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ORIGINAL ARTICLE

JIACM 2021; 22(1-2): 6-11

mHealth based Mental Health Support Counselling Service for COVID-19 Suspect and Positive Patients in Isolation Facilities

Mina Chandra, Chandra Bhushan Rai**, Vipindeep Kaur Sandhu**, Neelam Kumari**, Surabhi Vishnoi**, Sabah Aman**, Namit Gautam***

Abstract

Introduction: Psychological issues of COVID-19 suspect and positive patients in isolation and quarantine facilities can be addressed using mHealth.

Methodology: mHealth telecounselling framework for COVID-19 inpatients was established using existing manpower and standardised operating procedures. Separate WhatsApp groups were used to obtain contact data of consenting patients, allocate patients to counsellors, and clinical discussion. Telecounselling was documented in real-time in a Google form database and remotely monitored for adherence to the standard of care. Pilot anonymised scale based client satisfaction feedback was obtained from discharged patients using a Google form link shared on WhatsApp.

Results: 2918 telecounselling sessions were conducted between 21 March and 25 June 2020 for 643 inpatients (280 COVID-19 positive and 363 COVID suspect but later determined negative; mean age 49.57 years ± 15.23; male: female = 404: 239).

Psychological issues included anxiety (43.54%), low mood (9.79%), irritability (9.33%), insomnia (8.39%) boredom (8.24%), frustration (7.46%), fearfulness (3.57%) anger (1.24%) and Delusion of pregnancy in one non-compliant psychotic patient.

Interventions provided were supportive psychotherapy (57.69%), psychoeducation (52.72%), counselling regarding testing protocol (41.21%), sleep hygiene (20.06%), relaxation techniques (14.61%), activity scheduling (6.22%). Only 9 (1.39%) patients needed pharmacotherapy.

Most respondents expressed satisfaction on pilot anonymised feedback (n = 115: M: F = 73: 42) with 83% recommending the programme for other COVID-19 settings despite concerns for possible lack of privacy and confidentiality (31.1%).

Conclusion: Telemental Health Counselling Programme is a low cost, feasible, culturally acceptable, and sustainable mHealth initiative which can be easily transposed in other COVID-19 settings.

Key words: COVID-19, Mental Health, Telemental Health, mHealth.

Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by a new virus against which there is no immunity in the community[1]. Given the speed of international spread aggressive case identification by testing, quarantine, and isolation are essential to contain the pandemic.

COVID-19 suspect or positive status can cause significant psychological distress, exacerbated by stringent isolation and quarantine guidelines, and concerns about having possibly infected family members and friends[2,3]. Lack of awareness about COVID-19, its course and outcome coupled with economic challenges due to lockdown result in uncertainty, confusion, and psychological distress, requiring mental health support.

Psychological impact of quarantine and isolation in the COVID-19 pandemic includes anxiety, symptoms of acute stress, anger, fear, grief, insomnia, low mood, depression, frustration, boredom, and confusion in the acute stage and symptoms suggestive of Post-Traumatic Stress Disorder later[3–5].

WHO advises providing psychological support and First Aid which helps people affected by sudden disasters, for which they have no coping mechanism in place, to recover psychologically with dignity[6]. Prevention efforts from a psychiatric perspective must include screening for mental health problems, psychoeducation, and psychosocial support for patients in isolation and quarantine facilities[5].

mHealth initiatives have been advocated extensively to

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reduce treatment gaps and address healthcare inequity[7]. As it is, mental healthcare in India is underserved due to the paucity of psychiatrists, psychologists, and psychiatric social workers[8,9]. At the same time, the risk of acquiring COVID-19 infection to the limited number of counsellors can be mitigated by replacing in-person face-to-face sessions with remote counselling by Telemedicine/ Telepsychiatry approaches.

Dr Ram Manohar Lohia Hospital, New Delhi is a dedicated COVID-19 designated Hospital (CDH) with facilities for screening, testing, isolation, and Corona Intensive Care Units (Corona ICUs). To provide daily mental health support counselling for COVID-19 suspect and positive patients while ensuring the safety of mental health counsellors by preventing avoidable exposure, an innovative strategy of commencing Telemental Health support counselling service was undertaken under the mHealth paradigm.

Methodology

Telemedicine norms had already been notified by Medical Council of India in March 2020[10]. The telemedicine model was utilised to design a mental health support program for COVID-19 suspect and positive patients.

Objectives

To provide Tele Mental Health Support Counselling to all Corona suspect or positive patients admitted in various wards of Dr RML Hospital on a daily basis from admission till discharge.

Deliverables

Low cost, feasible, culturally acceptable, and sustainable Tele Mental Health Support Counselling Programme for all COVID-19 suspect and positive patients using mobile Health (mHealth) paradigm and existing trained manpower who may not be able to physically reach the hospital due to lockdown.

Establishment of Tele Mental health support counselling framework

A low cost sustainable tele mental health counselling framework was established in the third week of March 2020 using smartphones and social networking application WhatsApp which was already being used for intradepartmental and interdepartmental academic and administrative communication at our institute. The framework of RMLH Telemental Health Support Counselling Service is given in Fig. 1.

The process of ensuring tele mental health support counselling for all COVID-19 suspect and positive patients without missing any case required development of a Standardised Operating Framework and Standardised Operating Procedure. A core team was constituted for daily monitoring under the supervision of Chief Supervisor (Chandra). The core team (Vishnoi, Rai, Gautam, Gupta T, Aman, Gupta R) set up three WhatsApp groups.

The first WhatsApp group was a daily telephonic number updation and liaison group comprising of nursing incharges of all COVID-19 positive and suspect wards, Gynaecologist in charge of COVID-19 Labour room (a dedicated facility for delivery of COVID-19 suspect and positive pregnant women), Additional Medical Superintendent and Dean (Fig. 1). A format was made for communicating the mobile phone numbers of all admitted COVID-19 suspect and positive patients and shared with nursing incharges of all the wards.

The nursing staff attending COVID suspect and positive patients in different wards were sensitised regarding the need to share the mobile numbers of patients diligently every morning in addition to their patient care duties. They were also trained to fill and update the required format with details of patients, unique hospital id, mobile numbers, new admission, discharge, transfer or death status on a daily basis and share them on WhatsApp groups for collation on a shared excel sheet by a dedicated team member

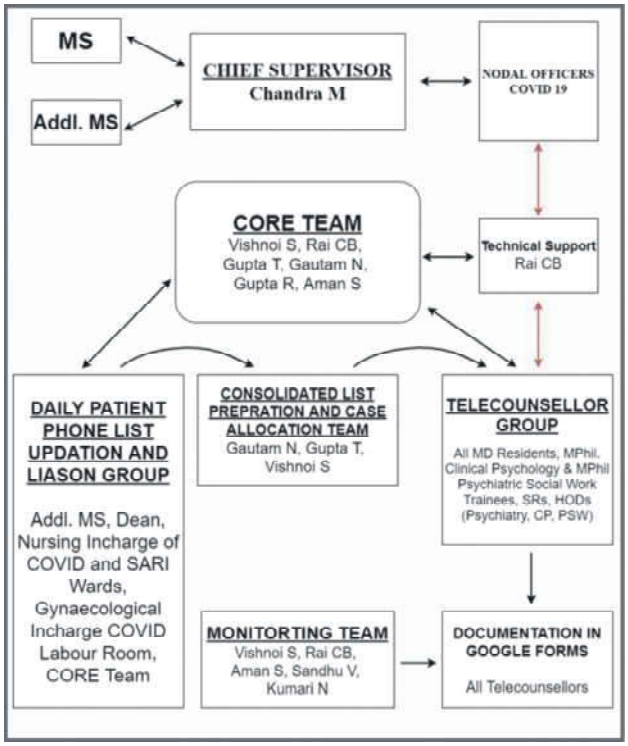


Fig. 1: *mHealth based Mental Health Support Counselling Service framework for COVID 19 suspect and positive patients in isolation facilities.*

(Gautam) and allocation of telemental health counsellors for each patient.

A pool of available counsellors was identified which included 12 MD (Psychiatry) residents, 13 MPhil (Clinical psychology) trainees and 9 MPhil (Psychiatric Social Work) trainees under the overall supervision of lead author (Chandra) (Fig. 1). All the counsellors were briefed regarding the nature of telemental health counselling service delivery, anticipated psychological issues and suggested interventions which can be delivered on the phone. These counsellors were included in a second WhatsApp group along with, Heads of Departments of Psychiatry, Clinical Psychology and Psychiatric Social Work, Core Team and Chief Supervisor. The counsellors received preliminary training on translation of clinical skills on to tele-mental health modality.

The third WhatsApp group was used by the core team to collate contact data of consenting patients from all COVID 19 wards and allocate subsets of patients to different telemental health counsellors on a daily basis, internal communication and problem solving.

A Google form database was created (Rai) and filled in real-time by counsellors with remote monitoring by core team subgroup (Vishnoi, Aman, Sandhu, Kumari). The google form contained mandatory fields like name, age, gender, mobile number. The counsellors documented each session as per a defined format including psychosocial concerns elicited and the psychotherapeutic interventions administered. This ensured adherence to standard of care and standardisation of documentation.

The chief supervisor and members of the core team interacted with the two nodal officers, for COVID-19 in the institute on patient-related issues, periodically on virtual platforms. The chief supervisor briefed Additional Medical Superintendent and Medical Superintendent periodically and sought their help in administrative issues, as required.

There was no face-to-face interaction between team members due to COVID-19-related restrictions and lockdown. The programme was managed remotely with regular interaction between team members on virtual platforms.

Procedure

All the patients admitted in Dr RML Hospital with COVID-19 Suspect or Positive status were provided with an option for Tele Mental Health Support Counselling beginning 21 March, 2020. The counselling continued for the duration of stay on a daily basis until the patient was discharged.

All the consenting patients were contacted by designated counsellors on their mobile number. The tele counsellors assessed the allocated patients telephonically and provided appropriate psychosocial interventions like Supportive Psychotherapy, Sleep Hygiene, Grief Counselling, etc. Any issue that they could not address themselves was posted in a WhatsApp group for first level advice by the core team and second level guidance by Chief Supervisor (Chandra). The status of these cases was updated on WhatsApp till transfer, discharge or death.

Any distress reported by patients was managed as per scientific literature and guidelines issued specifically to tackle the COVID-19 pandemic scenario[11]. If needed, case specific discussion was done with the core team, mentors and supervisor. Formal in-person psychiatric assessment, management and follow-up was done by MD Psychiatry resident under guidance of senior resident (Psychiatry) if required. The list was updated every day with new admissions, discharges/transfers/death by nursing officers of respective wards. All invalid phone numbers of patients were also updated with the help of the nursing staff.

A thematic analysis of data collected in the first month of operations (21 March to 20 April 2020) was conducted. The dominant themes elicited and common interventions provided were incorporated into Version 2 of the google form for better recording of data.

A preliminary assessment of client satisfaction was planned using a 5 item survey called COVID-19 Telecounselling client Satisfaction Scale (COTS) (Appendix) which was derived from TeSS (Telehealth Satisfaction Scale)[12] (after taking due permission from the author) along with open-ended questions on how the counselling help them and any suggestions regarding the provision of Tele Mental Health Support Counselling. The COTS is given in Appendix 1. The discharged patients were shared a link for google form through WhatsApp for providing anonymised feedback. The preliminary results were collated for improving the Telemental health support programme.

Two focused group discussions were held using WhatsApp conference calls after 4 weeks and 7 weeks of the start of the programme on cultural acceptability, feasibility, sustainability of this programme to serve as a model for telemental health support elsewhere in COVID 19 facilities in India and abroad Anecdotal reports on cultural acceptability were also provided by Nodal Officers of COVID 19, Physicians, Anaesthetists, Nursing officers and hospital administration.

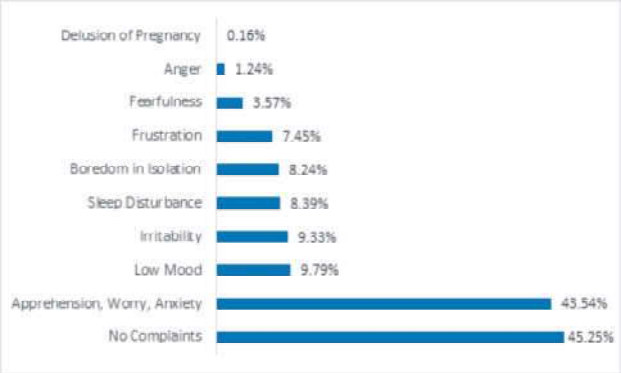
Results

The results of the thematic assessment of dominant psychosocial themes and common interventions for the period 21 March to 25 June, 2020 are as follows.

Of the 877 adult patients admitted in COVID-19 suspect and positive wards, only 658 were in the physical condition to receive tele mental health support services. (Mean age 49.62 ± 15.17 years; Male: Female = 411: 247). 288 patients were COVID-19 positive while 370 patients were COVID-19 suspect but later determined to be COVID negative. 32 patients died during the hospital stay.

2,951 sessions were taken, in which 301 (45.74 %) patients reported no psychosocial concerns spontaneously, 120 (18.23%) patients reported only one psychological issue while 237 (36.01%) patients reported multiple psychological complaints.

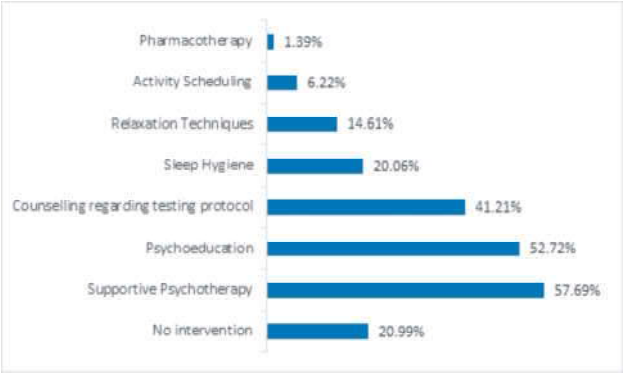
The most common psychological issues were apprehension, worry and anxiety (n = 283; 43.00%), low mood (n = 63; 9.57%), irritability (n = 60; 9.11%) sleep disturbance (n = 56; 8.51%) and boredom in the isolation facility (n = 53; 8.05%), frustration (n = 48; 7.29%), fearfulness(n = 23; 3.49%) and anger issues (n = 9; 1.36%). One patient (< 1%) with pre-existing psychotic illness and not taking any psychotropics currently was found to have Delusion of Pregnancy on Mental Status Examination (Graph 1).



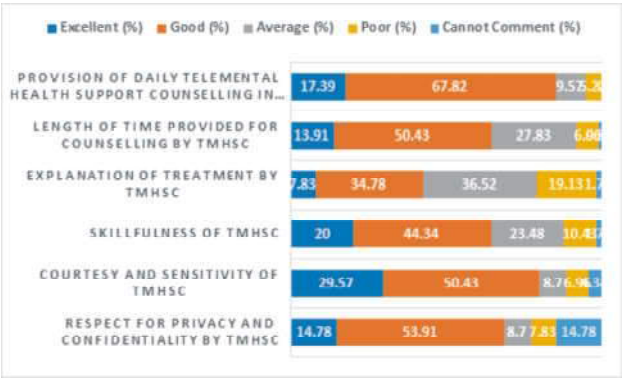
Graph 1: *Psychological complaints elicited in Telemental Health Counselling.*

Only 140 (21.27%) patients did not need any psychological intervention. The most common psychosocial interventions were supportive psychotherapy (n = 374; 56.83%), psychoeducation (n = 348; 52.88%), counselling regarding testing protocol (n = 269; 40.88%), sleep hygiene (n = 130; 19.75%), relaxation techniques to deal with anxiety (n = 95; 14.43%), activity scheduling (n = 40; 6.07%). Only 9 (1.36%) patients needed pharmacotherapy (Graph 2).

