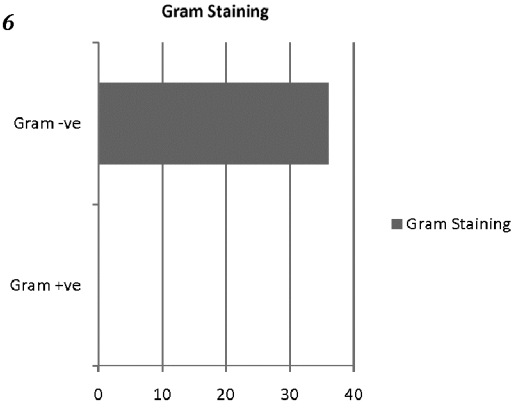

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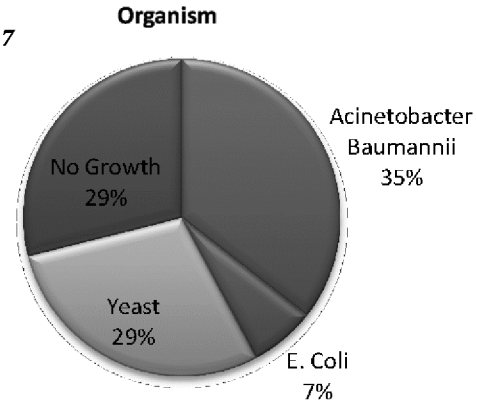

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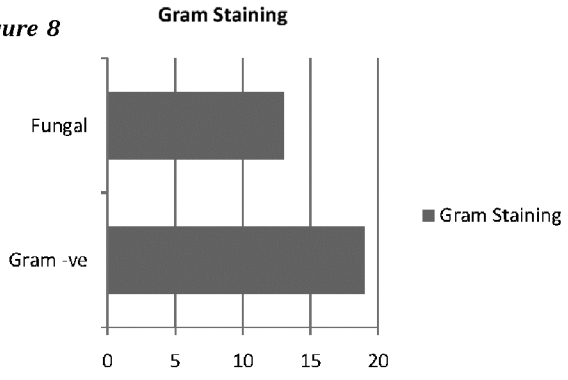
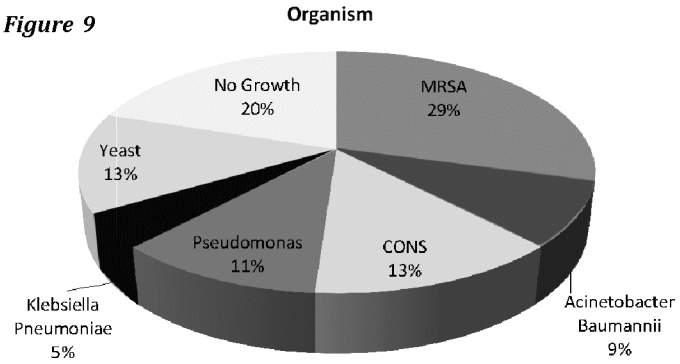


Growth profile:

When compared as a whole, out of total 45 cases studied, there was no growth seen in 5 of them (equivalent to 11.11% of cases) in any of the cultures (blood, central line tip, urine and tracheal aspirate).

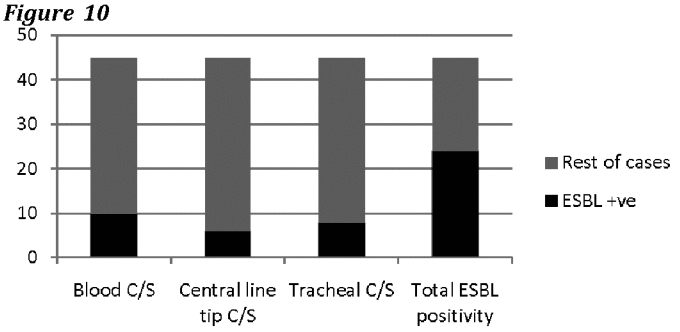
Figure 9



5. Microbial analysis:

Bacteria showing ESBL positivity: *Klebsiella pneumoniae* 22(92%) and *Citrobacter* species 2(8%).

Figure 10



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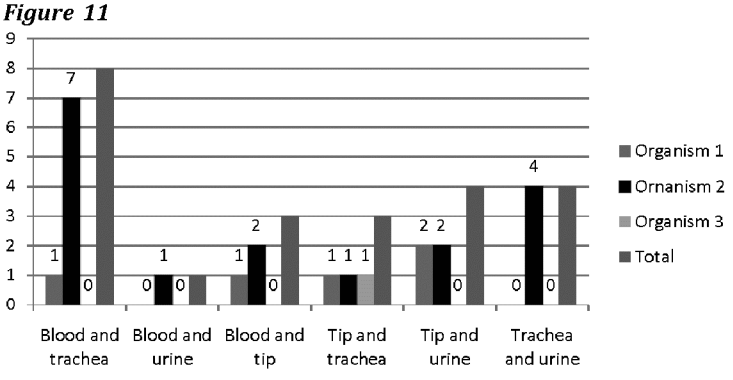

6. Comparative analysis of different cultures

In Blood and tracheal aspirate culture yeast was common in one case and *Klebsiella pneumoniae* in seven cases. In blood and urine culture yeast was the common organism in one case. In blood and catheter tip culture *Klebsiella pneumoniae* was common in one case and MRSA in two cases. In case of central line catheter tip and tracheal aspirate culture yeast, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* were common in one case each. In case of central line tip and urine culture yeast and *Acinetobacter baumannii* were common in two cases each. In case of tracheal aspirate and urine culture *Acinetobacter baumannii* was common in four cases.

7. Consolidated antibiotic sensitivity picture as per different culture and sensitivity results:

(A) Blood:

1. CONS: Cefoxitin, cotrimoxazole, linezolid, vancomycin >>Ciprofloxacin, linezolid.

2. *Klebsiella pneumoniae*: ESBL+ve: Imipenem, tigecycline, amikacin, gentamicin. ESBL-ve: colistin, tigecycline.

3. *Citrobacter:* Amikacin, meropenem, imipenem, tigecycline.

4. MRSA: Linezolid, tetracycline, ticoplanin, cotrimoxazole, erythromycin.

5. *Spingomonas paucimobilis*: High level gentamicin, tetracycline, aztreonam, tobramycin, polymyxin-B, ciprofloxacin, netilmycin, imipenem.

6. *Acinetobacter baumannii*: Linezolid, meropenem, tigecycline.

(B). Endo tracheal tube:

1. *Acinetobacter baumannii*: Tigecycline, meropenem >> levofloxacin, ampicillin sulbactum, piperacillin tazobactum.

2. *Klebsiella pneumoniae*: ESBL +ve: Tigecycline, colistin. ESBL –ve: Meropenem, tigecycline, tetracycline>> ampicillin sulbactum.

3. *Klebsiella oxytoca*: Meropenem, ciprofloxacin.

4. *Pseudomonas aeruginosa*: Colistin, imipenem, meropenem ciprofloxacin, aztreonam, polymyxin-B>> ceftazidime, meropenem, tigecycline, piperacillin tazobactum.

8. (C) Central line:

1. MRSA: Linezolid, cotrimoxazole, vancomycin, tetracycline>> ciprofloxacin, erythromycin.

2. *Acinetobacter baumannii*: Tigecycline >> imipenem, aztreonam.

3. CONS: Cefoxitin, linezolid, clindamycin, tetracycline, ticoplanin.

4. *Klebsiella pneumoniae*: Tigecycline >> meropenem.

5. *Pseudomonas aeruginosa*: aztreonam, polymyxin-B.

(D). Overall:

1. *Acinetobacter baumannii*: Meropenem, Tigecycline.

2. *Klebsiella pneumoniae*: ESBL +ve: Tigecycline, imipenem, colistin.
ESBL –ve: Tigecycline, colistin, meropenem.

3. *Klebsiella oxytoca*: Meropenem.

4. *Pseudomonas aeruginosa*: Tracheal: Colistin, Imipenem, meropenem.
Overall: Aztreonam, polymyxin-B.

5. CONS: Cefoxitim, linezolid.
MRSA: Linezolid, tetracycline.

As per CLSI 2017, no disk diffusion interpretive criteria available for colistin; only MIC detection is possible for detecting susceptibility profile of colistin.[5]

DISCUSSION :

Out of 45 cases, routine Blood culture showed growth for 32 patients (71%) and same in case gram stain, gram positivity was in 12 patients (37.5%) and negativity in 17 patients (53%). When same was compared with urine culture gram negativity was found in 19 patients (59%), no gram positive growth was seen in urine culture and interestingly fungal growth was seen in 13 patients out of 32 (21%). This varying pattern of the

organism in gram stain commonly seen in *E. coli*[6] but in our status it was found to *Acinetobacter baummannii*. The contamination of the blood was not from urosepsis but rather identified to be different species. When compared between blood culture and catheter tip culture it was found to be positive for the same organism in two cases, one belong to *Klebsiella pneumoniae* and one belong to MRSA. As the blood culture was done before the central catheter tip culture so the catheter tip was not responsible for organism present in blood culture in remaining cases which may be independent to the catheter tip. All cases were ventilated for more than 48 hours with disposable sterile circuit and HME filter. In case of tracheal aspirate culture 10 cases showed double infection. Not a single case was found to be gram positive. The pattern of organism in tracheal culture was dominant by *Klebsiella pneumoniae* 17(33%) versus *Pseudomonas aeruginosa* 10(19%). Here we can presume that in spite of the precautions of sterile circuit and filter there is every chance of growth of organism like *Klebsiella* and *Pseudomonas*. The growth of organisms in tracheal culture which did not reveal signs of sepsis doesn't require use of antibiotics. This should be taken as colonisation of organism rather than pathogenesis of the organism (colony count in urine culture and tracheal aspirate culture > 10^5CFU/ml and >15 colonies in case of catheter tip culture)

The two positive cases is sample collection for catheter tip and blood culture during the same period. The number of 7 positive cases (16%) of CONS is possibly due to the contamination of the skin from the loss of integrity of the antibacterial cap which was replaced by normal cannula cap. It may also be due to catheter lying directly in contact with the skin though a tegaderm cover was given after proper anti septic care. Otherwise, it may be due to poor collection of the samples from the catheter tip. The contamination in tracheal culture did not show any CONS because there is no chance for contamination from skin. The prevalence of organism in our ICU is mostly Gram –ve in Blood, Tracheal and urinary culture and Gram +ve in central line tip culture. With regard to ESBL positivity when all cultures are considered, it was dominated by *Klebsiella pneumoniae* in our set up (92% of all positive cases) followed by Citrobacter species. Fungal strain showed positivity in urinary culture. Urinary culture shows 29 % growth of yeast which could have been prevented by daily dressing change at the meatus level with betadine solution soaked gauge. While considering antibiotic sensitivity most of the supplied antibiotics were in the higher generation. We couldn't try the lower generation antibiotic due to the non availability of antibiotic basket.

Worldwide there has been a change in trend within past 25 years with gram-positive bacteria being the most common organism implicated in sepsis at present.[6] There has also been an increase in the fungal cause of sepsis over these years.[7]

In case of respiratory tract infection gram negative organism continue to be the most dominant organism in the ICU's worldwide with multidrug-resistant organisms, including *Pseudomonas aeruginosa, Acinetobacter baumannii*, and extended-spectrum â-lactamase (ESBL)–producing or carbapenemase-producing Enterobacteriaceae most commonly reported.[8]

In case of hospital acquired UTI, gram negative organisms predominate the microbial profile with *E. coli* followed by *P. aeruginosa*, *Klebsiella* species, *Enterobacter* species and *A. baumannii* being the most common organisms in decreasing order.[9]

In case of central line associated infections worldwide data suggest a predominance of gram negative organisms with *Staphylococcus* (*S. aureus* and CONS), *Enterococci* and fungi being the most predominant organisms.[10]

Thus concluding our data with respect to worldwide, culture and sensitivity pattern of organism were similar in case of tracheal aspirate and urine except catheter tip culture which shows opposite growth of gram positive bacteria and

blood culture which also showed opposite growth of gram negative bacteria.[7,8,9,10]

CONCLUSION :

Pertinent with the high rise of sepsis in ICU, evidence based information with regard to measures to prevent catheter associated infection should be strongly adhered to.[11] Other measures like use of catheter impregnated with antiseptic or antibiotic or both[12] or use of chlorhexidine impregnated dressing[13]may be used whenever possible, availability and more importantly cost effectiveness being the major issue in our set up. Available data do not support the use of antibiotic impregnated or silver coated urinary catheter for prevention of urosepsis as yet. Another major pitfall causing immense difficulty in treating patients in our set up is the erratic supply of antibiotics in the range from lower to higher generation.

We took total care of sepsis bundle for collecting sample from urinary, blood, catheter tip etc. Routine betadine soaked solution is advisable in all urinary catheter which is economical and with a good outcome

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Original Article

WHOQOL-BREF as a tool for Evaluation of Quality of Life and its predictors in Type-2 Diabetics: A cross-sectional study in Visakhapatnam, Andhra Pradesh

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ABSTRACT

Background: Impairment in Quality of Life (QoL) can influence regime compliance and disease management in diabetics. Hence, there is a need to evaluate their QoL.