The preliminary results of the pilot patient feedback on COTS was encouraging (Table I; Graph 3). Most patients (N = 115; Male: Female = 73:42) were satisfied with the m Health enabled counselling provided in the domains of the provision of the service, length of time for the sessions, explanation of treatment by counsellors, skillfulness, courtesy and sensitivity of counsellors.



Graph 2: *Common interventions provided to COVID 19 suspect and positive patients.*



Graph 3: *Patient satisfaction with mHealth based TeleMental Health Support Counselling (in %).*

On open-ended question for feedback, most respondents opined Telemental Health support Counselling for COVID-19 suspect and positive patients to be a good initiative. 83% respondents also opined that mHealth based Mental Health Support Counselling should be provided in all COVID-19 Isolation and Quarantine Facilities. However, the respondents expressed concern (31.1%) for possible lack of respect for privacy and confidentiality resulting in a repeat briefing of all counsellors by core team for ethical issues, privacy and confidentiality was conducted.

There were some adverse responses too. One patient wanted on-demand round-the-clock calling facility for being able to call back counsellors whenever he wanted, which was not feasible. As per protocol, any patient wanting additional telemental health support after having received the counselling call, was attended by Psychiatry resident on duty. Another patient also recommended right to refuse counselling and this was already available in the programme. However, no inpatient declined any telemental health support session.

Some patients opined that counsellors should not repeatedly inquire about socio-demographic data as they had access

to Google form records. The patients also wanted counsellors to provide non-mental healthcare information regarding COVID status reports, expected date of discharge which was in the purview of the physician responsible for the patient and not the telemental healthcare counsellor.

Results from two virtual focused group discussions after 4 weeks and 7 weeks of the start of the programme supported cultural acceptability, feasibility, sustainability of this programme to serve as a model for telemental health support elsewhere in COVID-19 facilities in India and abroad. The programme continued without any break with no additional requirements of resources or financial outlay indicating toward the feasibility and sustainability of the programme. Anecdotal reports on cultural acceptability provided by Nodal Officers of COVID-19, Physicians, Anaesthetists, Nursing officers, and hospital administration were also favourable.

Discussion

The guidelines from MOHFW and WHO and scientific literature emphasises the importance of social distancing and quarantine for suspected cases and isolation for confirmed cases during COVID-19 pandemic which compounds the stress of being COVID-19 suspect or positive patient[13,14].

Using mHealth based mental health services for counselling inpatients in isolation facilities provides relief and confidence that if needed, mental health support is just a call away[7]. With the use of m Health based service delivery system; a large number of patients can be catered from the place of convenience of telecounsellor remotely. Calling every patient daily helps in tapping their problems at a very early stage and timely intervention.

The development of m Health based Telemental Health Support Counselling programme for COVID-19 suspect and positive patients was made possible by the efforts of all streams of mental health professionals working in the multidisciplinary Centre of Excellence in Mental Health in our institute. This was a low cost programme utilising available manpower and existing resources at no additional cost to the institution.

The Telemental Health Support Service programme was designed to provide counselling to all COVID-19 suspect and positive patients and not just those who showed active psychological symptoms as symptoms are often masked and may not be picked up by non-mental health staff of doctors and nurses who managed COVID-19 facilities and who had no prior psychiatric training.

Clear and real time documentation in google forms allowed seamless takeover of cases by different telemental health counsellors thereby minimising the impact on mental health care delivery. Further, real time mentoring and discussion on difficult cases enhanced the confidence of the telemental health counsellors and improved mental healthcare delivery.

The option of formal in-person psychiatric consultation and psychotropic treatment by Psychiatry resident under the supervision of senior resident (Psychiatry) allowed for early therapeutic intervention whenever needed. In addition, liaison with Nodal Officers COVID-19 allowed for resolution of related issues of test reports, home isolation of caregivers, etc.

We had constant support from Additional Medical Superintendent to resolve administrative issues and Medical Superintendent to implement the programme confidently. This ensured that the programme became sustainable and sought after even by healthcare staff providing medical and nursing care to COVID-19 suspect and positive patients. A separate telemental health support helpline was launched for the benefit of residents, faculty and nursing staff in early May 2020 followed by a dedicated telemental health support helpline for police personnel as requested by Delhi Police after the preliminary success of this programme.

There were several limitations as well. Lack of co-operation from some nursing staff of one ward resulted in a subsection of COVID-19 patients admitted in that ward not receiving telemental health counselling for more than two weeks. Even in these two weeks, psychiatric support was provided to patients exhibiting psychological distress by Psychiatry residents. Alternative arrangements were done by psychiatry residents to obtain phone number list from this ward by liaison with Doctor in charge of that ward. Finally, the situation was resolved with administrative support from hospital authorities.

The newer COVID-19 facilities like COVID-19 Labour Room for pregnant COVID-19 suspect and positive patients and Obstetrics wards started participating later in the programme.

The patients in ICUs who were ambulatory, communicative, and maintaining oxygen saturation could have been provided Tele mental health counseling but the hospital policy of no mobile phone access in ICUs came as a setback. The Telemental Health Support team was not able to receive the mortality data in real time thus preventing therapeutic engagement for bereaved caregivers.

Another limitation of the model was the sharing of the mobile number of tele-counsellors with the patients and caregivers which can impact their privacy though no untoward incident has been reported in our programme till date. In addition, some patients did not have smart phones and the entire session had to be conducted on audio with no video support to assess for facial expression, general appearance and behaviour.

It is anticipated that there are likely to be psychiatric sequelae of COVID-19 infection in short and long-term. Our telemental health support counselling programme also demonstrated the utility of m Health based mental health services in COVID-19 pandemic and other similar disasters. It would be of interest to find out the utility of providing early psychosocial support through telecounselling in mitigating short- and long-term psychiatric sequelae in the coming months[15,16].

Conclusion

COVID-19 pandemic has resulted in a global medical, social, and economic crisis. Suspected COVID-19 infection and admission in isolation wards is a traumatic experience in the context of real risks and amplification by conventional and social media. The need for mental health support is real and apparent along with risk of counsellors contracting COVID-19 infection during in-person sessions. The Telemental Health Support programme addressed both these issues as a low cost, feasible, sustainable, and culturally acceptable solution. This model can be replicated in other COVID-19 facilities with existing mental health resources.

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We would also like to thank PG residents from different departments who liaised with us to effectively implement the Telemental Health Care Support programme and helped avoid possible exposure of core team members. These are Dr Prashant Bankar, Dr Khaise Hareed (MD Anaesthesia residents), Dr Shikha Priya, Dr Arnesh Bhattacharya, Dr Arpit Shastri and Dr Ayushi Singhal (MD Medicine residents).

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ORIGINAL ARTICLE

JIACM 2021; 22(1-2): 12-15

Symptomology of Patients Presenting to the Medicine OPD of a Tertiary Care Hospital with Special Reference to Temporal Variation: A Survey from Eastern India

Rudrajit Paul, Dipanjan Bandyopadhyay***

Introduction

Internal medicine department has the highest patient footfalls in any hospital. Since this department utilises a vast array of medicines, it is often very difficult to keep a steady supply of all drugs without facing the dual problem of drug shortage and drug wastage. In this backdrop, it would be highly desirable to have an idea about the relative percentage of different symptoms with which the patients present to the medicine OPD (outpatient department). Since the treatment strategy for a significant proportion of patients at first contact is symptomatic relief, this data about the relative percentage of different symptoms would help the hospital authority in planning the supply of different drugs. This is particularly relevant for the remote or rural public hospitals, where procurement of medicines is a lengthy process. Also, physicians equipped with this data will be able to devise protocols for the treatment of common conditions. This will help in speeding up the process of patient care at already overloaded and understaffed hospitals of India.

However, the symptomology of patients is not uniform throughout the year. Changes in the length of daylight time, humidity and temperature can alter the intensity and duration of various bodily symptoms. Psychiatry is one field where a seasonal rhythm in various symptoms is well established[1]. Various psychiatric disorders are found to predominate at particular times of the year and this is also reflected in the relative bed occupancy ratio[2]. While this seasonal variation in psychiatric diseases is well-known, other clinical conditions have also been shown to have ups and downs in incidence throughout the year. Some of this can be simply explained by prevailing weather conditions with increase in vector borne diseases like scrub typhus and malaria during the monsoon season in tropical countries. But there are other non-infectious conditions too where there are inexplicable seasonal variations. For example, in a recent study from Kanpur, it was seen that even conditions like toothache and abdominal pain showed significant seasonal variation[3]. However, there are very few Indian studies in this regard.

This variation in symptomology with season has significant implications for the health system. In a resource-limited country like India, especially in the public sector, allocation of resources (medicines, manpower, or beds) is always a contentious issue. Some idea about this seasonal variation in presenting symptoms may help in better allocation of health resources at different times of the year (for example, commissioning a fever clinic or pain clinic at particular times). However, in a vast country like India, there will be considerable geographical variation in symptomology. The symptomology of patients in Medicine OPD will vary widely between the mountains, deserts, coastal areas and forested districts of India. Thus, loco-regional data will be needed to get a complete picture of symptoms of patients.

The present study is aimed at finding the symptomology of patients throughout the year in one urban medicine OPD clinic in a tertiary care hospital of Eastern India. This is expected to generate data which can be used by hospital administrators and health planners of this region.

Material and methods

This was an observational, cross-sectional, hospital-based, questionnaire-based survey. The study was done in the afternoon pay clinic (Medicine) of a Medical College in Kolkata. This particular clinic was functional for two days per week, two hours per day. This clinic was chosen as the general OPD is too crowded for conducting an academic study. The presenting symptoms of all patients presenting to this clinic were recorded. These were the symptoms which the patient described on entering the clinic, without any leading questions. Later, during analysis, the words which implied the same meaning were clubbed together under the same heading. For example, the Bengali terms, "gas", "indigestion" or "bloating" were all clubbed together as dyspepsia. Similarly, "pain in the throat", "blocked nose", "watery discharge from nose" and cough were all clubbed together as "cough and cold". Different Bengali/Hindi terms

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for pain like "Byatha", "Dard", "jontrona", "shulano", etc., were all clubbed together as "pain".

The study was done for a period of one year to capture the 12-month data. Consecutive sampling method was used as it suited the busy work schedule of the authors. One particular study subject was included in the data only once even if he/she came back multiple times for treatment. Only if they came back with a new symptom, they were considered as a new entry for this study.

The data was captured in data entry forms. Then, it was transferred to Microsoft Excel worksheet. Mainly a descriptive analysis of the symptoms was done using Excel software. $P < 0.05$ was considered significant.

Results

There were a total of 957 patients in this survey. Males constituted 55.5% of the patients. Average age was 40.6 ± 14.5 years with an age range of 8 - 88 years. As Table I shows, the maximum proportion (66.6%) of patients belonged to 21 - 50 year age group. Regarding occupation, the largest share was of homemakers (36.5%), followed by office workers (15%), (Table II).

Table I: Age and gender distribution of patients.

Age group (years)	Male (n)	Female (n)	Total (n)
≤ 20	32	42	74
21 - 50	341	296	637
> 50	158	88	246
Total	531	426	957

Table II: Occupation of the study subjects.

Occupation	Number	Percentage
Home maker	349	36.5
Businessman	127	13.3
Labourer	79	8.3
Farmer	32	3.3
In-service	142	14.8
Student	98	10.2
Others	130	13.6

53.2% of the patients had one symptom, 38.5% had two symptoms, 6.7% had three symptoms and 1.5% had four symptoms. In November, patients were more likely to present with multiple symptoms. 28.6% of the OPD patients in November had 3 or 4 symptoms.

Table III describes the main symptoms with which the patients came to this medicine clinic. It is seen that different types of pain were the commonest symptom (51.6%) followed by dyspepsia (16.6%). 7.8% presented with generalised weakness. However, there was great variation in the site of pain (Fig. 1). 32% complained of abdominal pain while 16% complained of hand and foot pain. Headache was complained by 14%.

Table III: Main symptoms with which patients presented to the clinic.

Symptom	Number (n)	Percentage
Pain (anywhere)	494	51.6%
Dyspepsia	159	16.6%
Constipation	47	4.9%
Weakness	75	7.8%
Vertigo	31	3.2%
Cough and cold	83	8.7%
Diabetes	66	6.9%

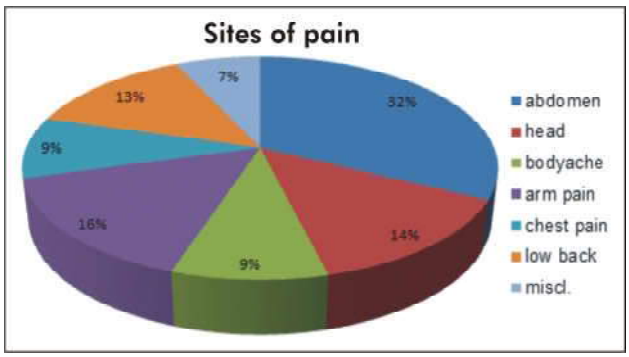

Fig. 1: *Pie chart showing the sites of pain, as complained by the patients.*

Fig. 2 shows the relative percentage of selected symptomology in different months of the year. As seen in this graph, abdominal pain was the commonest (25% of all patients) in October and December. Dyspepsia also peaked in December. Cough and cold peaked in January (around 20% of the patients) with a second smaller peak in October. Headache generally remained between 5 - 10%, except in July, when it showed a significant dip.

Weakness was another common symptom (not mentioned in Fig. 2). It was found that weakness, as the presenting symptom, was the highest in November (13%) followed by April (11.6%). The lowest percentage was in February (2.8%).

Table IV and Fig. 3 show the age and gender distribution of different symptoms/complaints. As seen here, dyspepsia was the commonest in 41 - 50 year age group (28.3%), while headache was commonest in 21 - 40 year group (61.8%). Diabetes, as expected, increased with age. Cough

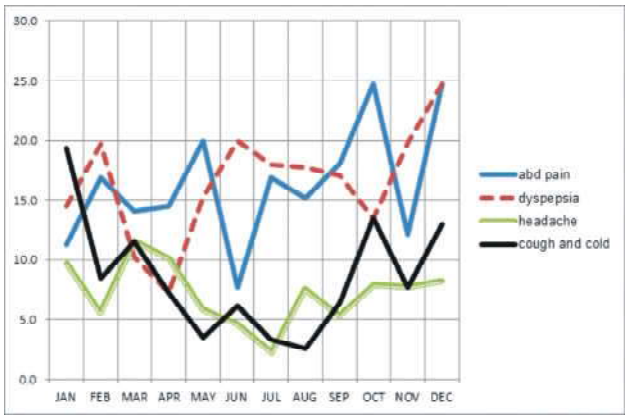

Fig. 2: *Line graph showing monthly relative percentage of some symptoms.*

and cold and constipation were most common in the above - 50 age group. Regarding gender, vertigo was commoner in females (54.8%), while constipation and dyspepsia were commoner in males (61.7% and 62.9% respectively).

Table IV: Table showing age-distribution of different symptoms.