Methods: 482 type-2 diabetics filled WHOQOL-BREF questionnaire for QoL evaluation. Independent 't' test compared the mean scores of different domains. Spearman rank correlation estimated the level of agreement between the domains. Multiple Logistic Regression was applied to determine the predictors of QoL.

Results: The mean age of diabetics was 53.18±10.55 years. The mean total score of WHOQOL-BREF scale was 55.10±8.52. The mean scores for physical health, psychological, social relationship and environmental domains were 53.38±8.33, 55.60±8.42, 53.40±14.6, 57.90±12.00 respectively. Age, education, physical activity, duration of DM and DM-related complications were strong predictors of QOL in diabetics.

Conclusion: Majority (53.94%) of diabetics had poor QoL. DM has significant impact on QoL, especially on physical health and social relationship domain. QoL is positively related to education, occupation and physical activity and negatively correlated to gender, age, duration of DM and DM related complications.

Keywords : *Type-2 diabetes mellitus, Quality of Life, WHOQOL- BREF scale, domains.*

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INTRODUCTION :

Evaluation of Quality of Life (QoL) has annexed a new dimension both in research as well as assessment of interventions and healthcare outcomes for implications of policy decisions and allocation of healthcare funds. As per World Health Organisation (WHO), "QoL" is defined as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns"[1]. Incorporation of QoL evaluation introduces a humanistic element to healthcare delivery system, thus emphasizing on a 'patient-centric' approach rather than 'laboratory report-centric' approach.

Ranking second worldwide in 2017, India homes 72.9 million diabetics consequential to population growth, rising age, urbanization, unhealthy diet and increasingly sedentary lifestyles[2]. Diabetes Mellitus (DM) management comprises of self-care, lifestyle modifications and pharmacotherapy to maintain near-normal glycemic control. Associated co-morbitidies may result in functional decline, dependence on care-givers, loss of autonomy, disruption of social, occupational and financial status and depression thus impairing QoL in diabetics[3].

QoL is depicted by WHO–QOL brief version (WHOQOL- BREF) questionnaire as four domains namely Physical health, Psychological, Social Relationship and Environment[4]. Adjunct to

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traditional indices like mortality and morbidity, evaluation of QoL is also an important indicator for diabetic care assessment. So, the objective of the study was to measure QoL of diabetic patients in each domain and to determine the predictors of QoL so as to identify specific limitations and needs at different stages of disease.

METHODS AND MATERIALS:

This hospital-based cross-sectional study comprised of subjects with type-2 DM over 18 years attending the Outpatient Department (OPD) of General Medicine, GVP IHC & MT, Visakhapatnam between February–June 2018. The study protocol was approved by Institutional Ethical Committee. Participation in this study was voluntary. After explaining the purpose of the study, informed written consent was obtained from the subjects, assuring them confidentiality.

The diagnosis of DM in the subject was confirmed as per guidelines of American Diabetic Association[5]. Exclusion criteria included (1) age <18 years (2) type-I DM (3) pregnancy or lactation (4) any psychiatric illness or use of any psychotropic medications (5) other endocrine disorders like thyroid disorders or on glucocorticoids medications (6) severe cognitive impairment (7) history of any major traumatic event like financial loss, divorce, separation, accident or death in the family, etc; within 6 months of data collection as it would affect the assessment of the various domains (8) refusal to participate.

Data collection :

Data were collected with face to face interviews. According to standardized procedure, following information were recorded prospectively: (1) socio-demographic information; (2) characteristics of DM and associated co-morbidities; (3) anthropometric measurements (4) vital signs (5) biochemical profile included Fasting and Post-prandial blood glucose and (6) World Health Organization–QOL brief version (WHOQOL-BREF) scale.

The socio-demographic information included age, gender, education, marital status, employment status, smoking status, alcohol consumption, diet, physical activity. Co-morbid conditions and/or complications were recorded based on history taking, complete clinical examination and clinicain's progress notes.

Research tool: WHOQOL- BREF scale.

This generic health-related questionnaire developed by the WHOQOL group is an abbreviated 26-item version of WHOQOL-100 and used by many Indian researchers[3,6,7,8]. It has excellent psychometric properties with good cross cultural validation[4]. It emphasizes on subjective remarkson life conditions, being assessed for past 2 weeks.

WHOQOL-BREF included 2 'benchmark' items for rating Overall QoL and satisfaction of General Health and 24 items divided into (Domain 1) Physical health with 7 items, (Domain 2) Psychological Health with 6 items, (Domain 3) Social relationships with 3 items, (Domain 4) Environmental health with 8 items. Each item was assessed on a 5-point Likert scale from 1 to 5. The first transformation converted raw domain scores for WHOQOL-BREF to a range of 4-20 score[9]. The mean scores of items within each domain was used to calculate the domain scores which were scaled in a positive direction (higher scores implied better QoL). The second transformation coverted domain scores to a 0-100 scale[9].

WHOQOL-BREF was self-administered by subjects. The instrument was translated into Telugu (local language) after a series of forward and backward translations to ensure content validity[10]. An experienced interviewer assisted most of the patients due to low literacy levels. It took 10-15 mins to complete the questionnaire and 10 mins to score.

Dependent and independent variables

Four domains of WHOQOL-BREF questionnaire were considered as dependent variables. The independent variables included sex, age, education, marital status, physical activity, employment status, duration of DM, existence of co-morbid diseases and DM-related complications.

Age-wise subjects were represented in binary fashion: <55 years vs. e"55 years. BMI (kg/m^2) was categorized as d"22.99 vs. e"23[11]. Duration of DM was classified as <10 years vs. e"10 years[12]. Other variables were dichotomized as yes/no or present/absent [literate (yes/no); employed (yes/no); married (yes/no); physical activity (present/absent); co-morbidities (present/absent); DM-related complications (present/absent).]

The information collected was organized with the Statistical Package for Social Sciences (SPSS) software version-22. Transformed scores of domains were utilized for analyses. Descriptive analyses were performed including Frequencies (N), Percentages (%), Ranges, Means, and Standard Deviation (SD). Spearman Rank Correlation determined the level of agreement between four domains of WHOQOL-BREF. Independent 't' test was used to investigate the association between participants characteristics and the mean scores of QOL in different domains. Multiple Logistic Regression was performed to determine the strongest predictors of QOL and Odd's ratio with 95% confidence interval were obtained. The level of significance was set at P-value < 0.05 for all analyses.

RESULTS :

In this study, 500 subjects with type-2 DM attending General Medicine OPD filled WHOQOL-BREF questionnaire. 18 questionnaires had more than 20% missing data and so were excluded from the study. Thus, the analysis was restricted to remaining 482 respondents.The baseline characteristics of 482 diabetic subjects were represented in Table: 1. The mean (±SD) age of the subjects was 53.18±10.55 years with the age in the range of 25-83 years. 319(66.18%) of the subjects were either housewives or unemployed or retired and were financially dependent on others. The highest mean raw score was seen for personal relationship followed by mobility (both scaled in positive direction) as per Table: 2. The lowest score was seen with leisure activity followed by sexual activity.

Table 1 : Baseline characteristics of the subjects having DM

Variables		Figures	
Gender #	Male	201	(41.70)
	Female	281	(58.30)
Age (in Years) #	20-30	2	(0.42)
	30-40	41	(8.50)
	40-50	128	(26.56)
	50-60	144	(29.87)
	60-70	145	(30.08)
	70-80	21	(4.36)
	>80	1	(0.21)
Education #	Illiterate	234	(48.54)
	1-10th std	193	(40.05)
	11-12th std	11	(2.28)
	Degree	37	(7.68)
	Post graduation	7	(1.45)
Marital status #	Single	3	(0.62)
	Married	429	(89.00)
	Widow	50	(10.38)
Employment status #	Unemployed	264	(54.77)
	Salaried	77	(15.98)
	Self employed	86	(17.84)
	Retired	55	(11.41)
Family history of DM #		168	(34.85)
Addiction #	Alcohol	43	(8.92)
	Tobacco	41	(8.50)
	Both	27	(5.60)
Physical activity#	Present	153	(31.74)
BMI (kg/m^2) $	≤ 22.99	248	(51.45)
	≥ 23.00	234	(48.55)
BMI (kg/m^2) $	Average	23.08 ± 3.76	
Duration of DM (in years) $		4.66 ± 5.30	
Associated co-morbidities #	Hypertension	176	(36.51)
	CAD	38	(7.88)
	CVA	40	(8.30)
	Cataract	74	(15.26)
	Orthopedic issues	38	(7.89)
DM-related complications #	Retinopathy	10	(2.07)
	Neuropathy	196	(40.66)
	Vasculitis	33	(6.85)
	Nephropathy	18	(3.73)
	Gastroparesis	11	(2.28)
Anti-DM medications #	None	7	(1.45)
	OHA	406	(84.23)
	Insulin	76	(15.77)
	Both	35	(7.26)
FBG (mg %) $		170.74 ± 67.50	
PPBG (mg %) $		245.62 ± 83.82	

BMI – Body Mass Index
SBP – Systolic Blood Pressure
DBP – Diastolic Blood Pressure
CAD – Coronary Artery Disease
CVA – Cerebrovascular Accident
OHA – Oral Hypoglycemic Agents
FBG – Fasting Blood Glucose
PPBG – Postprandial Blood Glucose
$ – mean (±SD)
# – N (%)

Diagram 1 : Comparison of the of the WHOQOL BREF transformed scores in four domains

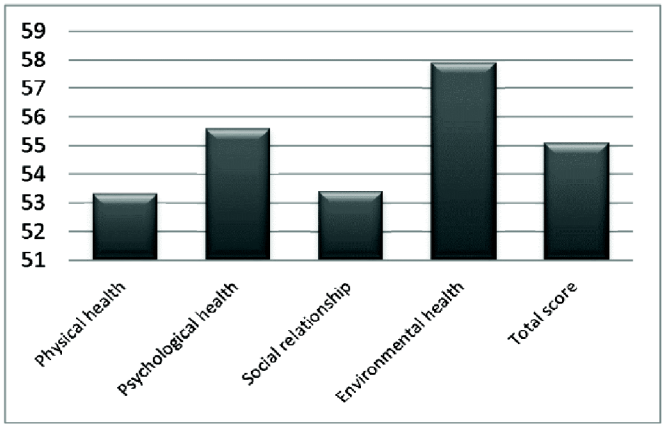

Table 2 : Raw scores for each item of WHOQOL-BREF in DM subjects

WHOQOL- BREF Item / domains	Direction of scale	Mean	SD
Q1 Overall QOL	+	3.51	0.50
Q2 General health	+	3.26	0.59
Domain 1: Physical Health			
Q3 Physical Pain	−	2.68	0.80
Q4 Dependence on Medication	−	2.59	0.69
Q10 Energy	+	3.31	0.69
Q15 Mobility	+	3.73	0.65
Q16 Sleep and Rest	+	3.20	0.86
Q17 Activities of Daily Living	+	3.29	0.69
Q18 Working Capacity	+	3.20	0.67
Domain 2: Psychological Health			
Q5 Life Enjoyment	+	3.49	0.58
Q6 Personal belief	+	3.43	0.53
Q7 Concentration	+	3.40	0.97
Q11 Body appearance	+	3.19	0.43
Q19 Self esteem	+	3.27	0.61
Q26 Negative feelings	−	2.55	0.70
Domain 3: Social Relationships			
Q20 Personal relationship	+	3.80	0.45
Q21 Sexual activity	+	1.97	0.92
Q22 Social support	+	3.63	0.79
Domain 4: Environment			
Q8 Safety	+	3.66	0.55
Q9 Physical environment	+	3.56	0.56
Q12 Financial resources	+	3.66	0.82
Q13 Accessibility of information	+	2.63	0.76
Q14 Leisure activity	+	1.92	0.80
Q23 Home environment	+	3.73	0.62
Q24 Access to health care	+	3.70	0.59
Q25 Transport	+	3.17	0.46

Correlation between 4 different domains of WHOQOL-BREF was represented in Table:3 and was statistically significant.

Various socio-demographic variables and disease parameters were compared with respect to transformed scores of each domain in Table: 4. Males, literates, employed, married, physical activity, absence of both co-morbid diseases and DM-related complications were having statistically significant better scores in Physical Health, Psychological and Social Relationships domain. For Environmental domain, Males, literates, employment, married, duration of DM, and absence of DM-related complications had statistically significant better scores.

Table 3: Determination of the level of agreement between 4 domains of WHOQOL-BREF

Domains	Statistics	Domain 1	Domain 2	Domain 3	Domain 4
Domain 1 (Physical health)	r-value	1.000	0.513**	0.547**	0.345**
	P-value		<0.001	<0.001	<0.001
Domain 2 (Psychological health)	r-value		1.000	0.507**	0.459**
	P-value			<0.001	<0.001
Domain 3 (Social relationships)	r-value			1.000	0.403**
	P-value				<0.001
Domain 4 (Environmental health)	r-value				1.000
	P-value				

*indicates level of significance at 5%
**indicates level of significance at 1%

Table 4 : Comparison of transformed scores of WHOLQO-BREF in 4 domains with respect to socio-demographic variables and course of disease in diabetic patients

Variable	Frequency (%)	Physical health	Psychological health	Social relationship	Environmental health	Total score
Gender						
Male	201(41.70)	55.84±8.61	57.25±9.40	59.60±14.71	60.62±13.27	58.33±9.21
Female	281(58.30)	51.67±7.68	54.48±7.44	48.93±12.81	55.89±10.66	52.74±7.13
P value		<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
Age group						
< 55 years	244(50.62)	55.19±7.90	57.6±8.40	57.5±13.09	58.29±11.61	57.15±7.68
≥ 55 years	238(49.38)	51.58±8.37	53.62±7.97	49.15±14.88	57.43±12.47	52.94±8.81
P value		<0.001*	<0.001*	<0.001*	0.43	<0.001*
Education						
Illiterate	234(48.55)	51.2±8.30	52.9±7.09	48.3±13.64	52.91±9.07	51.3±6.92
Literate	248(51.45)	55.45±7.85	58.18±8.78	58.17±13.86	62.53±12.62	58.58±8.40
P value		<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
Occupation						
Unemployed	319(66.18)	51.24±7.87	53.93±7.41	48.72±12.82	56.48±11.00	52.59±7.33
Employed	163(33.82)	57.7±7.55	59.0±9.25	62.5±13.56	60.58±13.47	59.9±8.61
P value		<0.001*	<0.001*	<0.001*	<0.001*	<0.001*
Marital status						
With partner	429(89)	53.83±8.26	56.02±8.56	54.74±14.57	58.37±12.25	55.74±8.54
No partner	53(11)	49.96±8.14	52.57±6.45	42.4±9.28	53.79±9.29	49.68±6.00
P value		<0.001*	0.002*	<0.001*	0.007*	<0.001*
Physical activity	153(31.74)	56.4±8.22	58.7±9.48	60.16±13.71	59.18±13.02	58.60±8.92
Present	329(68.26)	52.03±8.03	54.22±7.47	50.22±13.93	57.25±11.52	53.43±7.80
Absent		<0.001*	<0.001*	<0.001*	0.1	<0.001*
P value						
DM Duration						
< 10 years	407(84.44)	53.41±8.31	55.58±8.34	53.32±14.08	57.08±11.41	54.85±8.15
≥ 10 years	75(15.56)	53.41±8.45	55.92±8.87	53.71±17.28	62.09±14.35	56.28±10.22
P value		0.99	0.75	0.83	<0.001*	0.18
Comorbidities						
Present	259(53.73)	52.63±8.30	53.95±7.68	51.08±14.39	57.92±12.39	53.89±8.38
Absent	223(46.27)	54.31±8.30	57.6±8.81	56.04±14.42	57.8±11.63	56.44±8.47
P value		0.007*	<0.001*	<0.001*	0.63	0.001*
DM-related complications						
Present	258(53.53)	51.17±7.88	53.72±7.60	49.59±14.32	55.7±11.19	52.55±7.81
Absent	224(46.47)	55.98±8.10	57.84±8.78	57.75±13.7	60.35±12.51	57.98±8.37
P value		<0.001*	<0.001*	<0.001*	<0.001*	<0.001*

* - statistically significant

The results of Multiple Logistic Regression were displayed in Table: 5. As the mean total transformed score obtained was 55.10±8.52, the

Table 5 : Multivariate Logistics Regression to determine Predictors of QoL in diabetics

Variable	Category	N	Good QoL N=222	Poor QoL N=260	Odds Ratio	95% Confidence interval	P- value
Gender	Male	201	125	76	0.273	(0.27 - 0.76)	0.12
	Female	281	97	184			
Age group	< 55 years	244	144	100	2.686	(2.69 - 4.4)	<0.001*
	≥ 55 years	238	78	160			
Education	Illiterate	234	64	170	0.328	(0.33 – 0.51)	<0.001*
	Literate	248	158	90			
Occupation	Unemployed	319	111	208	0.840	(0.84 – 2.29)	0.733
	Employed	163	111	52			
Physical activity	Present	153	98	55	0.540	(0.54 – 0.88)	0.013*
	Absent	329	124	205			
Duration of DM	< 10 years	407	184	223	2.100	(2.1 – 3.86)	0.017*
	≥ 10 years	75	38	37			
Comorbidities	Present	259	108	151	0.892	(0.89 – 1.4)	0.619
	Absent	223	114	109			
DM-related complications	Present	258	84	174	2.563	(2.56 – 3.95)	<0.001*
	Absent	224	138	86			

* - statistically significant

cutoff value for QoL was set at 55. Among 482 subjects, 222(46.02%) reported better QOL. Age e"55 years, illiteracy, physical inactivity, duration of DM e"10 years and presence of DM-related complications had statistically significant correlation with poor QOL, thus reflecting them to be the strong predictors of QOL.

DISCUSSION :

In the present study, 260(53.94%) diabetics reported poor QoL thus reflecting DM to have profound negative impact on QoL of patients.

The mean reported age of diabetics was 53.18±10.55 years. Majority [272(56.43%)] belonged to age group of 40-60 years similar to reports by Wild[13]. Advancement of age was associated with significant decrement in QoL of patients (P<0.001) similar to studies by Raghavendra[7]. Female diabetics had significant lower scores of QoL than males in all domains due to poor self-care, paucity of solidarity and increased suspectibility to achieve glycemic control similiar to Mexican survey by Salcedo-Rocha AL et al[14].

HTN was reported in 176(36.51%) diabetics as the most predominant co-morbidity comparable to 30.8% as observed by Gautam[15]. The commonest complication was Neuropathy in 196(40.66%) diabetics similar to reported prevalence of 38% by Ramanathan RS[16]. The average BMI observed was 23.08±3.76 kg/m^2 of which 248(51.45%) had BMI d" 22.99 kg/m^2 which correlated with the occurrence of 'Asian Phenotype' DM[17] characterized by younger age, genetic predisposition for dyslipidemia and development of premature artherosclerosis[13].

Subjects with duration of DM e"10 years reported poor QoL due to the occurrence of complications following long-term DM, comparable to study by Liu et al[12] stating that the prevalence of complications had positive correlation with duration of disease, irrespective of the patient's age.

Illiteracy and unemployment were associated with poor QoL in all domains. Low education and financial constrains may hinder with treatment costs and adherence. Married patients had better QoL as compared to single/widowed patients particularly significant in social relationship and physical health domains similar to findings as Patel[8], may be due to physical care and mental support by care-givers.

In this present study, environmental domain was least affected. Highest score was reported among literates as education may influence diabetes-related information, interactions with healthcare providers and adherence to complex regimens and healthier lifestyle. As observed, Physical health domain was impaired the most in diabetics attributed to lower energy, mobility and poor sleep quality. It had positive correlation with physical activity which helps in glycemic control, weight loss and improves well-being[18].

In this present study, the score obtained in Social relationships was almost similar to Physical health domain. It had positive association with education, employment, exercise and absence of co-morbidities and complications. DM had negative

impact on Sex life[19] as evident by lower response for item: sexual activity. Also, physical pain and disability may hinder sociability with family and community thus impairing social QoL.

DM demands continuous monitoring, lifestyle modifications and pharmacotherapy which can have negative psychological impact on affected individuals[4] leading to perception of poor QoL. Employment, exercise and younger age were having positive impact on psychological domain. DM, being a chronic progressive disease, significantly affected QoL of patients in terms of physiological limitations, reduced sense of well-being, impaired productivity and decreased sociability. QoL and glycemic control should be targeted as distinct and attainable goals for diabetics[20]. Periodic QoL assessment and counseling, supplemented with physical and psycho-social rehabilitation, should become an integral part of DM management.

This study had few limitations. It was a cross-sectional study. HbA_1C was not obtained to determine correlation of glycemic control with QoL. Better conceptualization of substantial health determinants in diabetics for development of policies and interventions targeting QoL is a fertile quest zone.

CONCLUSION:

In the present study, majority 260(53.94%) diabetics had poor QoL. DM had significant impact on QoL, especially, on physical health and social relationships domains. QoL was positively related to education, occupation and physical activity where as it was negatively correlated to gender, age, duration of DM and DM-related complications. 'Individualized' approach focusing on patient's needs and satisfaction is required for better QoL in spite of limitations related with DM.

Acknowledgement

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Article Submission

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Original Article

Immunofluorescence pattern of antinuclear antibody and its association with autoantibody profile in SLE

R R Marak[*], D Doley[**], S Kakati[***], I H Choudhury[****]

Abstract :

Background : Antinuclear antibody (ANA) test by indirect immunofluorescence (IIF) reveals distinct patterns. Each pattern is associated with antibodies to certain nuclear antigens.

Objectives : To study the immunofluorescence pattern of ANA and to look for any concordance between ANA-IIF and Line Immunoassay in Systemic lupus erythematosus(SLE).

Methods : Sera of 134 diagnosed cases of systemic lupus erythematosus(SLE) were tested for ANA by Indirect Immunofluorescence(IIF) on HEp-2 cell and Line Immunoassay(LIA) using AESKUBLOT © ANA-17 pro which has 17 antigens per test strips. Concordance between the IIF patterns and LIA results was checked.

Results : 44(32.8%) sera exhibited the coarse speckled pattern, followed by homogenous in 24(17.9%), fine speckled in 20(14.9%), cytoplasmic, rim and centromere in 2(1.5%) each and Golgi pattern in 1(0.7%). 39 (29.1%) sera exhibited a mixed pattern. 20(14.9%) patients had no positivity on LIA profile. The most frequently found autoantibody was anti-SSA(Ro 60) in 65(48.5%) patients followed by anti-dsDNA in 64(47.8%), anti-SSA(Ro52) in 50(37.3%) and anti-histone in 46(34.3%) patients.The coarse speckled pattern (29.9%) correlated with antibodies against SSA, dsDNA , Sm, histone, and nucleosome. Among dsDNA positive patients, the most frequently encountered were coarse speckled and mixed patterns in 15.7%. But there was no further concordance between IIF and LIA.

Conclusion:There was high rate of discordance between IIF and LIA. Thus, there is a need to perform both and see which matches the clinical profile of the patient better.

Keywords : *Line Immunoassay, Systemic Lupus Erythematosus*

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INTRODUCTION :

Systemic lupus erythematosus (SLE) is an autoimmune disease characterised by various autoantibodies against extractable nuclear antigens (ENA) and chromatin components. Antinuclear antibody (ANA) test by indirect immunofluorescence (IIF) is highly sensitive with good specificity. ANA-IIF reveals distinct staining patterns. Each pattern is associated with antibodies to certain nuclear antigens. Positive fluorescence staining indicates the presence of ANA but it doesn't allow accurate identification of these antibodies. Further some specialized technique like Line Immunue Assay (LIA), western blotting or ELISA are employed for detection of specific autoantibodies.The study was done with the aim to study the immunofluorescence pattern of ANA in Systemic Lupus Erythematosus and to look for any concordance between ANA-IIF patterns and Line Immunoassay in systemic lupus erythematosus.

In this study, serum samples of SLE patients were analysed for ANA testing by Indirect immunofluorescence (IIF) methods and further processed for identification of specific autoantibodies by Line Immunue Assay(LIA). The results were correlated with one another to establish any definite link between the fluorescence pattern and specific autoantibodies. If a definitive correlation is found between the ANA patterns and immunueprofile, one could use ANA-IIF patterns to predict the presence of autoantibodies to diagnose SLE.

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METHODS :

A total of 134 diagnosed cases of SLE attending the OPD of Rheumatology and Medicine wards of Assam Medical college,Dibrugarh from July,2015 to Jun 2017 were enrolled in the cross-sectional study. Blood was drawn from SLE patients and sera were separated by centrifugion. Sera was stored at 4^0C if testing was done within 72 hours and -20^0C if testing done after 72 hours. Sera were tested for ANA by Indirect Immunofluorescence on HEp-2 cell and Line Immunoassay (LIA) using AESKUBLOT © ANA-17 pro which has 17 antigens per test strips.

Indirect immunofluorescence was done by available kit in the market. Slides were prepared from human epitheloid cells (Hep2 cells)as a substrate and were incubated with diluted serum. The presence of autoantibodies was detected by fluorescent anti-immunoglobulin antibody, and characteristics morphology patterns of fluorescent staining were observed under fluorescent microscope. A titre >1:80 were taken as positive.

The serum sample further processed using Line Immunue Assay(LIA). For LIA, AESKUBLOT ANA-17 PRO test strips were used which has 17 antigens arranged on test strips.It is a membrane based enzyme immunue assay for qualitative detection of IgG antibodies against dsDNA,nucleosomes,histones,smD1, PCNA, Ribo-P0, SSA/Ro60kDa, SSA/Ro50kDa, SS-B/La, CENP-B, Scl-70, U1-snRNP, AMA M2, Jo-1, Pm-Scl, Mi-2 and Ku in human serum or plasma. Antigens are located as parallel lines at exactly defined positions on a nitrocellulose membrane along with control band. Serum was diluted using dilution buffer in 1:110 and left on horizontal shaker for 30 mins. After this, washing was done for 5 min with wash solution for 30 min, followed by adding conjugate to strip for 30 min. Again the washing step was repeated. To the washed strip, substrate was added and left for 10 min. Afterwards, the reaction was stopped by adding stop solution for 2 min. Then, the strips were dried and evaluated by comparing with the intensity of positive control line.