Age group (years)	Dys-pepsia	Consti-pation	Weak-ness	Vertigo	Head-ache	Cough and cold	Dia-betes	Abdo minal pain	LBP
≤ 20	7	1	4	2	10	7	0	21	1
21 - 30	30	9	16	7	23	12	1	44	12
31 - 40	44	14	18	4	19	23	7	40	18
41 - 50	45	8	18	12	10	16	28	35	25
> 50	33	15	19	6	6	25	30	20	11

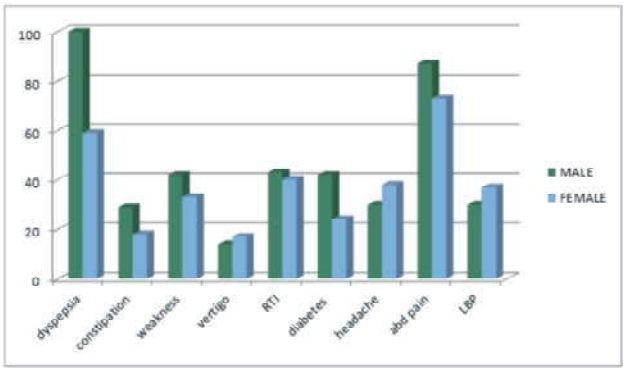

Fig. 3: *Bar diagram showing the gender distribution of some select sympoms.*

Discussion

The present study was a survey undertaken as a public health exercise. This survey has shown that in Eastern India, pain of different in is the commonest symptom of presentation the medicine OPD. Symptoms like abdominal pain and respiratory infection showed considerable seasonal variation.

A similar study was done in a primary health centre of Kanpur[3]. There, the authors observed that presentation with gastritis was the highest in the month of May-June. In our study, abdominal pain and dyspepsia were highest in December. In the study from Kanpur, respiratory infections were the highest in the months of July-August, while in our study we found higher prevalence in December-January (Fig. 2). Overall, the commonest diseases presenting at the OPD in Kanpur health centre were skin infections, respiratory infections, COPD and gastritis. This is quite different from the symptomology of our subjects. But this may be explained by the fact that our study was a medicine OPD based survey in a tertiary centre, where the patients get channelled into severe specialities. But in a PHC, all patients will come to the same OPD.

A survey done in Nepal showed that acute respiratory infections (ARI) were the commonest cause of OPD visit, followed by wound infection, acid peptic disease and diarrhoea[4]. But this survey was done between the months of July and September and thus, gives no idea of the symptomology at other times of the year. Common symptoms like diarrhoea and minor wounds are more likely to be treated at a local level and thus, the patients coming to tertiary care hospitals like ours are likely to have other problems.

Similar to our study, Sharma *et al* also documented higher prevalence of ARI in winter months[5]. They also found that ARI was commoner in females. But in the present study, no such gender difference in ARI was found (Fig. 3). Sharma *et al* also reported higher presentation with diarrhoea in the summer months. But in our study, the number of diarrhoea patients was too small for analysis.

A study done in the OPD of a tertiary care hospital of Sri Lanka in 2012 reported that the main symptoms at OPD visit were body aches, cough and cold and abdominal pain[6]. They also reported that body ache was the commonest presenting symptom for both genders while abdominal pain and cough were the commonest symptoms in the 20 - 40 year age group. In our study, headache and abdominal pain were the commonest in the 21 - 40 year age group; in females, vertigo, headache and low back pain (LBP) were more common than males. In another recent (2015) study from Pune, it was seen that ARI and musculoskeletal pain were the two commonest causes of OPD visit[7]. Like our study, they also found a peak in ARI in January. They reported very small number of gastritis/dyspepsia cases. Symptoms like low back pain and ARI were commoner in females in Pune.

The reason for higher prevalence of body ache or low back pain in our sample patient population is a matter of speculation. Low back pain is not one uniform entity but there may be multiple causes for this symptom. Similarly dyspepsia is a heterogeneous entity. This survey establishes that non-communicable diseases like peptic ulcer disease or musculoskeletal pain constitute a significant proportion of the patients in the medicine OPD and physicians must be aware of the various management options of these symptoms like dietary modification and biofeedback manoeuvres.

Limitation

There are some limitations of this study. Firstly, this study was conducted in a tertiary care hospital. So, the data may not represent the community based symptoms.

Secondly, the present study is limited by the small number of patients. Also, this survey was conducted in a biweekly medicine clinic of the hospital. Inclusion of OPD patients from all weekdays can give a better idea of the overall symptomology. Also, the symptomology of inpatients was not included here.

Finally, while the symptomology is important, the data on the actual diseases affecting the patients (like diabetes or COPD) is also important for health planning. This can help in manpower deployment during particular seasons. Such studies are planned in the future.

Conclusion

This present study is probably the first of its kind from Eastern India. This study generates data for health planners and hospital administrators which can be used to decide on drug supply and also physician training priorities.

Recommendations

- In view of the high proportion of patients presenting with different types of pain, a separate "pain clinic" may be arranged in the tertiary hospitals of this region. This can be in association with other departments like psychiatry, physical medicine and neurology.
- Supply of medicines for respiratory infections must be increased during the winter months, December and January.
- Physicians attending geriatric clinics must be well versed in the management of conditions like constipation, respiratory infection, or diabetes.

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ORIGINAL ARTICLE

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Risk Factors and Outcome Variables of Cerebral Venous and Sinus Thrombosis in a Tertiary Care Hospital

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Abstract

Introduction: Cerebral venous and sinus thrombosis (CVT) is one of the common causes of stroke in young people. It is a relatively uncommon neurologic disorder that is potentially reversible with prompt diagnosis and appropriate medical care. The purpose of this study is to identify the risk factors and outcome determinants.

Methods: A prospective observational study was conducted at a tertiary care centre in coastal Karnataka from November 2015 to May 2017. Demographic details, symptomatology and history pertaining to risk factors were noted. Outcome and prognosis were assessed by Modified Rankin Scale (mRS) at the time of admission and follow-up after 4 to 6 weeks. Chi-square test was used to compare mRS score at admission and follow-up in relation to outcome variables.

Results: A total of 45 adults with CVT were included. Males (53.3%) were more affected than females (46.7%), mostly in the 3rd decade. The most common risk factors were polycythaemia (31.1%) followed by oral contraceptive pill intake (17.7%). Based on mRS score at admission, 23 patients were functionally independent (mRS≤2) and 22 were functionally dependent (mRS > 2). At 6 weeks' follow-up 73.3% of the patients were functionally independent. Nine patients (20%) underwent decompressive craniotomy, of which seven patients improved, one deteriorated and one expired. The mortality rate was 2.2 %. Two patients were lost to follow-up.

Conclusion: The most common risk factors were polycythaemia followed by intake of oral contraceptive pills. Functional independence was achieved in 73.33% of patients at follow-up. The determinants of poor outcome were altered level of consciousness, presence of neurological deficits and intracerebral haemorrhage at the onset of illness.

Key words: Cerebral venous and sinus thrombosis, stroke, polycythaemia, mRS score.

Introduction

Cerebral venous and sinus thrombosis (CVT) is a type of cerebrovascular disease marked by thrombosis of blood in the cerebral veins, or dural sinuses, and cortical veins. CVT accounts for 0.5% of all strokes and its annual incidence is estimated to be 3 - 4 cases per 1 million population[1]. Strokes in the young account for nearly 30% of all cases of stroke in India and CVT accounts for 10 - 20% of these cases[2]. The mortality is relatively lesser compared with arterial stroke and most of the patients have a good long-term prognosis[3]. There are only few Indian studies on the risk factors, outcome and prognostic factors of cerebral venous thrombosis. The present study will assess the risk factors and outcome determinants of CVT.

Meterial and methods

This was a prospective observational study conducted at Kasturba Hospital, Manipal from November 2015 to May 2017. Data collection was commenced after obtaining ethical clearance certificate (IEC 635/2015) from Kasturba Medical College and Hospital Ethics Committee. A total of 56 patients diagnosed with CVT were considered for screening and enrolment into the study. Of these, 11 patients were excluded based on the exclusion criteria (patients with arterial infarcts and arterial malformations and those that developed as a result of diagnostic and treatment procedures that pierce the dura mater) and 45 patients with CVT of age greater than 18 years, radiologically proven either by CT/MRI brain with MR venography were included in our study after taking written informed consent.

Information regarding baseline patient characteristics, history pertaining to risk factors of CVT, such as intake of oral contraceptive pills, were compiled. All the patients underwent MRI brain with MR venography and treated in the intensive care unit with anti-epileptics, anti-oedema measures (mannitol, furosemide, and glycerol) and anticoagulation as per standard guidelines and protocols. Modified Rankin Scale (mRS) was used for measuring the degree of disability or dependence in the daily activities of living in our study. This scale describes 6 grades of disability (grade 6 denotes death; and grade 0 denotes no symptoms

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at all). mRS score of ≤ 2 was considered as functionally independent and score of > 2 was considered as functionally dependant. mRS score was documented at admission, at discharge and follow-up at 6 weeks.

Laboratory tests such as haemogram, serum homocysteine levels, antinuclear antibody tests and coagulation studies were done to identify the thrombophilia risk factors. Diagnosis of Polycythaemia Vera was made based on the WHO 2016 criteria[4]. Diagnosis of Antiphospholipid syndrome (APS) was made based on the revised Sapporo APS Classification Criteria (also called the Sydney criteria)[5]. Cut-off values for raised serum homocysteine levels were taken as > 15 mg/100 ml in those below 60 years, and > 20 mg/100 ml in those above 60 years of age[6].

Statistical methods

Data analysis and interpretation was done with Statistical Package for the Social Sciences (SPSS) version 15.0. The mean, standard deviation and Chi-square test was used to analyse the data and p value < 0.05 was taken as statistically significant. Chi-square test was used to compare mRS score at admission and follow-up in relation to age, gender, Glasgow Coma Scale (GCS) at presentation, presence of neurological deficits and intracerebral haemorrhage.

Results

A total of 45 patients were included in the study, of which 24 (53.3%) were males and 21 (46.7%) were females. Mean age of the patients was 36.13 ± 13.47 years with 31 (68.9%) patients below 40 years and 14 (31.1%) patients above 40 years of age.

The most common aetiology was polycythaemia (31.1%, n = 14) followed by intake of oral contraceptive pills (17.7%, n = 8), Antiphospholipid syndrome, pregnancy and puerperium, and hyperhomocystinaemia as shown in Fig 1. Out of 14 patients with polycythaemia, 7 (50%) were diagnosed with polycythaemia vera. The others had secondary polycythaemia with 5 (35.7%) having history of cigarette smoking and 2 (14.3%) having history of chronic obstructive pulmonary disease (COPD).

Outcome analysis

Based on mRS score at admission, 23 patients were functionally independent (mRS≤2) and 22 were functionally dependent (mRS>2) as shown in Table I. At 6 weeks, 100% of patients with mRS ≤ 2 at admission remained functionally independent with 65% (n = 15) returning from mRS 2 to mRS 0. Forty-five per cent (n = 10) of the patients with mRS >2 at admission recovered to mRS≤ 2 and were functionally

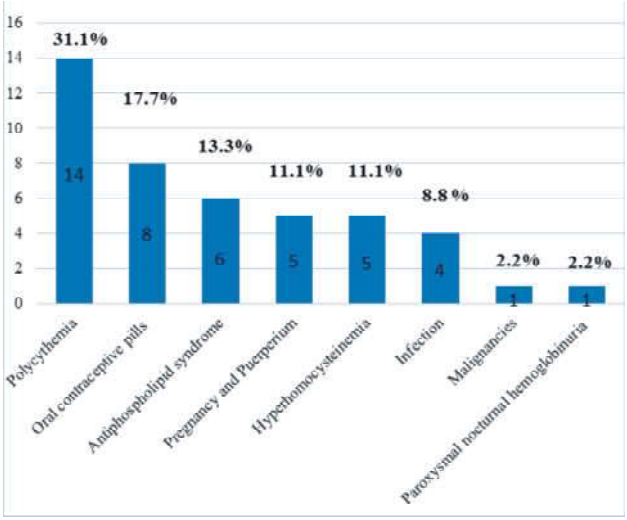

Fig. 1: *Risk factor analysis.*

independent at 6 weeks. Nine patients (20%) underwent decompressive craniotomy, of which seven patients improved, one deteriorated and one (2.2%) expired, which was probably due to cerebral oedema with transtentorial herniation. Two patients (4.4%) were lost to follow-up during the study. Last documented mRS score was taken for evaluation of patients lost to follow-up.

Table I: mRS scores of patients at admission and 6 weeks follow-up.

mRS score	At admission	Follow-up after 6 weeks
	No. of patients (%)	No. of patients (%)
≤ 2	23 (51.1%)	33 (73.3%)
> 2	22 (48.9%)	12 (26.6%)
Total	45	45 (93%)

In patients with baseline mRS ≤ 2 at admission, irrespective of age group, 100% remained functionally independent at 6 weeks follow-up. In patients with mRS > 2 at admission, age cut-off of 40 years was not a predictor of functional independence at 6 weeks follow-up. Age and gender showed no association with outcome as shown in Table II.

There were 15 patients (33.3%) with altered level of consciousness (2 patients in comatose state) at admission. Altered level of consciousness at presentation (i.e., GCS < 15) was associated with poor prognosis as the p value (0.003) was statistically significant. There were total of 19 patients (42.2%) with neurological deficits (11 had hemiparesis, 6 had paraparesis and 2 had quadriparesis). Presence of neurological deficits was associated with poor prognosis as the p value (0.034) was statistically significant. 13 patients (28.8%) had intracerebral haemorrhage at

admission. Presence of intracerebral haemorrhage was associated with poor prognosis as the p value (0.034) and was statistically significant.

Table II: Prognosis based on age and gender.

Demographic characteristics		mRS* ≤ 2	mRS* > 2	p value
Age < 40 years	Admission	18	13	p = 0.468
	Follow-up	24	7	
Age ≥ 40 years	Admission	5	9	
	Follow-up	9	5	
Males	Admission	8	16	p = 0.5
	Follow-up	16	8	
Females	Admission	13	8	
	Follow-up	17	4	

**Modified Rankin scale.*

Table III: Outcome based on GCS, neurological deficits and intracerebral haemorrhage status at admission.

		mRS ≤ 2	mRS > 2	p value
GCS < 15		6	10	p = 0.00005
GCS = 15		27	2	
Neurodeficits	Yes	9	102	p = 0.0007
	No	24	2	
ICH*	Yes	9	10	p = 0.0007
	No	24	10	

*ICH: Intracerebral haemorrhage

Discussion

The study revealed that a significant number of patients affected by CVT were in the 3rd decade of life with mean age being 36.13 ± 13.47 years, which was similar to the observations from various Indian and Western studies such as Pai *et al*[7], Narayan *et al*[8], Wassay *et al*[9] and Ferro *et al*[1]. Most of the earlier case series from India and Western studies like Wassay *et al*[9] and Ferro *et al*[1] have reported a higher proportion of women suffering from CVT, than men. This gender bias was usually attributed to gender specific risk factors like the usage of oral contraceptive pills (OCPs) and the influence of other factors such as pregnancy, puerperium, and hormone replacement therapy. In our study male gender was predominant (53.3%) which was consistent with the observations of recent Indian studies like Pai *et al*[7] (M: F - 3: 2) and Narayan *et al*[8] (M: F - 1.16: 1). The plausible reason for this change in gender trends over the last two decades could be due to usage of less thrombogenic oral contraceptive pills containing levonorgestrel and norethisterone in the recent years[7] or difference in healthcare availability to females.

The most common identified risk factors in our study were polycythaemia (31.1%) followed by intake of oral contraceptive pills (17.7%). Eight patients (17.7 %) had a history of intake of oral contraceptive pills (OCP) with mostly norgestimate and drospirenone as progestins. The incidence of oral contraceptive pills in the causation of CVT is gradually decreasing over the recent years due to the usage of less thrombogenic oral contraceptive pills (containing levonorgestrel and norethisterone).

Six patients (13.3%) were identified having antiphospholipid syndrome as a risk factor, of which 5 patients had primary antiphospholipid syndrome and 1 patient had secondary antiphospholipid syndrome with history of SLE in the past. There were a total of 5 pregnant and puerperal patients (11.1%) and all these patients developed CVT in their third trimester and puerperium, i.e, 6 weeks after delivery. The plausible reason was pregnancy being a hypercoaguable state, which induces several prothrombotic changes in the coagulation system and it worsens after delivery as a result of volume depletion and trauma. During the puerperium, additional risk factors which contribute to causation of CVT include infection and instrumental delivery or caesarean section.

Five patients (11.1%) were detected having hyperhomocysteinaemia and four patients (8.8%) were found to have infection as a risk factor and these infections were identified as paranasal sinusitis, tuberculous meningitis, chronic suppurative otitis media and severe dengue fever with hemoconcentration. One patient (2.2%) had essential thrombocytosis and one patient (2.2%) had paroxysmal nocturnal haemoglobinuria (PNH).

Pai *et al*[7], Narayan *et al*[8], Wassay *et al*[9] have shown that polycythaemia was the most common risk factor for the development of CVT. Ferro *et al* study[1] showed that oral contraceptive pills were the commonest risk factor. The risk of CVT among pregnant and puerperal patients in our study was almost similar to the above studies. The risk of infections leading to CVT was slightly higher than other Indian studies such as Pai *et al*[7] and Narayan *et al*[8]. The reason could be due to our hospital being situated in a rural area and lack of awareness about the significance of these infections among the people.

The risk of malignancy in the causation of CVT in our study was comparable with the other Indian studies such as Pai *et al*[7] and Narayan *et al*[8]; however, western studies like Wassay *et al*[9] and Ferro *et al*[1] have shown higher risk in comparison to Indian studies and the reason could be due to various dietary habits and malignancies being detected more common in developed countries than developing

countries. The incidence of hyperhomocysteinaemia in our study was almost similar with the results of other Indian studies such as Pai *et al*[7] and Narayan *et al*[8]; however, western studies such as Wassay *et al*[9] and Ferro *et al*[1] have shown lower risk and the reason could be due to higher incidence of vitamin B12 deficiency in the Indian population.

In our study, genetic thrombophilia markers such as protein C deficiency, protein S deficiency, antithrombin deficiency, and factor V Leiden (FVL) mutation were not tested due to the financial constraints of our patients, as the hospital being situated in a rural area and majority of patients belonged to low socio-economic standards. However, Pai *et al*[7], Narayan *et al*[8], Wassay *et al*[9] and Ferro *et al*[1] studies have showed that genetic thrombophilia contributes up to 18%, 12.3%, 10% and 22.4% for the causation of CVT, respectively.

Functional independence (assessed by mRS score ≤ 2) was achieved in 73.33 % of patients at 6 weeks of follow-up in our study. 9 patients (20%) underwent decompressive craniotomy, of which seven patients improved, one deteriorated and one expired probably due to cerebral oedema with transtentorial herniation. 14 patients (31.1%) required mechanical ventilation during the hospital stay. 2 patients (4.4%) were lost to follow-up during the study.

Patil *et al*[10] have shown that 84% of patients were discharged with partial and/or total recovery from illness in the form of hemiplegia or monoplegia. 3 patients (6%) underwent decompressive surgery, of which 2 patients improved and 1 succumbed. Eight patients (16%) died with cerebral oedema with transtentorial herniation. Thota Naveen *et al*[11] have shown that 20% of patients underwent decompressive craniectomy as the part of the treatment. 35 (70%) of the 50 patients had complete functional recovery, 9 (18%) had partial recovery independent, 3 (6%) had partial recovery dependent, whereas 3 (6%) died during the hospital stay.

Natarajan *et al*[12] have shown that 43 out of 48 patients (89.6%) recovered without any neurological disability; 2 out of 48 patients (42%) were discharged with minimal residual paresis. Total mortality in their study was 6.2%, i.e., 3 patients expired. Ferro *et al* have shown that 86.6% of the patients recovered without any neurological disability (mRS score ≤ 2). 52 patients (8.3%) had expired. 9 patients (1.4%) had decompressive craniotomy or hematoma evacuation and 7 (1.1%) required mechanical ventilation.

Our study has shown that gender and age have no association with the outcome of patients with CVT. Altered level of consciousness at presentation, presence of neurological deficits and intracerebral haemorrhage were associated with poor outcome. Ferro *et al* also showed that important prognostic factors for poor outcome were age > 37 years, male sex, coma on admission, mental status disorder, intracerebral haemorrhage on admission CT scan of the brain, which were similar to our study. Wassay *et al* study[9] also showed that altered level of consciousness at presentation and intracerebral haemorrhage were the strongest predictors of poor outcome in CVT.

Conclusion

The most common identified risk factors were polycythaemia followed by the intake of oral contraceptive pills. Functional independence, assessed by mRS score of ≤ 2, was achieved in 73.33 % of patients at follow-up. The mortality rate was 2.2%. The determinants of poor outcome in CVT were altered level of consciousness at presentation, presence of neurological deficits and intracerebral haemorrhage.

Strengths of study: All the patients in our study underwent MRI brain with MR venography and the abnormalities in the cerebral venous system were documented and confirmed by qualified radiologists. Majority of the patients were followed-up for 4 to 6 weeks and their functional neurological status was reassessed.

Limitation of study: Our hospital being situated in a rural area and most of the patients belonged to low socio-economic standards, genetic prothrombotic factors leading to cortical vein thrombosis was not evaluated due to financial constraints.

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ORIGINAL ARTICLE

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Pulmonary Hypertension in COPD Patients and its Correlation with Exercise Capacity and Quality of Life of Patients

Ankit Deshwal, Rehbar Khah**, Khamendra Kumar***, Devendra Kumar Singh****, Santosh Kumar*****, Saurabh Srivastava*******

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is associated with extrapulmonary effects and comorbidities that affect both morbidity and mortality[1]. It is difficult to diagnose pulmonary hypertension (PH) clinically at an early stage. The aim of this study was to estimate the prevalence of PH in COPD patients and its correlation with exercise capacity and quality of life of patients.

Material and methods: Detailed history, multisystem clinical examination, random blood sugar, complete blood count, chest radiography and spirometry were done in all patients. COPD patients were enquired for exertional dyspnoea, fatigue and angina, and examined for increased jugular venous pressure, reduced carotid pulse, palpable right ventricle (RV) impulse, loud P_2 right-sided fourth heart sound and peripheral cyanosis. PH was diagnosed by 2D-Echocardiography. Six Minute Walk Test (6MWT) for exercise capacity and Modified Borg's Scale questionnaire and St George's respiratory questionnaire for quality of life were also done.

Results: Out of 97 patients of COPD, 39 patients (40.20%) had PH. Majority of them had mild PH (26.8%). Only a few had severe PH (3.09%). Of total 39 patients having PH, 66.67%, 25.64% and 7.69% had mild, moderate and severe PH, respectively.

Conclusion: The prevalence of PH increased as the age and severity of COPD increased. The exercise capacity and health-related physical quality of life was found to be significantly correlated with PH in COPD patients. Rehabilitation programs, oxygen inhalation or other means to avoid or to delay PH in COPD patients should be implemented timely.

Key words: chronic obstructive pulmonary disease, pulmonary hypertension, extrapulmonary, exercising capacity, quality of life.

Introduction

Chronic Obstructive Pulmonary Disease is the fourth leading cause of deaths globally[1]. Global burden of COPD is projected to increase in coming decades due to continued exposure to risk factors and aging world population. According to Global Burden of Disease study, COPD is expected to become the third leading cause of death by 2020[2,3].

Like many chronic inflammatory conditions, COPD is associated with extrapulmonary effects and comorbidities that affect both morbidity and mortality[1]. In recent years, pulmonary vascular pathology is increasingly being recognised in the pathogenesis of PH. The consequence of pulmonary vascular involvement is an increase in the pulmonary vascular resistance (PVR) and pulmonary artery pressure (PAP) leading to increased afterload or the right ventricle. PH has generally been viewed as a late stage development occurring in patients with severe airways obstruction and a chronic hypoxemic state. Clinical recognition of early stages of PH is difficult.

Pulmonary hypertension is defined as an increased resting mean PAP above 25 mmHg with a pulmonary capillary wedge pressure (PCWP), left atrial pressure or left ventricular end-diastolic pressure of less than 15 mmHg and PVR greater than 3 Wood units[4]. PH complicating COPD is the commonest type of PH presenting to a pulmonologist.

The prevalence of pulmonary hypertension in the general COPD population is undefined because stable COPD patients do not routinely undergo right heart catheterisation. Most studies published on this topic focus on patients with moderate-to-severe disease awaiting lung transplantation because haemodynamic data from cardiac catheterisation are part of the standard transplant evaluation.

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The rationale behind this study was to find the prevalence of PH in stable patients of COPD and effect of PH on exercise capacity and health-related quality of life. Patients of COPD who have PH can be enrolled earlier for pulmonary rehabilitation programme and efforts can be made to make their health-related quality of life and exercise capacity better.

Material and mathods

An observational, cross-sectional study was carried-out on 97 stable COPD patients of stage I, II, III, and IV, according to the criteria laid down by NHLBI/WHO-GOLD 2013, from January, 2013 to October, 2014, at a tertiary care center in North India.

Sampling was done by systematic sampling method. Every k unit of COPD patients in outpatient department (OPD) were selected (k = 4).

Inclusion criteria: All known or newly diagnosed cases of stable COPD on the basis of clinical history, physical examination, chest radiographs and spirometery, irrespective of present smoking status, were enrolled.

Exclusion criteria: Any patient with co-morbidities, which could influence occurrence or severity of PH such as chronic liver disease, rheumatologic disorders like scleroderma or systemic lupus erythematous, lung neoplasms, pulmonary fibrosis, drugs like dexfenfluramine and phentermine, heart diseases like aortic valve disease, left heart failure, mitral valve disease, congenital heart diseases, thromboembolic disease, obesity, sleep apnoea, high altitude and those who did not consent to were excluded.

Every patient was screened by detailed history, thorough clinical examination, complete blood count, random blood sugar, chest radiograph[5-11,12], ECG and spirometry.

All patients were inquired for exertional dyspnoea, fatigue and angina. They were examined for increased jugular venous pressure, reduced carotid pulse, palpable RV impulse, loud $P_{2,}$ right-sided fourth heart sound and peripheral cyanosis. Finally they were evaluated via 2D-echocardiography[12,13] to diagnose PH, six minute walk test (6 M WT)[14] for exercise capacity, modified Borg's scale questionnaire[15-17] and St George's Respiratory Questionnaire[18-20] for quality of life. The St. George's respiratory questionnaire was translated to Hindi and was validated.

Chest radiograph was obtained as part of the initial diagnostic work-up but widening of the descending right pulmonary artery to > 16 mm or the left descending pulmonary artery to > 18 mm was considered as criteria for diagnosing PH on the basis of chest X-ray[21].

Electrocardiogram (ECG)[12,13] findings suggestive of PH include: a) p pulmonale, P-wave amplitude > 2.5 mm in leads II, III, and/or aVF; b) S1, S2, S3 pattern; c) a S1, Q3 pattern; d) incomplete or complete right bundle branch block; e) evidence of RVH, R axis deviation >/= 100°, dominant R wave in lead V1 >/= 7 mm in amplitude, ST segment depression and T wave inversion in leads V1 to V4, and deep S waves in leads V5, V6, I and aVL with a QRS duration < 0.12 s; f) low voltage QRS[22].

Echocardiogram (2D-ECHO):[23-25] value of mPAP > 25 mmHg was considered as cut-off value for labeling the patient as PH. The criteria for severity of PH on the basis mPAP were as follows: mild PH > 25 - 40 mmHg mPAP, moderate PH 41 - 55 mmHg and, severe PH > 55 mmHg.

Statistical analysis: Data was collected, entered and cleaned in MS Excel. Data was analysed using SPSS (Statistical Programme for Social Sciences) Version 16. Categorical data was presented in the form of percentages and continuous data was presented in the form of means and standard deviation.

Calibration of examiners was done to reduce intra-examiner variability. Coordination among all investigators was maintained during study period to maintain the quality of data.

Approval was taken from institutional ethical committee. Nature of study was explained to all participants. Written consent was taken and patient information sheet was also signed by all participants.

Results

Out of the total 97 patients of COPD evaluated for PH, majority were in the age group 66 - 75 years (52.38%), followed by, 56 - 65 years (40%). 82 were male and 15 were female. Out of these 34 male (41.46%) and 5 female (33.3%) were found to have PH (Table I).

Table I: Prevalence of pulmonary hypertension in different age groups.

Age group (years)	Total number of subjects in each age group	Pulmonary HTN present	Pulmonary HTN not present	Prevalence of pulmonary HTN (in %)
46 - 55	26	8	18	30.76%
56 - 65	50	20	30	40%
66 - 75	21	11	10	52.38%

On GOLD staging, 11 patients (11.34%) were in GOLD stage I, 35 patients (36.1%) were in GOLD stage II, 34 patients (35.05%) were in GOLD stage III and 17 patients (17.52%) were in GOLD stage IV. Majority of patients having PH belonged to GOLD stage IV (76.47%), followed by GOLD

stage III (44.11%) (Fig. 1).

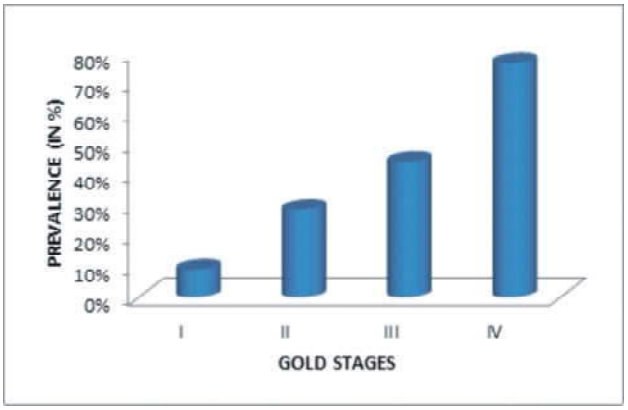

Fig. 1: *Prevalence of pulmonary hypertension according to the COPD GOLD stage.*

All patients of GOLD stage I and II had mild PH. In GOLD stage III, 80% had mild and 20% had moderate PH while in GOLD stage IV, 23% had mild, 53.85% had moderate and 23.07% had severe PH (Fig. 2).

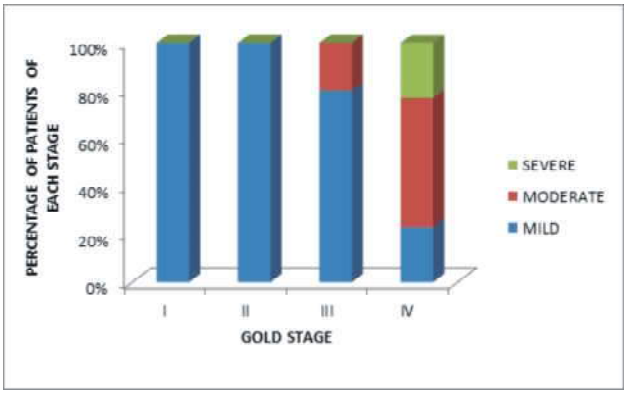

Fig. 2: *Prevalence of pulmonary hypertension, according to severity, in each COPD GOLD stage.*

Majority of patients with PH had mild PH (26.8 %). Only a few had severe PH (3.09%) (Fig. 3).

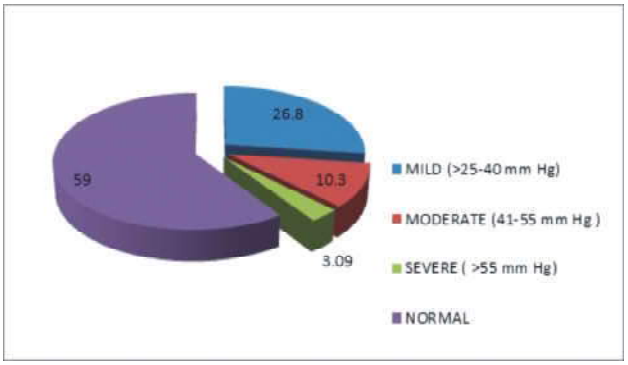

Fig. 3: *Propartion of severity of pulmonary hypertension in patients of COPD.*

In patients having PH (n = 39), 26 (66.67 %), 10 (25.64%) and 3 (7.69%) have been found to have mild, moderate and severe PH respectively.