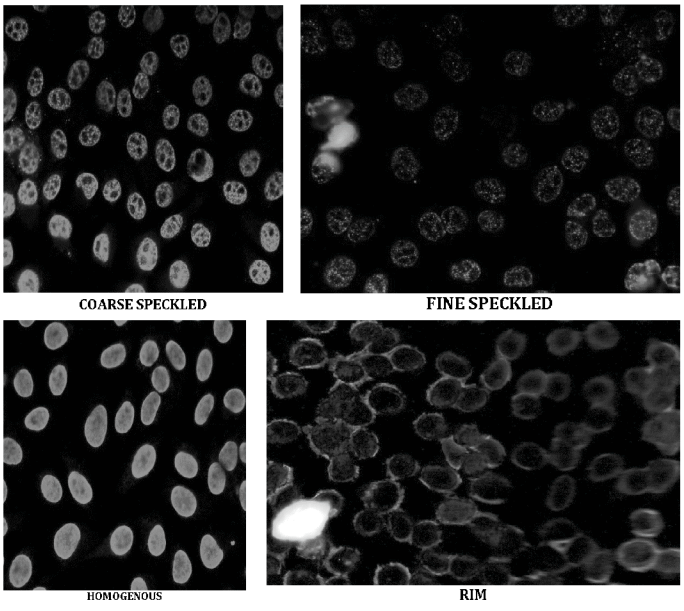
RESULTS :

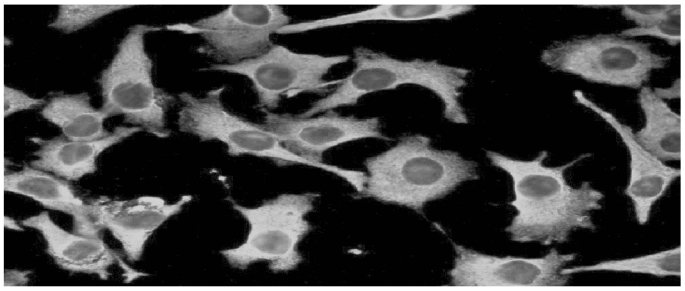
In this cross sectional study, 134 samples of SLE patients were analysed who were diagnosed by ARA (American Rheumatology Association) criteria. In this study, we tried to find out correlation between ANA IIF pattern with specific autoantibodies.

ANA IIF was found positive in 134 patients(100%); Among the sample, 44(32.8%) sera exhibited the coarse speckled pattern, followed by homogenous in 24(17.9%), fine speckled in 20(14.9%), cytoplasmic, rim and

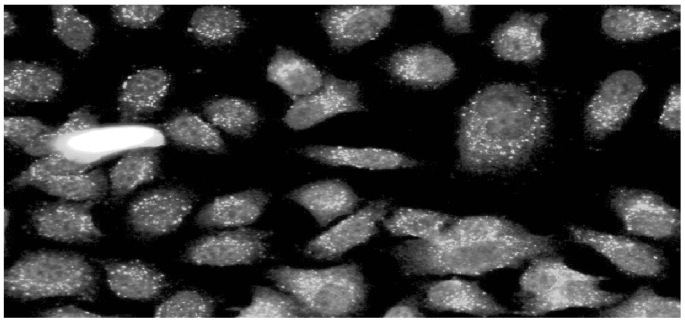
Table-1: Distribution of pattern of ANA

ANA PATTERNS	Frequency	Percentage
Homogeneous	24	17.9
Coarse Speckled	44	32.8
Cytoplasmic	2	1.5
RIM	2	1.5
Centromere	2	1.5
GOLGI	1	.7
Fine Speckled	20	14.9
MIXED	39	29.1





GOLGI



CYTOPLASMIC

TABLE-2: ENA PROFILE

	Frequency	Percentage
ds DNA	64	47.8
Nucleosome	25	18.7
Histone	46	34.3
SmD1	34	25.4
PCNA1	3	2.2
Rib-PO	37	27.6
SS-A (Ro60)	**65**	**48.5**
SS-A (Ro52)	50	37.3
SS-B/La	18	13.4
CENP_B	9	6.7
Scl-70	10	7.5
U1-snRNP	22	16.4
AMA-M2	8	6.0
Jo-1	8	6.0
PM-Scl	8	6.0
Mi-2	6	4.4
Ku	3	2.2

centromere in 2(1.5%) each and Golgi pattern in 1(0.7%). 39 (29.1%) sera exhibited a mixed pattern. 20(14.9%) patients had no positivity on LIA profile.

The most frequently found autoantibody was anti-SSA(Ro 60) in 65(48.5%) patients followed by anti- ds DNA in 64(47.8%), anti-SSA(Ro52) in 50(37.3%) and anti-histone in 46(34.3%) patients. The coarse speckledpattern (29.9%) correlated with antibodies against SSA, dsDNA, Sm, histone, and nucleosome. Among dsDNA positive patients, the most frequently encountered were coarse speckled and mixed patterns in 15.7%. The results are shown in the following tables.

TABLE:3

	ENA_PROFILE		Total
	Positive	Negative	
Homogeneous	19	5	24
	14.2%	3.7%	17.9%
Coarse Speckled	40	4	44
	29.9%	3.0%	32.8%
Cytoplasmic	2	0	2
	1.5%	0.0%	1.5%
RIM	2	0	2
	1.5%	0.0%	1.5%
Centromere	1	1	2
	.7%	.7%	1.5%
GOLGI	0	1	1
	0.0%	.7%	.7%
Fine Speckled	17	3	20
	12.7%	2.2%	14.9%
MIXED	33	6	39
	24.6%	4.5%	29.1%
TOTAL	114	20	134
	85.1%	14.9%	100.0%

TABLE:4

ANA PATTERNS	ENA PROFILE																
	DsDNA	NUCLEOSOME	HISTONE	SMD1	PCNA1	RIBP	SSA (RO60)	SSA (RO52)	SSB_LA	CENP_B	SCL70	U1RNP	AMA M2	JO1	PMSCL	MI2	KU
Homogeneous	13	6	11	2	1	3	10	8	4	3	3	1	1	1	1	1	0
	9.7%	4.5%	8.2%	1.5%	.7%	2.2%	7.5%	6.0%	3.0%	2.2%	2.2%	.7%	.7%	.7%	.7%	.7%	0.0%
Coarse Speckled	21	8	12	16	1	6	23	18	9	5	4	11	3	3	4	3	1
	15.7%	6.0%	9.0%	11.9%	.7%	4.5%	17.2%	13.4%	6.7%	3.7%	3.0%	8.2%	2.2%	2.2%	3.0%	2.2%	.7%
Cytoplasmic	0	0	0	0	0	2	1	0	0	0	0	0	0	0	0	0	1
	0.0%	0.0%	0.0%	0.0%	0.0%	1.5%	.7%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	.7%
RIM	2	2	2	0	0	2	0	0	0	0	0	0	0	0	0	0	0
	1.5%	1.5%	1.5%	0.0%	0.0%	1.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Centromere	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0
	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	.7%	.7%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
GOLGI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Fine Speckled	7	1	5	2	0	6	10	8	0	0	1	1	0	0	0	0	0
	5.2%	.7%	3.7%	1.5%	0.0%	4.5%	7.5%	6.0%	0.0%	0.0%	.7%	.7%	0.0%	0.0%	0.0%	0.0%	0.0%
MIXED	21	8	16	14	1	18	20	15	5	1	2	9	4	4	3	2	1
	15.7%	6.0%	11.9%	10.4%	.7%	13.4%	14.9%	11.2%	3.7%	.7%	1.5%	6.7%	3.0%	3.0%	2.2%	1.5%	.7%

DISCUSSION :

Anti-Nuclear Antibody (ANA) is the first immunologic test for diagnosis of Systemic lupus erythematosus (SLE). Detection of ANA by Indirect Immunofluorescence is the standard methods of diagnosing SLE .The immunufluorscence patterns correspond to specific autoantibodies against differnent nuclear antigen.

The present study analysed the correlation between ANA results detected by IIF and ANA profile by LIA in 134 patients with Systemic lupus erythematosus. There are many studies which had compared ANA results detected by IIF vs. ELISA in patients with suspected autoimmunue diseases. But there are only few studies which had assessed the results in patients with established autoimmunue disease. The present study is of one of its kind which had utilized both the tests(IIF and ANA profile by LIA)for establishing the diagnosis and then compared the performance of ANA profile with IIF pattern and correlated both the test results.

ANA IIF was found positive in 134 patients(100%). Among the sample, 44(32.8%) sera exhibited the coarse speckled pattern, followed by homogenous in 24(17.9%), fine speckled in 20(14.9%), cytoplasmic, rim and centromere in 2(1.5%) each and Golgi pattern in 1(0.7%). 39 (29.1%) sera exhibited a mixed pattern whereas in New York Gonzalez and Rothdfield reported that the homogenous and peripheral patterns with SLE and only a few produced a speckled pattern.[1]

In our study, the most frequently found autoantibody was anti-SSA (Ro 60) in 65(48.5%) patients followed by anti- ds DNA in 64(47.8%), anti-SSA(Ro52) in 50(37.3%) and anti-histone in 46(34.3%) patients. The coarse speckled pattern (29.9%) correlated with antibodies against SSA, ds DNA, Sm, histone, and nucleosome. Among ds DNA positive patients, the most frequently encountered were coarse speckled and mixed patterns. In USA, Mutasim and Adams also reported similar association between speckled pattern and various ribonuleoprotein in their study.[2] A study done by Sharmin S *et al.* reported speckled pattern as the commonest and antinuclear reactivity towards anti-RNP, then anti-sm, SSA and SSB; Peripheral and homogenous pattern as strongly associated with anti-dsDNA.[3]

Positive ANA IIF with negative ANA profile by Line Immunue Assay(LIA) was noted in 20 patients. A positive result with ANA IIF, together with the negative results in Line I mmunue Assay(LIA) was also noted earlier and attributed to the presence of anti-dsDNA antibodies. Vos *et al.* have found ANA positive samples negative with line immunue assay but found positive for anti-dsDNA antibodies

In the past, ANA negative lupus had been diagnosed based on simple assays, when this advanced ANA Profile was not available. This was also noted in other studies, where significant number of IIF assays missed reactivity to dsDNA which was picked by the subtype analysis.[4]

CONCLUSION :

ANA is used for screening of patients with SLE. Its fluorescent pattern could also predict the presence of certain specific antibodies in the sera. Detection of ANA by IIF may also yield false negative results even in the presence of high titre of antibodies, such as those directed to SS-A,Ro52, Jo-1 and others. A LIA is also performed for further confirmation and identification of particular antibody in the patient samples. A broad range of line immune assays are available and they are typically used to confirm autoantibodies previously identified by ANA IIF. In our study, there was high rate of discordance between IIF and LIA. Thus, there is a need to perform both and see which matches the clinical profile of the patient better.

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Original Article

Joint and Functional Assessment Following Secondary and Tertiary Prophylaxis in hemophilia

A Dutta*, S Kakati**, S Kar*, D Doley***

Abstract

Introduction : Sickle cell disease (SCD) is one of the most common monogenic disorders globally with an autosomal recessive inheritance. At least 5.2% of the world population carry a significant variant of normal haemoglobin. The primary pathophysiology of sickle cell disease is based on the polymerization of deoxy-HbS within the RBCs causing a distorted sickle shape which eventually leads to vaso-occlusion of sickle red cells. In this study, we aimed to describe the clinical characteristics, management and outcome of adult patients with SCD admitted to the Medicine department of a tertiary hospital. **Methodology :** This prospective observational study was carried out in Department of Medicine AMCH. Study was carried out on 20 sickle cell anaemia patients and its variants presented with crisis, whose age is 13yrs and above. Detailed history and careful clinical examination performed on each patient. A battery of investigations to detect crisis and organ failure was carried out during study period. **Results :** This study carried out on 20 sickle cell anaemia patients and its variants. Out of 20 patients, 12 [60%] belongs to Austro-asiatic ethnic group which includes the tea garden community. Out of 12, 7 had sickle cell disease, 4 had sickle cell beta thalassemia. Symptoms of acute chest syndrome are more common in sickle cell disease group. Abdomen pain is more common in sickle cell disease group. Most common sign was pallor [17 cases, 85%], followed by splenomegaly [16 cases, 80%]. Splenomegaly was present in all Sickle thalassemia patients. **Conclusion :** Among 20 patients, 12 are of sickle cell anaemia, 3 patients of sickle cell trait and 5 patients are of sickle thalassemia syndrome. Most common symptoms of presentation are Bone pain and Abdominal pain. Most common signs are Pallor, Fever and Splenomegaly. Splenomegaly was found more common in the adolescent age group, especially in Sickle thalassemia patients. Vaso-occlusive crisis is the most common crisis of presentation.