Chest radiograph and ECG findings suggestive of PH were used as preliminary investigations. Considering 2D-Echocardiography as the confirmatory diagnostic tool, CXR was found to have 58.97% sensitivity and 100% specificity and ECG was found to have 72.22 sensitivity % and 94.82% specificity.

Mean 6-Minute walk distance of COPD patients, was significantly correlated with Right Ventricular Systolic Pressure (Pulmonary Artery Pressure) as, $R^2 = 0.8842$ and coefficient of correlation, r = -0.9407 (Chart 1).

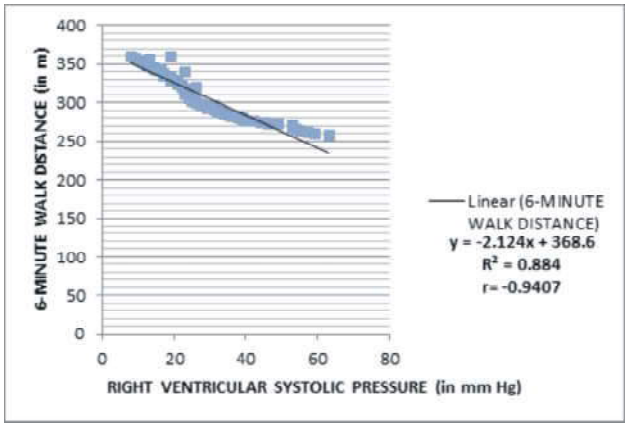

Chart 1: *Correlation of pulmonary artery pressure (Right Ventricular Systolic Pressure) with 6-minute walk distance of subjects.*

St. George's Respiratory Questionnaire (SGRQ) Score was significantly correlated with Pulmonary Artery Pressure (Right Ventricular Systolic Pressure) as, $R^2 = 0.859$, and co-efficient of correlation, r = 0.9272 (Chart 2).

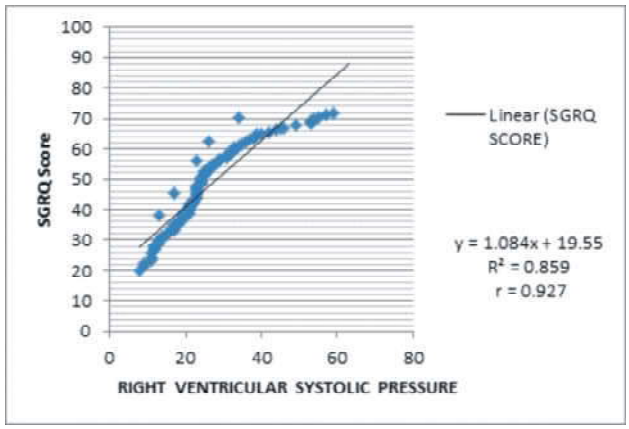

Chart 2: *Correlation of pulmonary artery pressure (Right Ventricular Systolic Pressure) with Health-related Physical Quality of life (St. George's Respiratory Questionnaire Score).*

The prevalence of PH was found to be 40.2% in patients of COPD. Prevalence of PH was found to be higher in male patients compared to female patients. The prevalence and severity of PH increased with severity of COPD, as all cases of moderate and severe PH were seen in patients of GOLD stage III and IV. Most of the COPD patients with PH had mild PH and there were only few (n = 3) cases of severe PH, that too, only in GOLD stage IV.

The exercise capacity and health-related physical quality of life was found to be significantly correlated with PH in COPD patients.

Discussion

In this study, using criteria for PH as mPAP of more than 25 mmHg, 40.20% had PH. The findings of the present study are in accordance with previous studies, Scharf *et al*[26] followed 215 patients being evaluated for lung volume reduction surgery or lung transplantation (mean FEV_1 24% predicted). Using a definition of pulmonary hypertension as a mPAP of more than 25 mmHg [patients with elevated Pulmonary capillary wedge pressure (PCWP) were excluded], the prevalence of pulmonary hypertension was noted to be 50.2%.

In the present study, mild and moderate PH were defined as mPAP 25 - 40 mmHg and 41 - 55 mmHg, respectively and 36 (90.00%) patients were found in this range. In the trials by Scharf *et al*[9] and Thabut *et al*[27] mild-to-moderate PH was defined as mPAP 20 - 35 mmHg and 35 - 45 mmHg, respectively, and 86 - 96% of patients were reported to fall in these ranges.

In this study, exercise capacity and health-related physical quality of life was found to be significantly correlated with PH in COPD patients. Unfortunately, the study on this topic, with the most robust exercise data has the smallest number of patients. Nevertheless, Jones *et al*[19] reported that the presence of PH was not associated with lower 6-minute walk distance or any variables measured during cardiopulmonary exercise testing. In contrast, Sims *et al*[14] evaluated 362 patients with severe COPD with right heart catheterisation and found that a higher mPAP was associated with shorter 6-minute walk distance after adjusting for patient demographics, lung function, and PCWP. They found an 11 meter decline in 6-minute walk distance for every 5 mmHg rise in mPAP (95% confidence interval (-21, 0.7; P = 0.04).

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ORIGINAL ARTICLE

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Ascitic Fluid Lactate Dehydrogenase (LDH) – A Marker for Spontaneous Bacterial Peritonitis

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Abstract

Ascites is defined as pathological accumulation of fluid in the peritoneal cavity. Evaluation of the cause of ascites is important for therapeutic and prognostic reasons. Bacterial infection of the ascitic fluid without any intra-abdominal surgically treatable source of infection is called spontaneous bacterial peritonitis (SBP). For evaluation of SBP, we rely upon serum ascitic fluid albumin gradient (SAAG), leucocyte count and fluid culture. At times, the diagnosis may not be clear and there may not be any other parameter to rely upon.

Aims and objectives: To study the significance of ascitic fluid lactate dehydrogenase (LDH) levels in SBP and to correlate the ascitic fluid LDH values to their corresponding blood values in SBP.

Material and methods: The study was a hospital-based cross-sectional study conducted in a tertiary care hospital of North India. Patients admitted with ascites due to any underlying aetiology were included in the study. Abdominal paracentesis was done under aseptic conditions, the ascitic fluid and corresponding blood samples sent for routine samples and LDH estimation.

Results and analysis: 170 patients were included in the study with the mean age of 54.38 years. Ascitic fluid LDH (AFLDH) was significantly raised in SBP as compared to non SBP patients (p < 0.0001). For SBP, AFLDH >/= 127.5 IU/L had sensitivity of 76.5%, specificity of 75.2%, PPV of 28.3% and NPV of 96.2%. For SBP, AFLDH/ SeLDH ratio with a cut-off value of >/= 0.50 had specificity of 81.2%, sensitivity of 47.1%, PPV of 25.7% and NPV of 93%. For AFLDH in SBP, the area under the curve was 0.820 with 95% CI 0.737 - 0.904 (p value < 0.001).

Conclusion: Raised AFLDH may be a useful parameter in diagnosis of SBP. So, in nutshell we can say that if the AFLDH is < 127.5 IU/ L, then chances of having SBP are very less.

Key words: Cirrhosis, portal hypertension, ascites, lactate dehydrogenase, spontaneous bacterial peritonitis.

Introduction

Ascites is defined as pathological accumulation of fluid in the peritoneal cavity. Normally, the peritoneal fluid volume is around 5 mls. in men and 5 - 18 mls. in women (depending on the phase of menstrual cycle). Atleast 1,500 mls of fluid needs to be present in the peritoneal cavity to be detected on clinical examination (much more in obese patients)[1]. Mild ascites may not cause symptoms, whereas moderate to massive ascites may lead to abdominal distension, development of abdominal hernias or respiratory distress[2]. Evaluation of the cause of ascites is important for therapeutic and prognostic purposes. Development of ascites in patients with cirrhosis of liver is associated with a mortality rate of 15% at one year and 44% at five years. Combined analysis of clinical profile along with the laboratory analysis of the ascitic fluid samples is needed to reach to the diagnosis[3]. Bacterial infection of the ascitic fluid without any intra-abdominal, surgically treatable, source of infection is called spontaneous bacterial peritonitis (SBP). The prevelance rate of SBP in patients with cirrhosis is 1.5 - 3.5% in the outpatient and 10% in hospitalised patients. With early diagnosis and treatment, the mortality rate in SBP has reduced from 90% to nearly 20%. For evaluation of SBP, we rely upon serum ascitic fluid albumin gradient (SAAG), leucocyte count and fluid culture. When the SAAG is > 1.1 gm/dl, its called transudative ascites (High SAAG) and is found in cirrhosis, right heart failure, and Budd Chiari syndrome. When the SAAG is < 1.1 gm/dl, its called exudative ascites (Low SAAG) and is found in patients with infections like tuberculosis, pancreatic ascites or malignancy[4]. SBP is an example of infected transudate characterised by SAAG > 1.1 gm/dl and neutrophil count of > 250 cells/mm^3,[5] in the ascitic fluid with or without culture positivity. Despite the use of sensitive methods, ascitic fluid culture is negative in 60% of the patients with clinical manifestations suggestive of SBP and increased ascitic fluid neutrophil count. The gold standard for ascitic neutrophil count is manual microscopy, which is labour intensive and associated with interobserver variability. So, at times, while

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using these parameters the diagnosis may not be clear and there may not be any other parameter to rely upon. As in Light's criteria used for pleural fluid analysis, LDH analysis has been explored for the ascitic fluid analysis. It has been reported that in patients with malignant ascites, ascitic fluid LDH (AFLDH) has high sensitivity but low specificity for the diagnosis of the disease[6]. According to Gokturk *et al*, LDH values were higher in patients with SAAG < 1.1 gm/dl as compared to those with SAAG > 1.1 ($p < 0.001$)[7]. However, the role of LDH in diagnosis of SBP has not been studied.

Aims and objectives

- To study the diagnostic significance of ascitic fluid lactate dehydrogenase (LDH) levels in evaluation of spontaneous bacterial peritonitis (SBP).
- To correlate between the ascitic fluid LDH levels and their corresponding blood levels in SBP.

Material and methods

The study was a hospital-based cross-sectional study carried-out in a tertiary care hospital of North India. The study was approved by the Institutional Ethics Committee on January 4th 2018 (Ref: 201801-033-IEC/CMCL-APPRVL-PG.THESIS/Medicine). Patients admitted with ascites due to any underlying aetiology over a period of 18 months were included in the study and abdominal paracentesis was done after taking an informed consent in writing. The ascitic fluid and corresponding blood samples were sent for routine investigations and LDH estimation. LDH values of ascitic fluid and blood were correlated with the clinical, pathological and radiological findings.

***Sample size*:** Sample size was 170 patients.

Inclusion criteria: All patients above the age of 18 years who had presented with ascites were included in the study after taking an informed consent in writing.

Exclusion criteria: Pregnant women and recent post-partum (within 6 months of delivery) were excluded.

The estimation of LDH was carried-out on C501 module of fully automated analyzer Cobas 6,000 by Roche. Other appropriate investigations were sent, as needed, for each patient.

Statistical analysis

Categorical variables were presented as number and percentage and continuous variables were presented as mean +/- SD and median. Normality of the data was tested by Kolmogorov-Smirnov test. If normality was rejected, then non parametric tests were used. The differences in AFLDH and AFLDH/SeLDH ratio between SBP and non-SBP group were compared using Mann-Whitney U test (as the data sets were not normally distributed). Receiver Operative Characteristics (ROC) curve was used to calculate the area under the curve and to define a cut-off value to predict SBP. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated using appropriate formulas. A p value of < 0.05 was considered statistically significant. The data was entered in MS Excel spreadsheet and analysis was done using Statistical package for social sciences (SPSS) version 21.0.

Results

The study was carried-out in the medical wards of a tertiary care hospital of North India over a period of 18 months. A total of 170 patients with ascites were included in the study. The mean age was 54.38 years and had 70.59% males. Abdominal distension was the commonest presenting symptom in 90.59% patients, weight loss in 61.18%, fever in 56.47% and pain abdomen in 12.94% patients (Fig. 1). Historically, 56.57% patients had jaundice and 31.17% patients had hepatic encephalopathy.

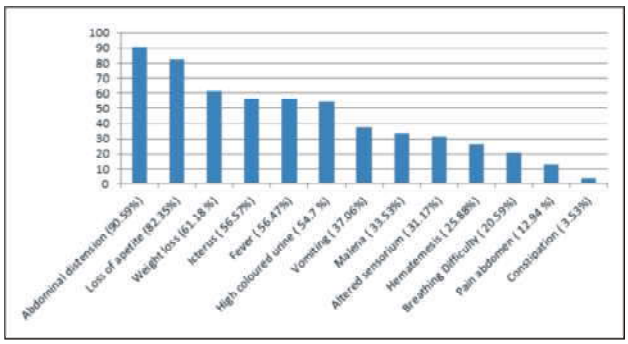

Fig. 1: *Presenting Symptoms in % age.*

Clinical examination revealed shifting dullness in 95.29% patients, fluid thrill in 81.17% patients, and pedal oedema in 61.76% patients. Signs of liver cell failure were present in nearly one-third (33.53%) of the patients, hepatomegaly in 20% and splenomegaly in 7.64% patient. Nearly one-third of the patients (30.58%) had asterixis and two-third had anaemia (Table I).

Liver function tests were abnormal in majority of the patients (Fig. 2). Hypoalbuminaemia (91.18%) was the commonest abnormality followed by hyperbilirubinaemia (77.06%). Thrombocytopenia was present in 64.12% and coagulopathy in 74.70%. Child Pugh grade C was present in 62.35% patients and grade B in the remainder (37.64%). On ultrasound examination, coarse nodular liver was present in 70%, splenomegaly in 40% and right side pleural effusion in 15.29%.

Table I: Presenting signs.

Presenting signs	Frequency (N = 170)	Percentage (%)
Shifting dullness	162	95.29
Fluid thrill	138	81.17
Pallor	115	67.65
Oedema	105	61.76
Icterus	89	52.35
Lacrimal gland enlargement	57	33.53
Gynaecomastia	53	31.17
Asterixis	52	30.58
Clubbing	41	24.11
Hepatomegaly	34	20
Dupuytren's contracture	33	19.41
Parotid gland enlargement	31	18.24
Splenomegaly	13	7.64
Spider naevi	11	6.47
Testicular atrophy	10	5.88
Palmar erythema	5	2.94

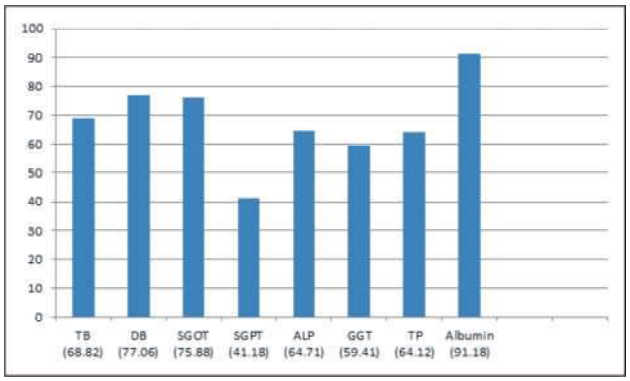

Fig. 2: *Abnormal LFT (%).*

Alcohol was the cause of liver dysfunction in 60.58% patients (85.83% males) and hepatotrophic viruses (HBV, HCV, and HIV) were detected in 17% patients. In 24 (14.11%) patients, ascitic fluid examination revealed high SAAG (> 1.1 gm/dl) with neutrophil count > 250/mm3 (Table II). There were 20 patients with malignancy. Amongst the remaining 150 patients, 16 fulfilled the criteria for SBP (n = 16). Diabetes mellitus was the commonest co-morbidity in 21.76% patients followed by hypertension in 17.05% patients (Table II).

Table II: Diagnosis

Diagnosis	Frequency (N = 170)	% age
Alcoholic liver disease	103	60.58
Diabetes mellitus	37	21.76
Hypertension	29	17.05
Spontaneous bacterial peritonitis	24	14.11
Cryptogenic	23	13.52
Malignancy	20	11.76
Hepatitis C virus	21	12.35
Tuberculosis	16	9.41
Hepatitis B virus	6	3.53
HIV	2	1.18
Hepatitis E virus	2	1.18
Cardiogenic	6	3.52
Hypothyroidism	5	2.94
Secondary peritonitis	3	1.76

Ascitic fluid LDH was estimated in all these 150 patients. It was found that patients with SBP had significantly raised ascitic fluid LDH (p = 0.001). The median (IQR) in SBP group was 201 IU/L (118 - 921.5) as compared to 74 IU/L (48 - 128) in non-SBP group (Table III).

Table III

	SBP (N = 16)	Non-SBP (N = 134)	
	Median (IQR)	Median (IQR)	p value
AF LDH	201 (118 - 921.5)	74 (48 - 128)	0.001
AF LDH/ Se LDH	0.50 (0.31 - 1.11)	0.24 (0.15 - 0.42)	< 0.001

Table IV: Test result variable(s).

	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower bound	Upper bound
AFLDH	0.820	0.043	0.000	0.737	0.904
AFLDH - SeLDH	0.749	0.060	0.001	0.631	0.866

The AFLDH >/= 127.5 IU/l was found to be suggestive of SBP. It had specificity of 75.2% and sensitivity of 76.5%, PPV was 28.3% and NPV was 96.2%. For AFLDH, the area under the curve was 0.820 with 95% CI 0.737 - 0.904 (p value < 0.001) (Table IV). The ratio of AFLDH to Se LDH was also significantly raised in the SBP group. The median (IQR) AFLDH/ SeLDH ratio was 0.50 (0.31 - 1.11) in the SBP group as compared to 0.24 (0.15 - 0.42) in the non-SBP group (p < 0.001). AF LDH/Se LDH ratio had a cut-off value of >/=

0.50. The specificity was 81.2%, sensitivity was 47.1%, PPV was 25.7% and NPV was 93% (Table IV).

Discussion

Higher level of AFLDH indicates high degree of peritoneal inflammation. In patients with malignancy, tuberculosis and pancreatic ascites, LDH is usually high (> 500 IU/L) and in liver related disorders it is generally low[8]. Tuberculosis and other conditions which have raised LDH have exudative ascites in contrast to SBP, which has transudative ascites. It means that if the ascitic fluid is transudative and the LDH is raised, then the chances of SBP are high.

Boyer *et al* observed that that the AFLDH levels were higher in malignant ascites (913 +/- 2,283 IU/L) as compared to ascites associated with liver disease (169 +/- 9 IU/L). Gokturk *et al* observed that AF LDH was higher in patients with SAAG < 1.1 gm/dl as compared to patients with SAAG > 1.1 gm/dl[7]. Touny *et al* reported that out of 41 patients of cirrhosis with ascites, 5 fulfilled the criteria of SBP. Out of these 5 patients, 3 had culture positive neutrophilic ascites and 2 had culture negative neutrophilic ascites. The ratio of AFLDH/SeLDH > 0.75 was present in the SBP group as compared to < 0.58 in non-SBP group[9]. Mortada *et al* reported that out of 30 patients of ascites, 13 had SBP and the AF LDH was significantly higher in this group as compared to the non-SBP group (p < 0.002). AF LDH/Se LDH > 0.5 had a sensitivity of 80%, specificity of 88%, PPV 66.7%, NPV 93.7% and accuracy of 63.3%[10].

Bedside criterion of neutrophil count > 250/mm^3 for the diagnosis of SBP is labour intensive and associated with inter-observer variability. So, to overcome these limitations, LDH can serve as a reliable parameter.

Conclusions

Ascitic fluid LDH can be a good biochemical marker for spontaneous bacterial peritonitis. AFLDH >/= 127.5 IU/l can be suggestive of SBP. It has specificity of 75.2%, sensitivity of 76.5%, PPV of 28.3% and NPV of 96.2%. AFLDH/ SeLDH ratio had a cut-off value of >/= 0.50. The specificity was 81.2%, sensitivity was 47.1%, PPV was 25.7% and NPV was 93%.

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ORIGINAL ARTICLE

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Hospital Outcomes in AES cases from Eastern India

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Abstract

Acute Encephalitic Syndrome (AES) is defined as acute onset fever of less than 7 days duration with altered sensorium and/or seizure.

104 consecutive patients of AES presenting to the Department of Medicine, North Bengal Medical College were studied to evaluate hospital outcomes and factors contributing to mortality and morbidity.

This study showed a male dominance of 65.38%. Aetiological diagnosis was reached in all cases with JE (72%), HSV Encephalitis (HSVE) (11.5%), Scrub Typhus Encephalitis (STE) (9.6%), Dengue Encephalitis (2.88%), Cerebral Malaria (1.8%), Bacterial Meningitis (0.9%) and sepsis (0.9%). We documented 25 deaths (24%) during the course of hospitalisation, with an aetiological breakup of JE 22 (29.3%), HSVE 2 (16.6%) and STE 1 (10%). Higher mortality was observed in patients GCS < 7 (47.6%) and seizure at presentation (38.8%). Among survivors, residual neuro-deficit was predominantly seen in JE patients, with 39.6% motor deficit, 17% sensory deficit, 20.7% autonomic deficit and 43% cognitive deficit.

Conclusion: GCS < 7 at presentation and seizures were found to be independent poor prognostic markers in patients of AES. Neurological sequelae in the form of cognitive, motor, sensory and autonomic deficits were common among AES patients, particularly in JE.

Introduction

Acute Encephalitis is defined as fever or recent history of fever with change in mental status (including confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures)[1]. The incidence of AES in India is 0.42/1,00,000 population per annum (1978 - 2011)[2]. The most common causative viral agents are Herpes Simplex (HSV1), Japanese Encephalitis, Dengue, Enteroviruses, Measles, Epstein-Barr virus (EBV), Tickborne Encephalitis (TBE), Human Herpesvirus 6 (HHV-6) and West Nile virus. Scrub Typhus, Cerebral malaria, acute pyogenic meningitis and non-infectious causes of encephalopathy need to be excluded while considering AES[3]. In West Bengal, the disease remains endemic (especially JE) in Bankura, Burdwan, and Howrah districts[4]. A study by Bandyopadhyay *et al* showed an incidence of 22.76% in 2011. In 1973, a JE outbreak was first recorded in the districts of Burdwan and Bankura in West Bengal, where 700 cases and 300 deaths were reported[5-9]. Japanese encephalitis virus (JEV), a mosquito-borne flavivirus, is the most common vaccine-preventable cause of encephalitis in Asia[11-15]. Japanese encephalitis (JE) occurs throughout most of Asia and parts of the Western Pacific[11,13]. Among an estimated 35,000 - 50,000 annual cases, approximately 20% - 30% of patients die, and 30% - 50% of survivors have neurologic or psychiatric sequelae[14,15].

Viral encephalitis can present with low or mild severity and recover spontaneously or much more aggressively with a poor prognosis and severe neurological sequelae in survivors. The prodromal signs and symptoms are those of a classic viral infection: fever and headache, possibly accompanied by nausea or vomiting[16]. After a few days, symptoms of CNS involvement become manifest with altered mental status, considerable irritability and agitation, personality changes; seizures (focal or generalised) may occur, sometimes accompanied by focal neurological signs. Patients may then become lethargic or comatose; death eventually ensues. Stiff-neck is a sign of meningeal involvement and heralds a poor prognosis[16].

Aims and objectives

The study was conducted from May 2018 to April 2019 on patients presenting with AES to the Department of Medicine of North Bengal Medical College, Darjeeling, West Bengal. All patients fulfilling inclusion criteria, after informed consent, were included in the study. The study was carried-out with an objective to evaluate the outcome of disease and factors contributing to clinical outcomes.

Material and methods

This was an observational, cross-sectional study done over a

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period of one year. Patients with a clinical diagnosis of AES admitted at Department of Medicine, North Bengal Medical College, Darjeeling were enrolled consecutively in the study from May 2018 to April 2019. A case of AES was clinically defined as a constellation of symptoms comprising of acute onset fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) and/or new onset of seizures (excluding simple febrile seizures)[1] in a person of > 12 years of age.

Inclusion criteria

a. Patients > 12 years, with

b. Diagnosis of AES (as defined by acute onset alteration of sensorium with fever of recent onset, i.e., 1 week or less duration).

Exclusion criteria

a. Fever of more than 1 week duration.

b. Patients having Metabolic Encephalopathy, Cerebrovascular Accidents, ICSOL, Trauma, Hypoxia.

c. Next of kin not providing consent for study and those who left against medical advice.

Parameters to be studied

a. Aetiology of AES cases.

b. Hospital outcomes (died or survived).

c. Residual neurodeficit at discharge.

d. Clinical factors influencing the mortality.

We evaluated all patients with a detailed history, with special attention to recent onset of altered sensorium and/or seizures. Clinical examination also focused on neurological assessment and residual neuro-deficit at the time of discharge from hospital. The lab evaluation included complete haemogram, blood sugar, LFT , urea, creatinine, malaria and Dengue antigens, Scrub typhus IgM, blood culture, serum serology for JE and Typhi-dot IgM. These were supplemented with CSF analysis for cytology, biochemistry and CSF for JE Mac Elisa and RT PCR for HSV. Neuroimaging in the form of MRI brain was advised for all patients. Ethical approval for the study was obtained from the Institutional Ethical Committee and written informed consent was taken from the next of kin.

Data analysis

Data was entered in Excel Microsoft Software to prepare Master table and is presented in various tables, charts and diagrams. The data was then analysed using SPSS statistical software V 12.2.

Results

Among 104 patients of AES enrolled for this study, males dominated the clinical picture with 68 out of 104 patients (65.38%).

An aetiological diagnosis was reached in all cases. 75 cases (72%) were caused by Japanese Encephalitis. The next most common causes were Herpes Simplex Encephalitis (12 cases; 11.5%) followed by Scrub Typhus (10 cases; 9.6%). Dengue Encephalitis was also found in 3 cases (2.88%).

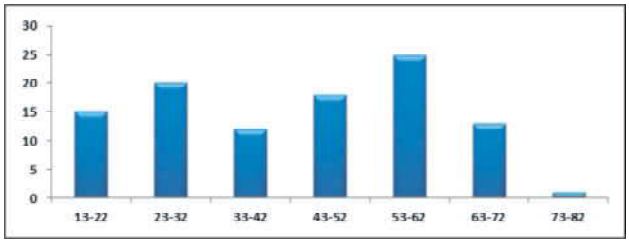

Fig. 1: *Age distribution of study population.*

Two cases initially diagnosed to have AES were found to have Cerebral Malaria and one case each was due to Sepsis and Acute Pyogenic Meningitis.

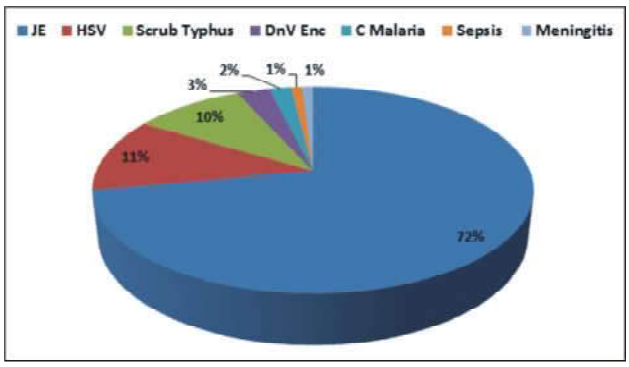

Fig. 2: *Aetiology of AES in the study population.*

The majority of patients (54.81%) were > 40 yrs of age as depicted above figure. Mean age of patients was 43.60 ± 17.23 years (Fig. 1).

Table I: Gender and Rural: Urban ratio, as per aetiology.

	Total (n=104)	JE (n=75)	HSV Enc (n=12)	Cer Mal (n=2)	Scr Typ (n=10)	Bact Men (n=1)	Sepsis/ MODS (n=2)	Dengue (n=3)
Male: Female	1.9: 1	1.8:1	2:1	1:1	3:2	0:1	1:0	2:1
Rural: Urban	1.8:1	2.5:1	1:1	1:1	1:1	1:0	0:1	0:3

The JE cases were mostly from the rural areas whereas the Rural: Urban distribution was equal in cases of Scrub Typhus and HSV Encephalitis. All three cases of Dengue

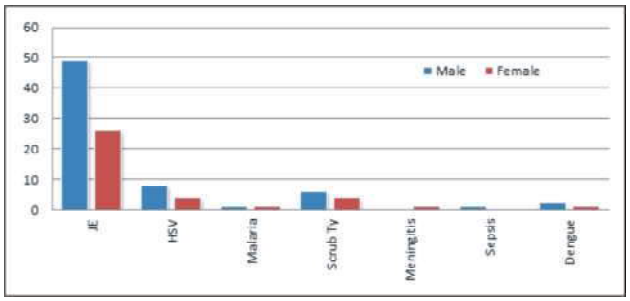

Fig. 3: *M: F ratio as per aetiology of AES.*

Encephalitis were residents of urban areas. Male: Female ratio was found to be highest in HSV and Dengue encephalitis followed by JE and Scrub Typhus (Table I; Fig. 3).

Table II: Mortality outcome with respect to aetiology.

	Total (n=104)	JE (n=75)	HSV Enc (n=12)	Cer Mal (n=2)	Scr Typ (n=10)	Bact Men (n=1)	Sepsis (n=1)	Dengue (n=3)
Survived	79	53	10	2	9	1	1	3
Mortality (%)	25 (24%)	22 (29.3%)	2 (16.6%)	0	1 (10%)	0	0	0

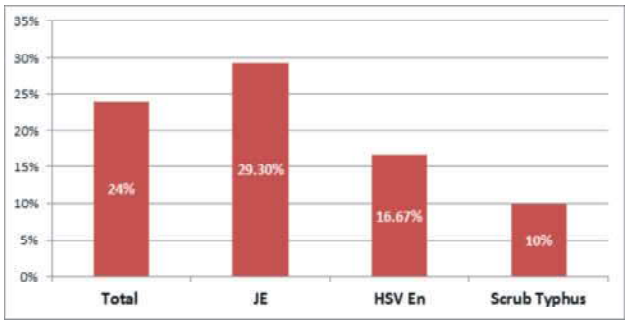

Fig. 4: *Mortality in relation to aetiology.*

Total 25 patients died, resulting in overall mortality rate of 24%, of which highest mortality was observed in JE (29.33%) followed by HSV encephalitis (16.67%) and Scrub typhus (10%) (Table II, Fig. 5).

During the study, it was noted that lower GCS at presentation carried poor prognosis in terms of survival. In the study group, 42 patients presented with a GCS of < 7 with a mortality of 47.6%. Those who had a GCS of more than 7 had a mortality of 8%. (p - Value < 0.0001, RR: 5.9 with 95% of Confidence Interval: 2.4 - 14.5) (Table III).

Table III: Correlation of mortality with GCS on presentation.