Keywords : *Hemophilia, Prophylaxis, Joint assessment, HJHS, Functional assessment, FISH*

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INTRODUCTION :

Hemophilia is an X-linked recessive disease which results in the deficiency of coagulation factors. The prevalence of hemophilia A is 1:5,000 male live births and of hemophilia B, 1:30,000 male live births.[1] The hallmark of hemophilia is musculoskeletal outcome. Though Primary prophylaxis can prevent joint damage but prophylaxis will not help repair joints that are already damaged. Prophylaxis is considered optimal care for hemophilia patients to prevent bleeding and to preserve joint function which may improve quality of life.[2] Prophylaxis is now the goal of treatment for people with hemophilia, allowing them to remain active and participate more fully in daily life. Unlike episodic or "on demand" treatment, which is given at the time of a bleed to make it stop, prophylaxis is given to prevent bleeding before it starts. Studies of secondary and tertiary prophylaxis in adolescents and adults have also shown benefit in reducing annual bleeding rate (ABR), rate of joint deterioration, and number of days lost from school or work compared to episodic treatment.[3,4]

Prophylaxis is the regular infusion of clotting factor concentrates in an attempt to raise clotting factor levels and to keep them at 1% or higher at all times. There are currently two protocols in use for which there is long-

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term data. One is the Malmö protocol in which Factor concentrate of 25-40 IU/kg is administered three times a week for those with hemophilia A and twice a week for those with hemophilia B. In the Utrecht protocol, factor concentrates of 15-30 IU/kg is administered three times a week for those with hemophilia A and twice a week for those with hemophilia B. In countries with significant resource constraints, lower doses of prophylaxis (e.g., 10-15 IU/kg, 3 times per week) may be an effective option.[5] According to a joint statement made by the World Health Organization (WHO) and the World Federation of Hemophilia (WFH), initiating prophylactic treatment at an early age is considered to be the optimal form of therapy for a child with severe hemophilia.[6–8] To be most effective, a prophylaxis protocol should be tailored to the individual based on their age, bleeding pattern, joint health, the level and timing of physical activity they engage in, their clotting factor levels, and their ability to adhere to a protocol. Prophylactic regimens should also be flexible enough to change with time as the individual patient's circumstances change.

Costs of clotting factor concentrate appear to be the main barrier preventing the widespread use of prophylaxis in developing countries including India. Currently, government schemes for hemophilia treatment in India are funding for these clotting factors. Most of the PWH from North East India used to receive infrequent episodic on demand factor replacement until recently when Assam State Government started procuring Factor VIII and Factor IX. These factors were provided to PWH free of cost at Government Medical Colleges of Assam. We, at Assam Medical College and Hospital started patient education workshops, Hemophilia Clinics, awareness programs and motivational activities for family members. This was followed by initiation of low dose prophylaxis treatment in eligible candidates in a structured way.

AIM:

To study the annual bleed rate (ABR), annual joint Bleed rate (AJBR), joint assessment using Hemophilia Joint Health Score (HJHS)and functional assessment using FISH in PWH three months and six months after receiving low dose prophylaxis.

METHOD :

The study enrolled all symtomatic hemophilia patients attending Assam Medical College and Hospital from 1st January 2017 and willing to take prophylaxis therapy instead of ondemand treatment. The PWH with more than 50 exposure days, no history of Inhibitors, history of hospitalization for bleeding events and index joint bleeding or involvement were included in the study. After proper consent taken in their mother tongue, they were assessed clinically with annual bleed rate, joint involvement using Hemophilia Joint Health Score (HJHS) and functional status using Functional Independence Score in Hemophilia (FISH). HJHS was used to assess joint health by measuring swelling, muscle atrophy, alignment and range of motion, joint pain, strength and global gait. The higher the HJHS score, the more severe the condition. FISH includes the assessment of eight activities: eating, grooming, dressing, chair transfer, squatting, walking, step climbing and running. Each activity is graded according to the amount of assistance required to perform it. The lower the FISH score, the more severe the condition. FISH and HJHS can be used to evaluate change in the scores over time or after the therapeutic intervention.

PWH (A & B) were initially started 10 IU/kg once a week every Saturday for one month to see whether they were compliant and motivated enough to continue prophylaxis. Once they started coming regularly, the dose in PWHA was increased to 10-15 IU/Kg twice a week on Tuesday and Saturday and in PWHB was increased to 15-20 IU/Kg once a week on Saturday. This was

supplemented with proper individualized physiotherapy sessions, patient education programs and one on one interaction with attendants and family members to address various social and non-medical issues. They were reassessed after three months. In PWH with break through bleeds and poor clinical improvement, dose escalation was done. In others, home therapy was encouraged with an aim to make the PWH totally independent with self infusion of factors or parents infusing them. Some patients were assigned to "guardian" health care providers from their locality, who gave them factors at home or at their nearest health care centre. They were again assessed after six months for joint health and functional status.

RESULTS :

We have 62 patients registered in Tinsukia Hemophilia society. Out of them, 53 are Hemophilia A, 8 are Hemophilia B and one factor X deficient. 37 PWH A and 8 PWH B were eligible and consented to start prophylaxis. After initial clinical examination, joint and functional assessment they were started on very low dose of prophylaxis weekly. Those who were motivated and compliant were escalated to our optimal dose of 10-15 IU/kg twice weekly in Hemophilia A and 15-20 IU/Kg weekly in Hemophilia B. Those who did not respond clinically were farther escalated 15-20 IU /Kg thrice weekly as shown below.

Figure 1: Dosage schedule in Hemophilia A

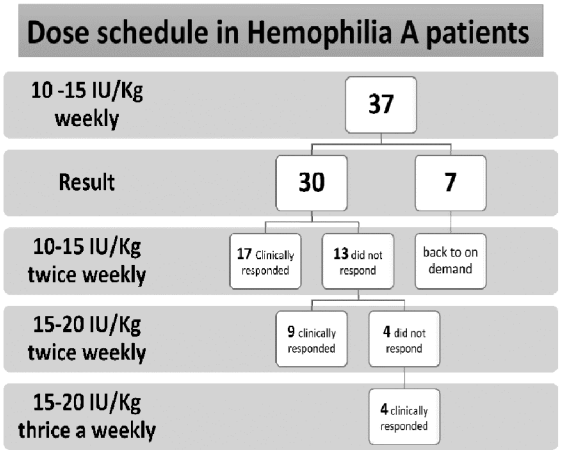
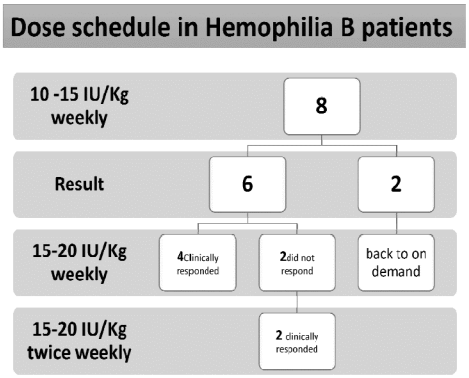


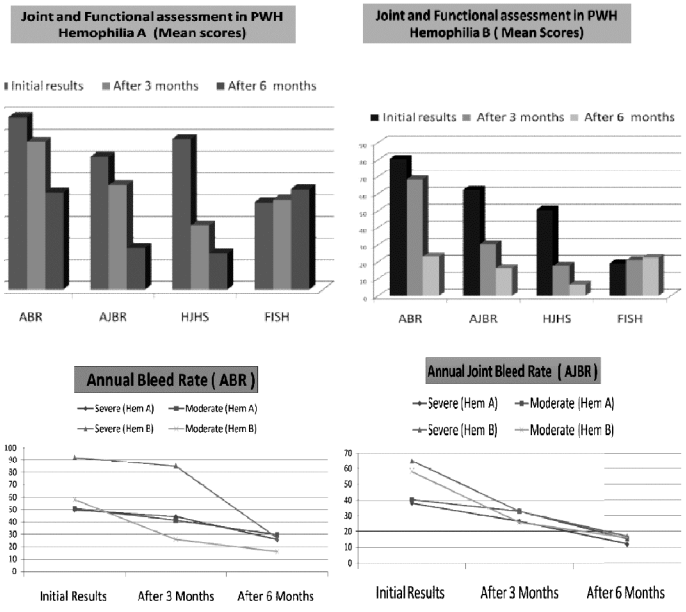
Figure 2: Dosage schedule in Hemophilia B

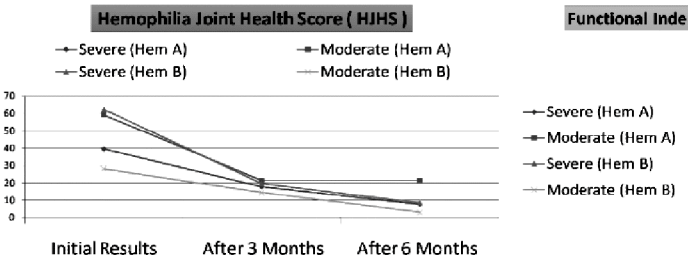


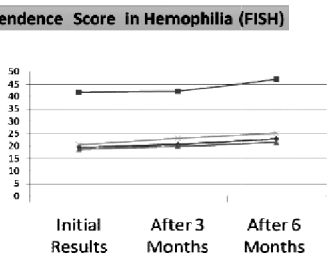
There was 43% reduction in ABR, 68% reduction in AJBR, 75% reduction in HJHS and 15% increase in FISH after 6 months of low dose prophylaxis in PW Hemophilia A. Similarly there was 71% reduction in ABR, 73% reduction in AJBR, 86% reduction in HJHS and 17% increase in FISH after 6 months of low dose prophylaxis in PW Hemophilia B.

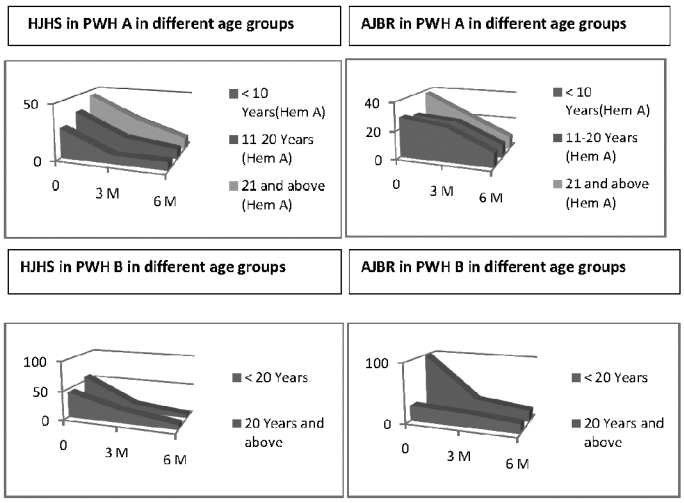
Severe PWH (Factor <1%) showed maximum improvement in all bleeding and joint assessment scores. Functional assessment (FISH scores) improved similarly in all patients. Younger PWH had better Joint scores to start with, in comparison with elder PWH but the joint health improved after 6 months of prophylaxis therapy in all PWH across different age groups.

Figure 3: Joint and functional assessment in Hemophilia A









DISCUSSION :

The key to a successful long term outcome in patients with Hemophilia is an efficient prophylaxis that prevents bleeding in joints for children and adults with hemophilia. Efficient prophylaxis requires taking into account the available resources (clotting factor concentrate, trough levels), the bleeding trigger (activity levels, chronic synovitis, already existing arthropathy) and most importantly the number of acceptable bleeds, especially joint bleeds. Depending on the available resources, the treatment objectives can vary between countries and treatment centers. In an almost ideal setting, the number of spontaneous bleeds should be minimized in order to prevent the manifestation of joint arthropathy. Moreover, joint arthropathy in a patient on primary prophylaxis develops very slowly, over a decade or even longer time periods. A number of published studies suggest that these patients benefit from lifelong prophylaxis.[9, 10] Prophylaxis has greatly improved joint health and is challenging joint outcome assessment. Because of the low number of about 1 joint bleed every 2 years resulting from intensive prophylaxis programs.[11-13] Clinical manifestation of joint disease has become a subtle process, starting mildly, sub clinically, and progressing slowly over years.

Studies have proven that patients in prophylaxis treatment have less haemorrhagic episodes, less progressive joint deterioration, reduced hospitalization and limited days lost from work or school compared to on demand treatment.[14,15] A study in Kerela shows that low – prophylaxis is effective and feasible in children with severe in resource limited setting such as Kerela, India. This treatment regime is also associated with better school attendance and reduced hospitalization among the children with haemophilia.[16]

In Sweden, prophylactic treatment of boys with severe haemophilia has been practised since 1958 in an attempt to convert the disease from a severe to a milder form. It appears to be possible to prevent hemophilic arthropathy by giving effective continuous prophylaxis from an early age, and preventing the VIII: C or IX: C concentration from falling below 1% of normal.[17] Petrini and colleagues reported the prevention of haemophilic arthropathy when prophylaxis was initiated before patients reached 2 years of age.[18] Aledort and others reported that prophylaxis slowed the progression of established joint damage.[19] The Canadian primary prophylaxis experience begins with a once-weekly regimen (50 U/kg body weight [BW]), that, depending on number of bleeds, is intensified in a first step to twice-weekly treatment (2 times 30 U/kg BW) and, in a third step, to every-other-day therapy (25 IU/kg BW).[20]

CONCLUSIONS :

Low dose prophylaxis therapy with factor concentrates along with patient education

programs and regular physiotherapy was very effective in hemophilia patients to improve the joint health and functional status within 6 months of initiation, especially in patients who were receiving on demand therapy, that too very often or infrequently. The results were most remarkable in PWH with sever factor deficiency (<1%).

Acknowledgement

We would like to acknowledge, Prof Pritikar Dowerah, Prof Adity Sarma, Dr Aditi Barua, Dr C J Borah, Dr Pranoy Dey, Dipjyoti Boruah, Papari Boruah, Washim Akramul Hoque PT for their cooperation and help in running the Hemophilia Care Center in Assam Medical college and being a part of this study.