GCS	Died	Survived	p value*
GCS < 7 (n = 42)	20 (47.6%)	22 (52.4%)	< 0.0001 (RR = 5.9)
GCS > 7 (n = 62)	5 (8%)	57 (92%)	
Total (n = 104)	25 (24%)	79 (76%)	

**Pearson chi square test.*

In our study, 54 patients had a presentation with seizures, mostly GTCS. 21 out of these 54 patients (38.8%) died whereas, among the rest 50 patients, who did not have any seizures, only 4 died (8%). So, presence of seizures had a significant positive correlation with mortality (p - value < 0.0002, RR - 2.01, with a 95% of confidence interval 1.47 to 2.74) (Table IV, Fig. 6).

Table IV: Correlation of Seizure with mortality.

	Death	Survived	p value*
Seizures (n = 54)	21 (38.8%)	33 (61.2%)	< 0.0002 (RR 2.01)

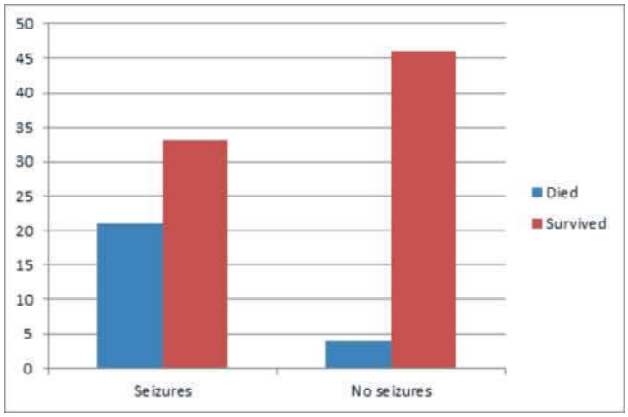

Fig. 5: *Relation of mortality in respect to seizure occurrence.*

No seizures (n = 50)	4 (8%)	46 (92%)	
Total (n = 104)	25 (24%)	79 (76%)	

**Pearson chi square test.*

Table V: Residual neurological sequelae among survivors.

	Neurological sequelae				
	Motor	Sensory	Autonomic	Cranial nerve	Cognitive Deficit
JE (n = 75)	21 (39.6%)	9 (17%)	11(20.7%)	2(3.7%)	30(56.6%)
HSV Enc (n = 12)	1(10%)	0	0	0	3(30%)
Cerebral Malaria (n = 2)	0	0	0	0	0
Scrub typhus (n = 10)	0	0	0	0	1(11%)
Bacterial meningitis (n = 1)	0	0	0	0	0
Sepsis (n = 1)	0	0	0	0	0
Dengue (n = 3)	0	0	0	0	0

27.8 % of survivors had some motor deficit at the time of

discharge from hospital, like monoparesis, hemi paresis, motor aphasia and dystonia mostly in the JE group (39.6% of survivors). 9 patients (17% of survivors) of JE had sensory abnormalities in the form of paraesthesias, tingling and numbness of the affected paretic limb. Two patients had residual facial deviation and 11 patients of JE (20.7% of survived) had some or other sort of residual autonomic abnormality such as loss of bowel and bladder control, blood pressure and heart rate variability. 34 (43%) patients had a cognitive deficit on discharge (MMSE < 25) in our study (Table V).

Discussion

104 consecutive AES patients presenting to the Department of Medicine, North Bengal Medical College , Darjeeling were enrolled during a period of one year, of which mean age was 43 years (Range 13 - 75 years) with a male: female ratio of 1.85: 1. Karmakar *et al* showed a male: female ratio of 1.71:1[17]. The male predominance might be due to the occupational exposure, as majority of them work in fields.

Aetiological diagnosis was reached in all 104 patients with a viral aetiology in 86.5% cases. Among the viral causes, JE was found to be the most common (72% of all cases) followed by HSV -1 encephalitis (11.5% of all cases) and Dengue Encephalitis (2.88% of all cases). Jain *et al* found JE as the most common cause of AES in her series of 4,092 patients of AES, followed by Dengue Encephalitis, Enteroviruses and HSV[18]. Karmakar *et al* found that only 8.7% tested positive for JE[17]. In another epidemic outbreak studied by Saxena *et al*, 55.3% patients tested positive for JE[19]. JE is emerging as the most common cause of AES in India. In recent times, after 2012, AES cases in India have shifted towards the JE aetiology. Based on reports, the Indian states of Uttar Pradesh (UP), Bihar, Assam, West Bengal, and Tamil Nadu were identified as JE endemic zones[20]. Also, huge population migration with availability of potential breeding sites for mosquitoes and local pig rearing at homes could be the dominating cause.

In our study, there was a positive correlation between GCS at presentation and mortality rate with a GCS of < 7 having a mortality of 47.6%. On the contrary, a GCS of > 7 had a mortality of 8%. (p value < 0.0001, RR - 5.9 with 95% confidence interval – 2.4 - 14.5). Rayamajhi *et al*[21] showed that a lower a GCS was associated with poor outcome. Farzana *et al*[22] showed a relatively poor outcome when the GCS was < 6.

Patients who presented with seizures, had a worse outcome (mortality 38.8%) in our study, with a positive correlation between poor outcome and seizures. the (p value < 0.0002, RR - 2.0, with a 95% of confidence interval – 1.4 to 2.7). Michael A Hansen *et al* also reported positive correlation between seizure and mortality (p value < 0.01)[23]. A similar observation on outcome of AES patients was reported by Takeshi Hatachi *et al* with 9,386 patients for 8 years where he opined that presence of epilepsy was a predictor of poor outcome[24].

Residual neuro-deficit was common among the survivor patients in the form of motor deficit (27.8%), sensory deficit (17%) and autonomic disturbance (20.7%). 34 (43%) patients had a cognitive deficit on discharge. Similar observation was reported by Rayamajhi *et al*[21], showing, 25% of all viral AES cases and 38% of JE cases had residual neurological sequelae.

Conclusion

Among adult patients with AES, JE was the most common cause, followed by HSV-1 encephalitis and Scrub typhus, in this region of the country. GCS at presentation and seizures were found to be independent poor prognostic markers. Residual neuro-deficits in the form of motor/sensory/ autonomic were common sequelae, particularly in cases of JE. Residual cognitive impairment was not uncommonly seen.

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ORIGINAL ARTICLE

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Clinical Determinants and Short-Term Prognosis of Hyponatraemia Present on ICU Admission

Agnivesh Sharma, Rajeev Gupta**, BS Gupta***, Shabbar HK Joad****, Sushil Kalra*****, Mukesh Kumar Sarna*******

Abstract

Background: Hyponatraemia is one of the most common electrolyte imbalances in hospitalised patients, encountered in 15 - 30% of patients. A major proportion of the data available on this subject is derived from work done outside India. Most of the studies are retrospective in nature and there is wide variation in the findings of different studies.

Objective: To identity the prevalence, aetiology, clinical determinants and outcome of hyponatraemia present on medical Intensive Care Unit (ICU) admission.

Methods: Patients getting admitted to medical ICU over a period of one year meeting inclusion and exclusion criteria were included in this observational, prospective study.

Results: Prevalence of hyponatraemia on ICU admission was 42.7% (n = 128). Prevalence of mild, moderate and profound hyponatraemia was 24%, 17.5% and 12.5%, respectively. Binary logistic regression analysis showed that age > 55 years (p = 0.036), chronic renal failure (p = 0.025) and use of thiazide diuretics (p = 0.010) were independent risk factors for the development of hyponatraemia. Kidney disease was the most common cause of hyponatraemia (29.69%). Fluid restriction was the most common treatment modality (33.59%). There was no significant association of hyponatraemia with increased mortality and adverse outcome.

Conclusions: Hyponatraemia was common on ICU admission, more so in Indian scenario. Old age, chronic renal failure and use of thiazide diuretics were independent risk factors for hyponatraemia. Regular monitoring of serum electrolytes, especially serum sodium, cannot be overemphasised in these specific populations. The association of hyponatraemia with increased mortality and adverse outcome has to be reconsidered in larger, multi-centre studies.

Key words: Hyponatraemia, ICU, risk factors, aetiology, prognosis.

Introduction

The interplay between pituitary (vasopressin/antidiuretic hormone) and renal system (relative salt and water excretion) is mainly responsible for maintaining normal level of sodium in the body. Hyponatraemia is decrease in the relative ratio of sodium (Na^+) to body water. Serum Na^+ < 135 mEq/l has been defined as hyponatraemia and serum Na^+ > 145 mEq/l as hypernatraemia. In the latest European guidelines, hyponatraemia has been further classified as mild (serum sodium between 130 and 134 mEq/l), moderate (serum sodium between 125 and 129 mEq/l) and profound hyponatraemia (serum sodium less than 125 mEq/l[1]. It is one of the most common electrolyte imbalances encountered, reported in 15 - 30% of hospitalised patients[2]. Hyponatraemia is more common in intensive care settings. Frequency of hyponatraemia among patients admitted to intensive care units (ICUs) has been reported to be between 17.7 and 34.3%[3-7]. Hyponatraemia can be hyperosmolar, isoosmolar or hyperosmolar based on the corresponding serum osmolality.

The symptoms of hyponatraemia, mainly caused by brain oedema and/or increased intracranial pressure, vary depending on the time of development of hyponatraemia and the absolute decrease in serum Na^+ level. While mild hyponatraemia is mostly asymptomatic; moderate-to-profound hyponatraemia can cause symptoms ranging from subtle ones like nausea, confusion and headache to severe ones like seizures and coma[1].

In more than one study, hyponatraemia has been reported to be an independent risk factor for poor outcome[5-7]. A major proportion of the data available on this subject is based on work done outside India. Most studies are

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retrospective and there is wide variation in the findings studies. The aim of this prospective study was to identity the clinical determinants and outcomes of hyponatraemia, present on ICU admission.

Objectives

To identity the prevalence, aetiology, clinical determinants, management and outcome of hyponatraemia, present on ICU admission.

Inclusion and exclusion criteria

Successive patients admitted in Medical Intensive Care Unit (MICU) over a period of one year (2017 - 2018) with/without hyponatraemia, with age > 18 years giving consent for participation in the study were included in the study. Patients not giving consent for participation in the study, age less than 18 years, pregnant patients at the time of admission and patients readmitted to MICU during the same hospitalisation were excluded from this study.

Material and methods

Patient's serum sodium level, demographics, volume status, relevant present medical and drug history, APACHE-2 score, SOFA score on day one, two and three of ICU admission, relevant investigations, clinical diagnosis, cause of hyponatraemia, treatment, outcome on transfer out from ICU and hospital discharge, were collected in a specially designed study proforma. Hyponatraemia was classified as mild (serum sodium 130 - 134 mEq/l), moderate (serum sodium 125 - 129 mEq/l) and profound hyponatraemia (serum sodium < 125 mEq/l) acoording to the European guidelines[1]. Chi-square test, Fischer's test, Student's t-test and non-parametric tests, when appropriate, were used for statistical analysis.

Results

In this study, prevalence of hyponatraemia at ICU admission was 42.66% (n = 128). Prevalence of mild, moderate and profound hyponatraemia was 21% (n = 63), 13.33% (n = 40), and 8.33% (n = 25), respectively (Fig. 1).

After univariate analysis, age more than 55 years (p = 0.002), hypertension (p = 0.003), chronic renal failure (p = 0.003), use of thiazide (p = 0.001) and loop diuretics (p = 0.025), and APACHE-2 score more than 12 (p = 0.027) were significant risk factors for hyponatraemia (Table I).

Many of the hypertensive and chronic renal failure patients were taking thiazide and loop diuretics, respectively and most of them belonged to the older age group. Age, along with serum creatinine level, are part of APACHE-2 score.

Binary logistics regression analysis was done to identify the significant independent risk factors. It showed that age more than 55 years (p = 0.036), chronic renal failure (p = 0.025) and use of thiazide diuretics (p = 0.010) were independent risk factors for the development of hyponatraemia (Table II).

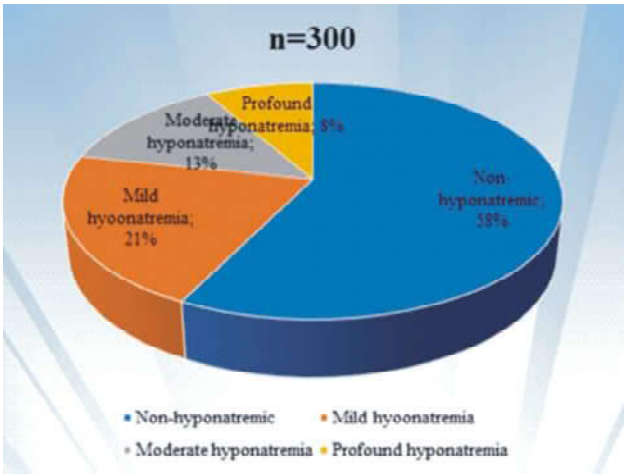
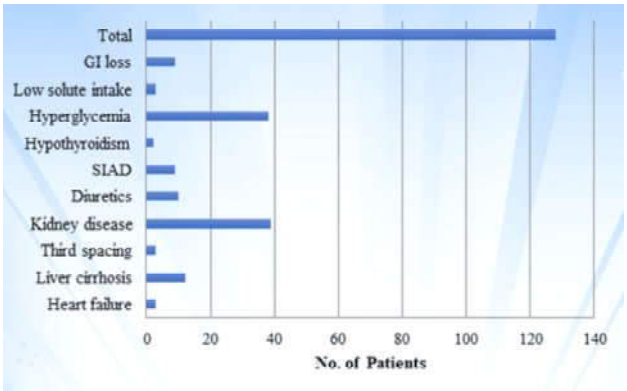


Fig. 1: *Distribution of the cases according to serum sodium level (mEq/l).*

Hypertension (49%) and diabetes mellitus (35.67%) were the most common comorbidities in the study population in both hyponatraemic as well as non-hyponatraemic groups. History of diuretic medications was given by 8.33% (n = 25) of total patients. Mean APACHE-2 score was 14.19 ± 6.57 for the hyponatraemic patients and 12.32 ± 8.20 for the non-hyponatraemic patients (p < 0.05) (Table I).

Kidney disease was the most common cause of hyponatraemia (30.46%, n = 39). It was followed by hyperglycaemia (29.69%, n = 38), liver cirrhosis (9.38%, n = 12), diuretic use (7.81%, n = 10), SIAD (7.03%, n = 9) and gastrointestinal loss (7.03%, n = 9) (Fig. 2).



GI loss: Gastrointestinal loss; SIAD: Syndrome of inappropriate diuresis.

Fig. 2: *Distribution of the cases according to cause of hyponatraemia.*

Table I: Univariate analysis for the risk factors of hyponatraemia.

	Hyponatraemic (n = 128)		Non-hyponataremic (n = 172)		Total (N = 300)	Odds ratio (95% confidence interval)	P value
	No	%	No	%	No		
	128	42.67	172	57.33	300		
Age > 55 years	97	49.24	100	50.76	197	2.253 (1.359 to 3.734)	0.002
Age ³ 55 years	31	30.10	72	69.90	103		
DM	53	49.53	54	50.47	107	1.544 (0.959 to 2.488)	0.095
Hypertension	76	51.70	71	48.30	147	2.079 (1.305 to 3.311)	0.003
Renal failure	26	61.90	16	38.10	42	2.485 (1.271 to 4.861)	0.011
Cardiac failure	1	25.00	3	75.00	4	0.444 (0.046 to 4.315)	0.833
CLD	13	61.90	8	38.10	21	2.317 (0.931 to 5.771)	0.105
Bronchial asthma	3	27.27	8	72.73	11	0.489 (0.127 to 1.881)	0.45
COPD	17	48.57	18	51.43	35	1.310 (0.647 to 2.655)	0.569
Malignancy	5	41.67	7	58.33	12	0.952 (0.295 to 3.072)	0.824
Thiazide diuretics	11	91.67	1	8.33	12	16.077 (2.048 to 126.217)	0.001
Loop diuretics	7	87.50	1	12.50	8	9.893 (1.201 to 81.452)	0.025
K^+ sparing diuretics	4	80.00	1	20.00	5	5.516 (0.609 to 49.958)	0.213
APACHE-II score							
> 12	71	72		143		1.730 (1.090 to 2.745)	0.027
< 12	57	100		157			
Mortality	22	38.60	35	61.40	57	0.812 (0.450 to 1.466)	0.582
Recovery	106	43.62	137	56.38	243		

DM-Diabetes mellitus; CLD-Chronic liver disease, COPD-Chronic obstructive pulmonary disease

Table II: Multivariate analysis for Identifying significant independent predictors for hyponatraemia by binary logistic analysis variables in the equation.