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Review Article

How do I manage patients with Acute lower gastrointestinal bleeding ?

Premashish Kar*, R Kothari**

Overt lower gastrointestinal bleeding (LGIB) accounts for 20% of all cases of gastrointestinal bleeding which needs invasive diagnostic evaluation.[1-3] Even though many times the bleeding stops spontaneously and have favourable outcome, morbidity & mortality is increased in older patient.[4] In most occasions, lower GI bleed presents with sudden onset hematochezia (maroon & red blood) passed per rectum. But some times patient may also present with history of malena when the bleeding site is in the caecum or right sight of colon.[5] Sometimes patient with brisk upper GI bleeding can also present with hematochezia. 15% of patients with presumed LGIB may have an upper GI source of Bleed.

Lower GI Bleed is defined as bleeding from source distal to the ligament of treitz and includes bleeding from the colon & rectum.[6] The common cause of lower GI bleeding is mentioned in table 1 .

Table 1 - Common causes of LGIB and their frequency[7]

1.	Diverticulitis	30-40%
2.	Infectious colitis	5-20%
3.	Haemorrhoids	2-15%
4.	Ischemic colitis	5-20%
5.	Angiodysplasia	5-10%
6.	IBD	3-5%
7.	Post polypectomy	2-7%
8.	Rectal ulcer	0-5%
9.	Radiation colitis	0-2%
10.	Stercoral ulcer	0-5%
11.	Colorectal varices	0-3%
12.	Dieulafoy's lesion	rare

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The management of the case should include -

1. Focused history, physical examination, laboratory evaluation at presentation to assess the severity of the bleeding & its possible location & etiology.

2. Hematochezia associated with haemodynamic instability is indicative of upper GI bleeding source. Therefore either a upper GI endoscopy or a nasogastric tube to be passed & ascertained to rule out upper GI bleeding & to focus on rectal/colonic cause of lower GI bleed.

3. Patient should received intravenous fluid resuscitation with normalisation of blood pressure & heart rate prior to any endoscopic evaluation / intervention.

4. Packed Cell transfusion is indicated to maintain a haemoglobin around 9 gm%.

5. Endoscopic haemostasis may be considered in patients with INR of 1.5-2.5 before or concomitant with administration of reversal agents . Reversal agents should be considered before endoscopy in patient with INR >2.5 . Platelet transfusion should be considered in patients with platelet count less than 50,000/cu mm. In patient with severe bleeding & those requiring endoscopic haemostasis.

6. In patients on anticoagulants, it should be decided whether to discontinue medication or use reversal agents to balance the risk of bleeding and thromboembolic events based on multidisciplinary approach.

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7. Colonoscopy should be the initial diagnostic procedure for nearly all patient presenting with overt LGIB. Colonoscopic evaluation should be done within 24 hours of patient presentation after adequate bowel preparation. The colonic mucosa should be carefully inspected during both colonoscope insertion and withdrawal, with aggressive attempts made to wash residual stool and blood in order to identify the bleeding site.[8] The endoscopist should also intubate the terminal ileum to rule out proximal blood suggestive of a small bowel lesion

8. Endoscopic therapy should be provided whereas there is evidence of active bleeding (spurting and oozing); non bleeding vessel and adherent clot. In a case of diverticular bleeding, endoscopic clips are recommended as clips are safer in the colon as compared to band ligation. For angioectasia bleeding, argon plasma coagulation is required. Post polypectomy bleed would require mechanical clips or contact thermal injury with or without use of dilute epinephrine injection. Epinephrine injection therapy (1:10000 or 1: 20000 dilution) can be used to gain initial control of active bleeding lesions and improve visualisation and achieve secondary haemostasis using mechanical or contact thermal therapy.

9. Surgical consultation should be sought with ongoing bleeding. Surgical interventions should be sought when therapeutic endoscopic options have failed. But before surgical resection, it is important to localise the source of bleeding.

10. Radiographic interventions should be considered in patients who have ongoing bleeding, have a negative upper endoscopy, have not responded to hemodynamic resuscitation and who are unlikely to tolerate bowel preparation and urgent colonoscopy. If a diagnostic test is required for localisation of bleeding site before angiography, CT Angiography should be considered. Though tagged RBC scintigraphy may be more sensitive for bleeding, CT angiography is a the first-line screening test if needed before angiography or emergency surgery as it is more expedient and accurate than tagged RBC scintigraphy.

PREVENTION OF RECURRENT LOWER GI BLEEDING:

It is important to remember that colonic diverticula and angioectasia are prone to rebleed. In patients with diverticular bleed ~15% of patients rebleed after combination injection plus thermal or clip therapy.[9] Angioectasias are also prone to rebleeding, and new lesions may form throughout the GI tract. The rate of rebleeding ranged from 37 to 45% at 1 year and 58 to 64% at 2 years.[10] Evidence for treatment with thalidomide or estrogen plus progesterone yields low outcome. The Rate of rebleeding were no different with reference to the use of argon plasma coagulation compared with heater probe and monopolar thermal coagulation.

It is important to remember that the management of antiplatelets and anticoagulants medications in patients with acute LGIB requires multidisciplinary individualised approach that balance the risk of rebleeding with the risk of thromboembolic events. It should be cautioned that aspirin should not be discontinued when used as secondary cardiovascular prophylaxis and dual dual antiplatelet therapy should not be stopped within 90 days of an acute coronary syndrome or 30 days of coronary stenting.

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CONSENT FORM FOR CASE REPORTS

For a patient's consent to publication of information about them in a journal or thesis

Name of person described in article or shown in photograph :_____

Subject matter of photograph or article : _____

Title of article : _____

Medical practitioner or corresponding author : _____

I_____ [insert full name] give my consent for this information about MYSELF OR MY CHILD OR WARD/MY RELATIVE [insert full name]:_____, relating to the subject matter above ("the Information") to appear in a journal article, or to be used for the purpose of a thesis or presentation.

I understand the following :

1. The Information will be published without my name/child's name/relatives name attached and every attempt will be made to ensure anonymity. I understand, however, that complete anonymity cannot be guaranteed. It is possible that somebody somewhere - perhaps, for example, somebody who looked after me/my child/relative, if I was in hospital, or a relative - may identify me.
2. The Information may be published in a journal which is read worldwide or an online journal. Journals are aimed mainly at health care professionals but may be seen by many non-doctors, including journalists.
3. The Information may be placed on a website.
4. I can withdraw my consent at any time before publication, but once the Information has been committed to publication it will not be possible to withdraw the consent.

Signed:_____ Date: _____

Signature of requesting medical practitioner/health care worker:

_____Date:_____

Case Report

Sheehan's Syndrome Presenting with hypernatraemia with refractory hypotension and hyponatremia

M P Das* A Agarwalla**, U Kalita**, S Kalita**

ABSTRACT

Sheehan syndrome (SS) or post partum necrosis of pituitary gland, is a rare complication of post partum haemorrhage usually presenting with failure of lactation and subsequent amenorrhoea.[1] It can also present acutely with circulatory collapse, congestive cardiac failure and hypotension.[2] We report two cases, one patient 28 year old with history of secondary amenorrhoea and lactational failure following child birth complicated severe post partum haemorrhage, who presented to us with anemia, hypotension and hypernatremia. Hormonal assays revealed low pituitary hormones, sub normal levels of cortisol and thyroid hormones, with magnetic resonance imaging of the brain suggestive of pituitary apoplexy.

Another case, a 30 year old woman presented with irrelevant talking, altered behaviour, loss of secondary sexual characters with lactational failure and hyponatremia. Hormonal assays revealed low pituitary hormones, sub normal levels of cortisol and thyroid hormones, with magnetic resonance imaging of the brain suggestive of SS with empty sella. Hence, there should be a high index of clinical suspicion for Sheehan's syndrome in women with secondary amenorrhoea and lactational failure with hypernatremia with refractory hypotension as well as hypernatremia.

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INTRODUCTION :

Sheehan syndrome (SS) or post partum necrosis of pituitary gland, is a rare complication of post partum haemorrhage, first described by H L Sheehan in 1937.[3] It occurs as a result of ischaemic injury to anterior pituitary due to severe post partum haemorrhage. Clinically, SS is suspected in a women presenting with a history of post partum haemorrhage with failure of lactation and subsequent amenorrhoea. However, clinical manifestations may be subtle and variable, from asymptomatic cases to lactational failure, secondary amenorrhoea, neuropsychiatric manifestation like psychosis and seizures etc [1], or electrolyte imbalance and hypotension. *Two cases of SS, one presenting with late onset of neuropsychiatric features characterised by a state of acute confusion and abnormal posturing along with hyponatremia, while other with refractory hypotension with hypernatremia, which is a uncommon presentation of the disease.*

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CASE 1

A 28-year-old mother, presented to the Emergency Department with hypotension with history of loose stools 4 episodes per day for two days. There was preceding history of low grade fever for 4 days.

There was no history of acute blood loss, vomiting, swelling of legs, decrease in urine output, intake of any drugs or any illicit substances or bladder dysfunction. The patient had no history of cardiac disease or diabetes mellitus.

On examination, she had pallor, hypotension (BP 70/50mm Hg), with tachycardia (pulse rate 104/min) and a respiratory rate of 25/min. She was conscious, oriented but restless. There were no signs of meningeal irritation, papilledema or focal neurological deficits. Examination of the other systems revealed no significant abnormalities. There was no pubic and axillary hair.

Laboratory investigations (Table 1) showed hypernatremia with hypokalemia with moderate anemia. The other electrolytes calcium and magnesium were normal. The liver function tests were normal. Serum creatinine was elevated. The chest X ray, ultrasonography of abdomen and electrocardiogram revealed no abnormality.

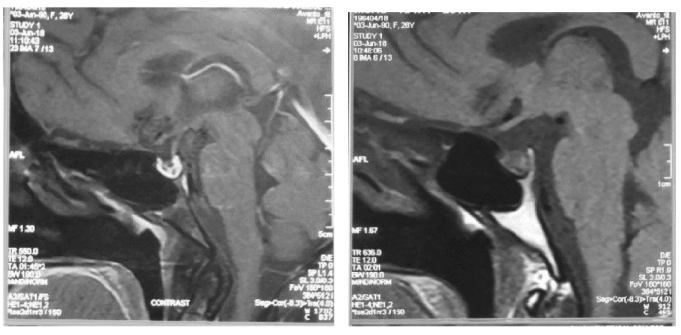
Table 1

Laboratory Parameter {units}	First Patient (case 1)	Second patient (Case 2)	Reference Values
Haemogram			
Hemoglobin (gm/dl)	8.4	8.5	13-15
Total Leucocytic count (x10³/µl)	10.43	4.1	4-11
Differential leucocytic count (%)			
N	85.7	73.3	37-72
L	9.0	14.3	20-40
M	5.2	9.3	2-10
E	0.1	4.2	1-6
Platelet count(x10³/µl)	152	160	150-400
Erythrocyte Sedimentation rate (mm/h)	100	70	20-40
Biochemistry			
RBS(mg/dl)	83	110	80-120
Urea (mg/dl)	21	17	19.3-22.8
Creatinine(mg/dl)	2.7	0.5	0.5-1.3
Serum Calcium (mg/dL)	**8.1**	**5.7**	**8.4-10.2**
Sodium (meq/L)	155	109	137-145
Potassium(meq/L)	3.1	3.7	3.5-5.1
Magnesium(mg/dl)	2	1.7	1.6-2.3
Bilirubin (mg/dl) Total	0.5	0.8	0.2-1.3
Direct	0.0	0.0	0.0-0.3
Indirect	0.1	0.3	0.0-1.1
AlT(lU/L)	46	37	17-59
AST(lU/L)	78	25	21-72
ALP (lU/L)	80	58	38-126
Coagulation Profile			
PT	19	17	16
INR	1.46	1.1	1
TotalProtein(g/dL)	4.9	5.1	6.3-8.2
S.Albumin(g/dL)	2.1	2.7	3.5-5
Hormonal Assay			
TSH (mIU/L)	1.08	1.40	0.46-4.6
FT3 (pmol/L)	1.88	2.2	4.2-8.1
FT4 (pmol/L)	1.71	4.98	10-28
FSH(mIU/L)	10.93	13.4	25.8-135
LH(mIU/L)	8.84	7.42	7.9-59
Cortisol(µg/dl) 8.00AM	5.1	2.1	6.22-19.4

On further enquiry, it was found that the patient gave birth to a preterm child at age of 21 years, followed by severe post partum haemorrhage leading to shock which required three units of blood transfusion. During the post partum period she failed to lactate, had decreased libido and developed amenorrhoea which was persisting.

We started on iv antibiotics and fluid replacement. We gave 0.9% NS and 0.45 % NS, oral plain water and oral rehydration salt was advised. Serial electrolyte monitoring was done. Hypernatremia got corrected with adequate fluid supplementation but the blood pressure remained low. Further inotropes (nor adrenaline) was started suspecting sepsis and later hydrocortisone was given following which patient improved and BP came to normal. Hydrocortisone along with antibiotics were continued for 7 days and hydrocortisone was tapered and discontinued. But the patient developed hypotension again and tests were carried out to investigate the cause of hypotension and secondary amenorrhoea. Hormonal assays (Table 1)showed low levels of free thyroxine (FT4) and (FT3). Also at 8:00am cortisol levels were below normal range. Measurement of plasma ACTH and cosyntropin challenge test could not be done. Magnetic resonance imaging of the pituitary gland showed reduced bulk of pituitary gland with few non enhancing areas in between suggestive of pituitary apoplexy (Figures 1 and 2).

Fig.1 and 2 MR imaging of the pituitary gland in Sheehan syndrome



With this clinical and laboratory findings, a diagnosis of Sheehan's syndrome with pituitary apoplexy presenting with refractory hypotension with hypernatremia was made. The patient was started on replacement corticosteroid (hydrocortisone and estrogen progesterone oral contraceptive tablets) and thyroxine. Initiation of replacement therapy normalised the blood pressure and the patient was discharged home and on follow up she is doing well.

CASE 2

A 30 year old woman presented to the Emergency Department with altered sensorium and history of irrelevant talking. There was no history of fever, acute blood loss, intake of any drugs or illicit substances or bowel or bladder dysfunction.

On examination she had pallor, BP was normal (96/60 mm Hg), with pulse rate of 80/min and respiratory rate of 20 /min. She was conscious but disoriented and restless. There were no signs of meningeal irritation, papilledema or focal neurological deficits. Examination of the other systems revealed no significant abnormalities.

Laboratory investigations (Table 1) showed hyponatremia with hypocalcemia and moderate anemia. The other electrolytes potassium and magnesium were normal. The liver function tests and renal function tests were normal. The chest X ray, ultrasonography of abdomen, electrocardiogram and CT brain revealed no abnormality.

On further enquiry, it was found that the patient gave birth at age of 22 years, followed by severe post partum haemorrhage leading to shock which required two units of blood transfusion. During the post partum period she failed to lactate, had decreased libido and developed amenorrhoea. With this clinical and laboratory findings a diagnosis of SS with pituitary apoplexy presenting with hyponatremia was made.

Sodium replacement (both intravenous and oral 3% NaCl) was initiated and serial electrolyte monitoring was done but there was persistent hyponatremia which was not being fully corrected after adequate sodium replacement. Further tests were carried out to find out the cause of secondary amenorrhoea and persistent hyponatremia. Hormonal assays (Table 1) showed low levels of free thyroxine (FT4), 8:00am cortisol and FSH and LH were also below normal range.

Magnetic resonance imaging of the pituitary gland showed atrophy of the anterior lobe of pituitary gland with empty sella without any focal lesion (Figure 3).

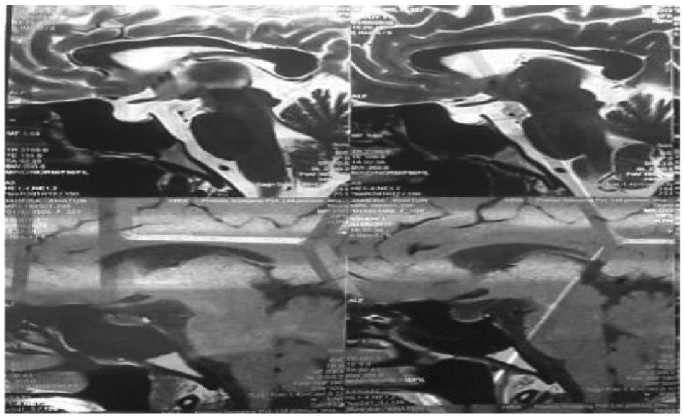


Fig. 3 MR imaging of the pituitary gland in Sheehan syndrome

With this clinical and laboratory findings a diagnosis of SS with pituitary failure presenting with delayed onset neuropsychiatric manifestations and hyponatremia was made.

The patient was started first on replacement therapy of hydrocortisone and estrogen progesterone tablets and later thyroxine was added to avoid aggravting pituitary crisis. Initiation of replacement therapy lead to gradual correction of hyponatremia and resolution of clinical symptoms. The patient was discharged home and subsequent follow up visits were normal.

DISSCUSSION :

Sheehan's syndrome is characterised by ischaemic anterior pituitary insufficiency usually preceded by post partum haemorrhage (PPH).

Enlargement of pituitary gland, small sellar size, disseminated intravascular coagulation and autoimmunity have also been suggested to play a role in the pathogenesis of the disease. SS is characterised by varying degrees of dysfunction of the anterior pituitary.[4] The anterior pituitary is mainly supplied by portal venous system which is a low pressure system. Enlargement of pituitary cells particularly lactotrophs occur during pregnancy, but without a corresponding matching increase in vascular supply.[5] So, whenever the pituitary becomes vulnerable to hypo perfusionin post partum period, ischaemic necrosis of pituitary gland occurs. It is commonly suspected when the mother complains of failure of lactation or difficulty in lactation and amenorrhoea following child birth. SS can range from pan hypopituitarism to selective hormone loss.[6] The mean age at diagnosis is variable[6] ranging from 48.2±10 to 60.1±3.4 years. Our cases presented at a comparatively younger age of around 30 years. The time in years between the inciting delivery and diagnosis is variable[7,8], ranging from 13.9±6.1 to 26.8±2.5 years. However our case had a much shorter time of presentation since inciting pregnancy of only 7-8 years. Thus in our case we see a relatively early presentation in younger patient, in comparison to the usually more delayed presentation of SS.

Also our patient was found to be moderately anemia. Anemia has been found to be reported in as many as 63.8% patients with SS in one study.[9] Overall, the prevalence of hyponatremia in cases of SS has been variable[7,9] ranges from 21-32%. There are several possible mechanisms by which hypopituraism can result in hyponatremia. Hypothyroidism can cause decreased in free water clearance and subsequent hyponatremia. Glucocorticoid deficiency can also free water clearance independent of vasopressin. Hypopituitarism itself can stimulate vasopressin secretion and can cause severe inappropriate secretion of anti diuretic hormone, which can also cause hyponatremia. The potassium level in these situations is normal, because adrenal production is not dependent on the pituitary.[10] Severe hyponatremia leading to neuro psychiatric manifestations and acute confusional state as presenting symptom in Sheehan syndromehas been rarely described in the literature.[11] Acute pituitary insufficiency, also called pituitary crisis, is a life threatening condition following a period of non specific symptoms due to chronic pituitary insufficiency, is caused by electrolyte imbalance, infection, trauma or other forms of stress. Volume depletion and low cardiac output are common in acute pituitary deficiency and recovery of normal cardiovascular status is rapidly achieved under volume and hormone replacement therapy.[2] Cathecholamine overproduction during stress may be toxic to the myocardium, which is unprotected by inadequate glucocorticoids, impairing cardiac function; glucocorticoid deficiency disturbs the transport function of the membrane calcium pump, affecting myocardial contractility.[12,13] The hypernatremia in our case of SS was probably because of more amount of fluid loss as compared to sodium loss due to diarrhoea which got corrected on giving fluids, but hypotension which not corrected by fluids and inotrophs and improved only by giving steroids, on a background history of post partum haemorrhage and secondary amenorrhoea arised a suspicion of SS.

CONCLUSION :

Diagnosis of SS is often challenging and a high index of suspicion and clinical acumen is needed to diagnose this entity. Deficiency of various pituitary hormones and their target hormones produces a myriad of clinical features. MRI of the brain and pituitary fossa may show an empty sella or evidence of haemorrhage but is neither diagnostic nor mandatory[14], which highlights the importance of proper history and clinical examination of patients of SS.

We report this two cases of SS one with refractory hypotension with hypernatremia and

other with hyponatremia. Keeping in view with varied clinical manifestations of SS, so the possibility of SS should be kept in the differential diagnosis whenever a woman comes with electrolyte abnormalities especially sodium, acute confusional state and refractory hypotension with a history of post partum haemorrhage and secondary amenorrhoea.

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Case Report

Human cutaneous dirofilariasis presenting as cervical lump

B Thakuria*, N Goswami, T Maitra***, P Dewraja******

ABSTRACT

Human dirofilariasis is a rare infection caused by the nematode Dirofilaria.The parasites are transmitted to man by mosquitoes.We report a case of human subcutaneous dirofilarisis caused by dirofilariaspp[1]. The patient presented with a cervical lump for two months. Since subcutaneous dirofilariasis is not uncommon In Assam, it should be considered as one of the differential diagnoses for cervical lump in this region.

Keywords: *Cervical Lump, Dirofilariainfection.*

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INTRODUCTION :

Human dirofilariasis is a rare infection caused by nematode Dirofilaria. The life cycle has two hosts, a vertebrate species (definitive host) i.e. domestic or wild animal; and blood sucking zoo anthrophilic arthropod like Culex, Anopheles, and Aedes; which act as intermediate hosts. Because human is an abnormal host, the parasite never develops fully in it.[1] Eosinophilia levels and antifilarial antibody titres are not commonly elevated. These infections usually do not respond to anti-filarial chemotherapy. Excisional biopsy is both diagnostic and curative.[2]

CASE REPORT :

A 53 years old male from central Assam presented to the medicine outdoor of GMCH with painless swelling in left side of neck for two months. There was no history of significant weight loss, cough or evening rise of temperature. It started as a small swelling and gradually increased in size.

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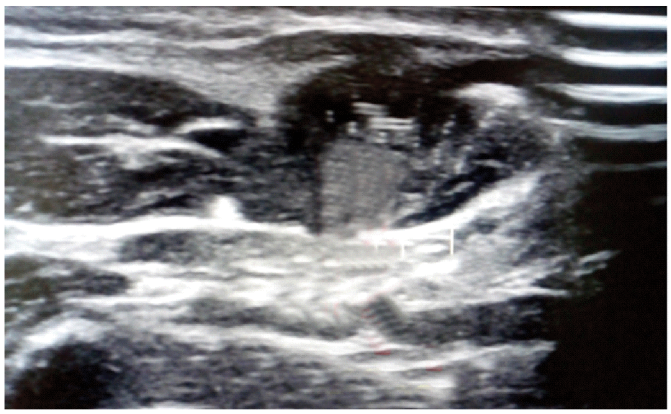
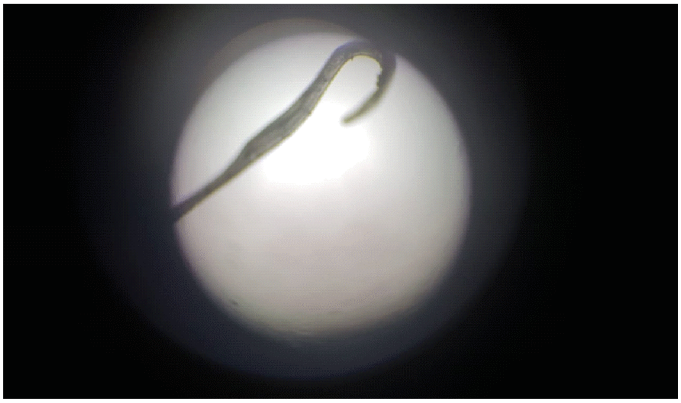
On clinical examination, the swelling was 2X2 cm^2, nontender, with no discharge or any punctum present.

Systemic examination was within normal limit. Investigations revealed: Total Count 7500(N:70% L:25 M4% E 1%), ESR 15mm, HB 12gm%,CXR normal.

USG neck showed an ill-defined hypoechoic lesion in the left lateral aspect of neck (? Lymphadenitis/? Parasitic infection).

Excision biopsy showed one live worm identified as dirofilaria spp.





DISCUSSION :

Zoonotic filariodoses are common in human. The number of human dirofilarisis reported in last 50 years has gradually increased, and it may be described as one of the emerging zoonoses. The first case of subcutaneous infection with Dirofilaria from India, in 1989, was a child manifesting as portal cavernoma with pulmonary dirofilariasis.[3] Simple excision is the treatment of choice for subcutaneous dirofilariasis and there is no role of antihelminthic drugs. In India, while dirofilariasis is considered endemic in Sothern India, it is not uncommon in Northeast India.[1] So it should be considered as one of the differential diagnoses for cervical lump in this region.

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Case Report

Family with Cook's Syndrome from North East India

D Balaji[*], H R Bharath[*], B Jain[*], A Dutta[**], A K Pegu[***], S M Baruah[****], C Dutta[*****]

ABSTRACT

Various genetic disorders of nails and digits have been described in literature with association of major organs like heart, liver, kidneys etc. Their identification in general examination may be a valuable clue to any underlying disease. We describe a patient with congenital anonychia-onychodystrophy, brachydactyly, absent distal phalenges, features of which were consistent with a rare genetic syndrome first described by Cooks *et al* in 1985, namely Cooks syndrome. Three successive generation of family members of this patient were also found to get affected reinforcing its autosomal dominant mode of inheritance. Very few cases of Cook's syndrome have been reported in world literature and this is the first case report from North East India.

Keywords : *Rare disease, Autosomal dominant, Brachydactyly, Onychodystrophy, Family members.*

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INTRODUCTION :

Several genetic disorders exist which can cause anonychia and onychodystrophy, such disorders often cause other anomalies such as deafness, mental retardation, defects of the hair, eyes and teeth. Cooks *et al* in 1985, described a rare such disorder called Cook's syndrome with no systemic anomaly.[1] It is a rare congenital syndrome with autosomal dominant mode of inheritance. It is characterized by anonychia, onychodystrophy, brachydactyly, hypoplasia or absence of distal phalanges of the hands and feet with out any systemic involvement. Till now, only 21 cases have been studied in world literature. Here we describe a patient with features consistent with Cooks syndrome with a positive family history of similar deformity.

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CASE STUDY :

A 63 year old male patient got admitted for complaints of vomiting and loose stools. We did routine investigation with routine stool and culture. Complete blood count shows raised total count with neutrophilia. Stool routine shows presence of pus cells, RBCs. He had moderate dehydration and sinus tachycardia. He was diagnosed as Acute Bacillary dysentery for which he received intravenous fluids and antibiotics and recovered well but interesting was that Clinical examination reveals short digits in both hands since birth except thumbs. Onychodystrophy was seen in 2^{nd},3^{rd},4^{th} digits in both hands. Anonychia was seen in little finger of both hands. Fifth digit in both hands showed severe hypoplasia as compared to other digits. Bulbous swelling was present in 2^{nd},3^{rd},4^{th} and 5^{th} digits. Examination of feet was found to be normal. No facial anomaly was present. Other skeletal structures were normal.

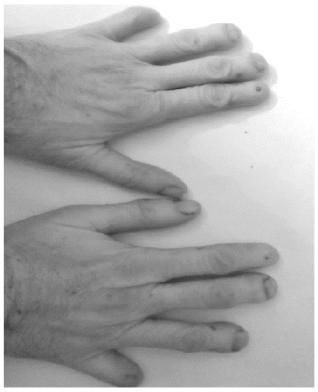


Figure 1: Anonychia of both little fingers, Onychodystrophy of 2nd,3rd,4th digit, Brachydactyly of little fingers.

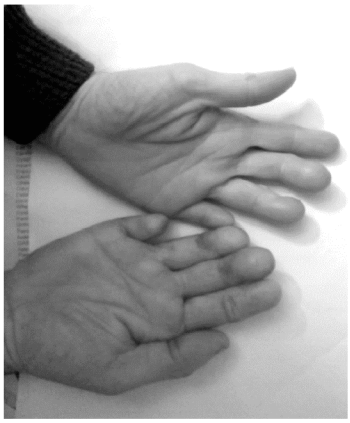


Figure 2: Bulbous swelling of 2nd,3rd,4th,5th digits

We did radiological investigations such as X ray both hand in AP and lateral view to look for malformation of digits such as aplasia/hypoplasia of phalanges and other anomaly .

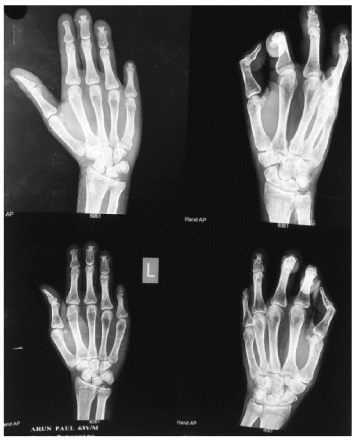


Figure 3: Loss of distal phalanges of 2nd,3rd,4th,5th digit with hypoplasia of middle phalanx of little fingers.

The patient was accompanied by his son and when we did clinical examination of his son, we also found similar features were present in his son's digits. Toe digits looked normal, no facial anomaly, no other bony deformity present. The following image shows digits of his son.

Figure 4: Hands of patient's son showing Brachydactyly of little digits, Thumb deformity, Onychodystrophy of index finger.

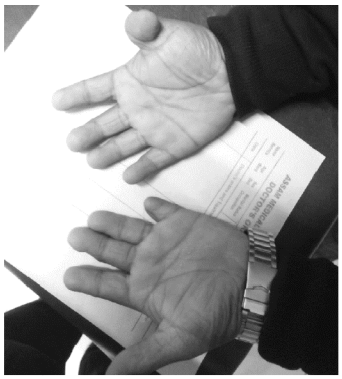
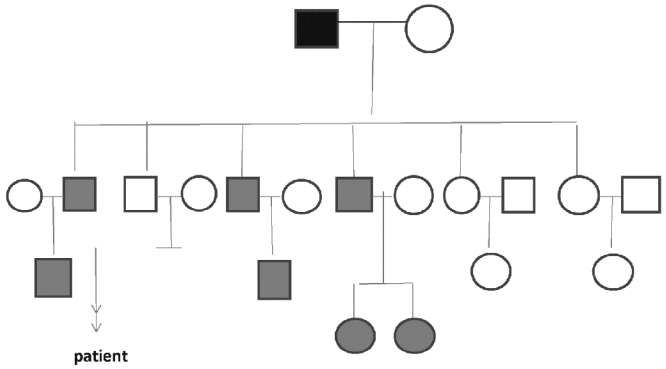


Figure 5: Hands of patient's son showing bulbous swelling of 3rd,4th digits.

On probing into the family history, the patient recalled that similar picture was present in his father, brother and his niece. No history of consanguineous marriage. There were also diffusely spread depigmented patches all over the body suggestive of Vitiligo. Hence, we did thyroid profile, diabetic profile, vitamin B12 study to rule out other autoimmune disease, but everything came to be normal. We also did Ultrasound of whole abdomen, Echocardiogram to rule out any congenital anomaly involving organs, but there was no other congenital anomaly.

Image 6 : Family tree of the patient



DISCUSSION :

Cooks *et al* in 1985, described a rare form of nail dysplasia along with bone abnormality without any systemic involvement which was not recognised previously in seven members of a family in two successive generations. In the hands, which Cooks *et al* described , there was progressive dysplasia of nails involving digits 1st,2nd and 3rd in both the hands whereas in digits 4th and 5th there was complete absence of nails. Fifth digits of both the hands were more shortened as compared to rest of other digits. Some affected members showed lengthening of 1st digit. In the toes, there was complete absence of nails in all digits. It was proposed that the inheritance of this disorder is autosomal dominant.

In 1995, N C Nevin *et al* described the presence of similar features as described by Cooks in four members of a family with three successive generations.[2] This was the second family where

Cooks syndrome was confirmed. Their study confirmed that the inheritance of this disorder as Autosomal dominant.

In 1999, a sibling pair born to normal non-consanguineous couple was found with Brachydactyly type B (BDB). Because the disorder principally involves the nails and distal phlanges, the study group concluded that Cooks syndrome and Brachydactyly type B (BDB) are same entity.[3] However, in 2007, a literature was carried out on 2 year old girl affected with Brachydactyly type B (BDB) in order to delineate the Cooks syndrome clinical spectrum from Brachydactyly type B (BDB) and it was found that the two syndromes were distinct clinically, radiologically and genetically.[4]

In India, Cooks syndrome variant[5] was reported in 2014, in a 45 year old male with congenital anonychia and brachydactyly of the left foot and in 2015, in a 4-day-old baby with congenital anonychia of all the digits in hands and toes with others features consistent with Cooks syndrome.[6]

The exact etiology of Cooks syndrome is still unknown, but microduplications on chromosome 17q24.3 involving SOX9 gene (non coding segment) have been implicated as a cause in some patients with Cooks syndrome. The SOX9 gene was necessary for chondrocyte differentiation and cartilage formation with defective gene resulting in nail and digital anomaly.

Although several genetic disorders exist which can cause Anonychia and Onychodystrophy, such disorders often cause other anomalies such as deafness, mental retardation, defects of the hair, eyes and teeth whereas Cooks syndrome doesn't cause any such anomaly.

In autosomal dominant Dermatosis, congenital anonychia was present along with long standing hypo- and- hyper- pigmentation involving axilla and groins, dry palmar and plantar skin and hair anomaly.

In autosomal dominant onychodystrophy and anonychia, congenital nail dysplasia and/or absent nails along with hypoplasia of metacarpals.

In several other syndromes involving nails and finger, other clinical features coexist.Neither the family described by Cook *et al*, nor the family described by our study had no anomaly involving organs, hair, teeth and no mental retardation.

CONCLUSION :

Cooks syndrome is a rare syndrome involving digits and phalanges of hands and digits with autosomal dominant mode of inheritance without any systemic involvement. In such way it differs from other syndrome involving nails and digits. Till now, only 21 cases have been described in the world with 3 cases reported in India.

Acknowledgement :

We would like to thank Dr. Purnabrat kashyap, Dr. Trinayani Barua, Dr. Bhabani Sankar Dhal, Dr Kaushik Kakoti, Dr. Amit Kumar, Dr. Sunita Lamicheny from Medicine unit 5, Assam Medical College and Hospital for their cooperation.

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Letter to Editor

Correlation of acetylcholinesterase levels with diagnosis, severity and prognosis of organophosphorous (op) compound poisoning

Sir Editor,

I have read with interest the article on "correlation of acetylcholinesterase levels with diagnosis, severity and prognosis of organophosphorous (OP) compound poisoning". In India organophosphorous compound poisoning is the third most common mode of suicide according to the National Poison Information Centre, India.[1] Therefore, when such patients come to hospital we need a reliable and ideal indicator for diagnosis and prognosis of organophosphorous compound poisoning and we were pleased to see that above study was conducted in the same direction. Above study has extensively studied various clinical presentations of OP poisoning with their frequency.

Acetylcholinesterase is inhibited by organophosphorous compound. It is present in serum and in RBC. There were studies which believed that estimation of both serum acetylcholinesterase and RBC acetylcholinesterase correlate well with the clinical condition.[2] Above mentioned study, very noticeably concluded the reliability of estimation of serum cholinesterase levels for diagnosis and prognosis of OP poisoning. Majidi M *et al.*[3] study showed that estimation of RBC acetylcholinesterase is more accurate than serum acetylcholinesterase. Estimation of acetylcholinesterase is not available widely, especially in the peripheries of India.

It was very interesting to note the observation from above study that acetylcholinesterase enzyme levels decreased till the first week of treatment; however, clinical improvement preceded the recovery of enzyme levels.

However, the present study did not mention anything about the type of OP compound. Eddleston *et al.* reported that different organophosphates have different chemical characteristics and poisoning outcomes, and the relationship between enzyme inhibition and mortality in one is not applicable to the other compound.[4] The study didn't mention about the relationship between dose of atropine with the cholinesterase level. In Hiremath P *et al*[5] study, they concluded that there was no relation between the two whereas in Avasthi G et al.[6]

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Medi-Quiz

D Das*

1. Which of the following clinical feature is least likely in a case of acute streptococcal pharyngitis?

a. Tonsillar exudates
b. Anterior cervical lymphadenopathy
c. Cough
d. Fever

2. False about Flatbush diabetes

a. Middle aged obese, hypertensive male with acanthosis nigricans
b. Ketosis prone
c. Absence of autoimmune markers
d. None of the above

3. Which of the following drug is used in male infertility which is produced from urine of post menopausal women?

a. Goserelin
b. Menotropin(hMG)
c. Synthetic FSH
d. Androgen

4. Which of the following influence the natural history of patients with COPD?

a. Smoking cessation
b. Oxygen therapy in chronically hypoxemic patients
c. Lung volume reduction surgery
d. All of the above

5. All are true about protein-losing enteropathy except

a. Low albumin
b. Normal globulin
c. Lymphopenia
d. Intestinal lymphangiectasia can be a cause.

6. False about Type 1 (distal) RTA

a. Nephrolithiasis
b. Hyperkalemia
c. Non anion gap metabolic acidosis
d. Urine pH>5.5

7. What length of time after first motor symptoms in GBS, immunotherapy is no longer effective?

a. 1week
b. 2weeks
c. 3weeks
d. 8weeks

8. Refeeding edema best relates to?

a. Calcium
b. Insulin
c. Oxytocin
d. Paratharmone

9. All are true about SAPHO syndrome except

a. Hidradenitis suppurativa
b. Bull's head sign in Bone scintigraphy
c. No HLA association
d. Drug of Choice is steroid

10. Which of the following produces Red Green birefringent needle crystals in urine?

a. Acyclovir
b. Uric acid
c. CPPD
d. Oxalate

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11. Components of CURB –65 scane are all except
a. Anemia
b. Blood pressure <90mmHg
c. Renal impairment
d. Confusion

12. All the following drugs used in parkinsons disease except
a. Donepezil
b. Levodopa
c. Tolcapan
d. Apomorphine

13. DIC – is seen in which type of AML
a. AML – M1
b. AML – M3
c. AML – M5
d. AML – M7

14. Whipples triad includes all except –
a. Hypoglycemia
b. Insulinomia
c. Response to treatment present
d. Refractory to treatment

15. Site of ghon focus in congenital tuberculosis-
a. Lungs
b. Liver
c. GIT
d. Brain

ANSWER

1: C. cough, in acute pharyngitis presence of cough goes in more favour of viral etiology.
2: D. None of the above
3: B. menotropin or human menopausal gonadotropin which contains FSH & LH.
4: D. All of the above
5: B. normal or high globulin goes against diagnosis of protein-losing enteropathy.
6: B. hypokalemia is a feature of type 1 & 2 RTA but hyperkalemia occurs in Type 4 RTA.
7: B 2weeks.
8: B. refeeding edema may be linked to increased release of insulin which directly increases tubular sodium reabsorption.
9: D. treatments available are NSAIDs, bisphoshonate, anakinra.
10: A. acyclovir.
11. C. Renal impairment
12. A. Donepezil
13. B. AML – M3
14. B. Insulinomia
15. B. Liver