		B	SE	Wald	df	Sig	Exp(B)	95% CI for EXP(B)	
								Lower	Upper
Step 1[a]	Renal failure	-.857	.383	5.012	1	.025	.424	.200	.899
	Thiazide diuretics	-2.764	1.066	6.718	1	.010	.063	.008	.510
	Loop diuretics	-2.055	1.085	3.587	1	.058	.128	.015	1.074
	APACHE-II score	-.006	.018	.127	1	.722	.994	.960	1.029
	Age	-.631	.302	4.378	1	.036	.532	.295	.961
	Hypertension	.058	.294	.038	1	.845	1.059	.595	1.885
	Constant	1.022	.400	6.512	1	.011	2.778		

a. Variable(s) entered on step 1: Renal failure, Thiazides, Loop diuretics, Apache 2 score, Age, Hypertension.

Fluid restriction was the most common treatment modality (32.03%), followed by glycaemic control (28.12%) and normal saline (16.40%). Hypertonic saline was used initially in 13.28% of hyponatraemic patients. Tolvaptan was used in 3 patients, being the primary treatment modality in one patient.

Table III: Comparison of outcomes in hyponatraemic patients.

	Non-hyponatraemia		Mild		Moderate		Profound		
	No.	%	No.	%	No.	%	No.	%	Total
Mortality	33	19.19	11	17.46	5	12.5	6	24	53
Recovery	139	80.81	52	82.54	35	87.5	19	76	247
	172	100.00	63	100.00	40	100	25	100	300

Chi-square = 1.668 with 3 degrees of freedom; p = 0.882.

Out of 300 patients, 53 (17.66%) died in the ICU, while 4 patients (1.33%) died after transfer out from ICU. Overall mortality in the study population was 57 (19%). Mortality in hyponatraemic patients was 17.19% (n = 22), with no significant difference from that in the non-hyponatraemic group (20.35%, n = 57) (p = 0.582). Mortality in the mild, moderate and profound hyponatraemia patients was 24% (n = 6), 17.46% (n = 11) and 12.5% (n = 5), respectively (Table III). In the hyponatraemic patients, mean duration of stay in ICU (5.42 ± 5.67 days) was not significantly different as compared with 6.44 ± 8.47 days in the non-hyponatraemic group (p = 0.239). Similarly mean BiPAP (bilevel positive airway pressure) support duration was 4.15 ± 3.31 days as compared with 8.41 ± 9.7 days in the non-hyponatraemic group (p = 0.131). Mean mechanical ventilator support duration was 5.88 ± 7.52 days in the hyponatraemic patients while it was 5.11 ± 6.11 days in the non-hyponatraemic patients (p = 0.644). In patients with profound hyponatraemia (serum sodium < 125), mortality was 24%, which was higher than that in the non-hyponatraemic patients but the association was not significant (p = 0.882).

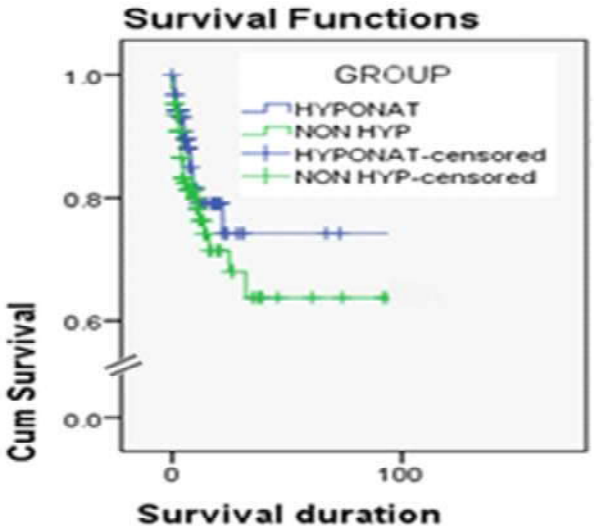


Fig. 3: *Kaplan-Meier survival analysis.*

Discussion

Hyponatraemia is one of the most common electrolyte imbalances seen in hospital ICUs. Yet there is a challenge in managing these patients as hyponatremia is not a single well-defined disease entity and the treatment varies, depending on the aetiology.

Prevalence of hyponatraemia (42.66%) is significantly higher in comparison with other studies, especially the studies done outside India[3-7]. The studies show similar distribution, with profound hyponatraemia having the least prevalence preceded by moderate and mild hyponatraemia. Overall, the prevalence of hyponatraemia on ICU admission appears to be higher in the Indian ICUs as seen in this study and the study done by Padhi *et al*[7]. Hyponatraemia was more common in the elderly patients. Similar trend was observed by Bhattacharjee *et al* where 84% of the patients had age > 84 years[8]. Age is significant risk factor for the development of hyponatraemia due to changes in body metabolism and dietary solute intake with increasing age. Also, comorbidities such as renal failure and hypertension

Kaplan-Meier survival Analysis

Table IV: Means and Medians for Survival Time.

Group	Mean[a]				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower bound	Upper bound			Lower bound	Upper bound
Hyponatraemia	249.663	35.251	180.570	318.755	373.000	.000	.	.
Non-Hyponatraemia	149.454	14.658	120.724	178.184	228.000	.000	.	.
Overall	222.682	26.286	171.161	274.202	228.000	55.518	119.185	336.815

a. Estimation is limited to the largest survival time if it is censored.

increase with age. There is relatively low consumption of high salt content processed food items by the Indian elderly population, as compared with their Western counterparts. Salt intake is further reduced based on doctor's advice for the control of hypertension. The situation is worsened by use of thiazide diuretics as anti-hypertensive medications, and routine monitoring of serum sodium is rarely done. These may be the possible reasons for higher prevalence of hyponatraemia in Indian ICUs.

Similar to the trend shown by Bhattacharjee *et al*[8], hypertension (49%) and diabetes mellitus (35.67%) were the most common comorbidities in the study population in both hyponatraemic as well as non-hyponatraemic groups. A greater number of patients with hypertension are likely to use diuretics as anti-hypertensive medications and prevalence of diabetes mellitus increases with age. Hyponatraemic hypertensive syndrome is a known clinical entity in which atherosclerosis of arteries in the elderly is associated with development of hyponatraemia[11]. Kidney disease itself is the cause of hyponatraemia due to urinary loss of sodium, so association is causal. Role of thiazide diuretics in hyponatraemia is already well established[1].

Kidney disease was the most common cause of hyponatraemia in this study, followed by hyperglycaemia, liver cirrhosis, diuretic use, SIAD and gastrointestinal loss. In contrast, Padhi *et al* reported SIAD to be the most common cause of hyponatraemia (36.25%)[7] while Bhattacharjee *et al* reported gastrointestinal loss as the most common cause (24%), followed by diuretics (20%), congestive cardiac failure (18%), liver cirrhosis (15%), SIAD (8%) and chronic renal failure (7%)[8]. This may be due to different settings where studies were carried out. Padhi *et al* had patients admitted in the mixed ICU as the study population, while Bhattacharjee *et al* had medicine ward patients as the study population. This study had medical ICU as the study population. As cardiac patients were admitted in a different cardiac ICU, number of patients with cardiac failure was less. More patients with end-stage kidney disease might have been admitted in the ICU. Similar to our study, Agarwal *et al* also reported fluid restriction to be the most common treatment modality (40%) in hyponatraemic patients with serum $Na^+ < 125$ mEq/l[10].

There was no significant difference in mortality in the hyponatraemic and non-hyponatraemic groups. Also, there was no significant difference between the two populations in terms of other parameters like mean duration of stay in ICU, mean BiPAP support duration and mean duration of mechanical ventilator support. This is in contrast to the previous studies where hyponatraemia has been shown to be associated with increased mortality and adverse outcome[5,7]. As compared with this study, hypernatraemic patients were excluded in the studies by Funk *et al*[5] and Padhi *et al*[7]. Hyperglycaemic patients were excluded by Padhi *et al*[7]. Even after adjusting the above two factors, mortality association was not significant. This may be attributed to higher contribution of the other associated diseases and risk factors in the study population, rather than hyponatraemia as the determinant of outcome.

Conclusions

This study shows that hyponatraemia on ICU admission is more common in Indian ICUs (prevalence = 42.66%). Old age, chronic renal failure, and use of thiazide diuretics were important risk factors for hyponatraemia. Emphasis on regular monitoring of serum electrolytes especially serum sodium is of utmost importance in these specific populations. Surprisingly, there was no significant association of hyponatraemia with increased mortality and adverse outcome. Hyponatraemia, when properly and promptly managed in intensive care settings, is a treatable condition with good patient outcomes.

Study limitations

1. As the site of study was adult medical ICU, it doesn't represent other ICUs (e.g., surgical, cardiac and paediatric ICUs).
2. Our hospital, being a private sector tertiary care centre, may not be representative of the lower socio-economic strata of the general population.
3. Further studies with larger sample size, using multivariate analysis, may be needed to substantiate or contradict the findings.

Recommendations

1. Elderly patients, prone to many other diseases, are more likely to develop hyponatraemia. Electrolyte imbalance as cause of presenting complaints in elderly should be given priority.
2. Indiscriminate use of thiazide diuretics for hypertension in older patients should be discouraged. If necessary, frequent monitoring of serum electrolytes especially serum sodium should be done for early detection of electrolyte imbalance.
3. Frequent monitoring of serum sodium, along with other electrolytes and maintenance of fluid balance is recommended in patients with chronic renal failure.
4. Association of hyponatraemia with adverse outcomes needs to be reconsidered with larger studies, in view of the present study findings. Newer diagnostic modalities and better treatment for diseases like chronic renal failure should be taken into account.

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ORIGINAL ARTICLE

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Haematological Parameters in COVID-19 and their Association with Severity and Mortality

Nikhil Gupta, Nalini Kurri**, Bhumesh Tyagi**, Satish Kumar**, Ashok Kumar Agarwal***, Suparna Dubey*****

Abstract

***Background:** Since the COVID-19 global pandemic emerged, the worldwide medical fraternity has been facing multiple challenges regarding its management. Patients with severe/critical illness have a poor prognosis. Hence, early detection and assessment of disease severity is vital to offer timely management. Recent studies indicate that altered haematological parameters may predict the disease severity and mortality. We aimed to investigate associations between haematological parameters and disease severity in patients with SARS CoV 2 infection.*

***Objectives:** This study was undertaken to find out the optimal cut-off values of haematological parameters that may significantly relate to the clinical severity of COVID-19 and to evaluate their utility as parameters to predict mortality.*

***Methods:** It was a hospital based prospective cohort study, conducted over a period of 4 months, from May, 2020 to August, 2020 at a level 3 designated COVID-19 facility in Uttar Pradesh. In our cohort, there were a total of 211 patients out of which 125 were non-ICU admissions and 86 were ICU admissions. Cases were classified as severe, moderate and mild based on their oxygen requirements and ICU care needs.*

***Results:** The mean age of non-ICU patients was 47.1 ± 16.2 years, ICU survivors, were aged 57.4 ± 11.4, and ICU non-survivors were aged 57.3 ± 15.2. There was no mortality in the non-ICU group. Of the 86 ICU admissions, 69 were male, of which 27 were non-survivors and 17 were female, of whom 5 were non-survivors. Amongst the deceased patients, there was a significant leucocytosis ($P < 0.001$), neutrophilia ($P < 0.001$) and increased NLR ($P = 0.026$). The pooled analysis revealed that the NLR cut-off of > 3.85 was associated with severity and prediction for ICU admission, while NLR of > 5.2857 was associated with mortality.*

***Conclusion:** In conclusion, advanced age, male sex, a high white blood cell count, neutrophilic leucocytosis or neutrophilia along with the elevated NLR were significantly associated with both the clinical severity and mortality.*

***Key words:** SARS COV-2, COVID-19, complete blood count, absolute neutrophil count, neutrophil lymphocyte ratio, acute respiratory distress syndrome.*

Introduction

On December 31, 2019, the World Health Organisation was notified of a cluster of pneumonia cases of unknown aetiology in Wuhan, China[1]. The aetiologic agent was identified as a novel beta-coronavirus, subsequently named SARS CoV-2 and the disease was designated COVID-19[2]. It has subsequently spread rapidly. The World Health Organisation (WHO) on March 11, 2020, had declared the novel coronavirus (COVID-19) outbreak a global pandemic[3].

Current information suggests that the incubation period ranges from 1 to 12.5 days (with median estimates of 5 to 6 days). Patients with SARS COV-2, develop a myriad of clinical symptoms like fever, dry cough, myalgia, dyspnoea, anorexia, rhinorrhoea, sore throat, anosmia, ageusia. Major complications include ARDS, arrhythmias, metabolic acidosis, coagulopathy, and septic shock. Most critically ill patients were older, around 60 years and had more underlying co-morbidities. Most patients require oxygen therapy and a minority of the patients need non-invasive and invasive ventilation[4-5].

There are no specific clinical symptoms which can accurately predict the severity and progression of COVID-19; consequently, we opted to rely on laboratory parameters to assess the severity of the disease. Complete blood count (CBC) is a simple, readily obtainable and affordable haematological investigation, that can provide comprehensive, yet reliable, information regarding the disease progression. SARS CoV-2 infection is characterised by the development and progression of inflammatory responses. Haematological parameters, such as white blood cells (WBCs) and their subpopulations like neutrophils and

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lymphocytes and also red cell distribution width, platelet count, mean platelet volume, platelet distribution width and derived markers such as neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and lymphocyte to monocyte ratio (LMR), are established biomarkers of inflammatory responses[6-9]. Several studies have been carried-out, comparing the various values and ratios obtained from CBC, in COVID-19 patients and COVID-19 negative individuals[10,11].

However, there is a lacuna regarding the haematological parameter comparison in COVID-19 patients and their association with disease severity. We aimed to study the differences in haematological parameters between ICU and Non-ICU cases of COVID-19.

Material and methods

The present work was a hospital-based prospective cohort study, conducted over a period of 4 months, from May, 2020 to August, 2020 at Sharda Hospital, a level 3 designated COVID-19 facility. Patients were triaged on admission according to Indian Central Medical Research (ICMR) guidelines and were categorised as mild, moderate, severe and critically ill[12]. Mild/moderate category of patients were admitted to wards and severe/critically ill cases were transferred to ICU. COVID -19 diagnosis was confirmed by SARS-COV-2 real time PCR (Qualitative) by obtaining nasopharyngeal or oropharyngeal swab. COVID-19 test was conducted as per kits approved by ICMR/CE-IVD/USFDA.

Inclusion criteria

- All patients aged > 18 years.
- Patients with a positive RT PCR for COVID 19/positive COVID-19 rapid antigen test.

Exclusion criteria

- Pregnancy or breastfeeding.
- Patients with documented haematological disorders like thalassaemia, sickle cell disease, haemolytic disorders, etc.

Study design

A total of 211 subjects were studied, out of which 86 were classified as severe cases of COVID-19 requiring ICU admission, while the rest were mild-to-moderate cases admitted to the ward.

An informed consent was taken from all subjects included in the study and prior approval of the institutional ethics committee of, Sharda Hospital and School of Medical Science and Research, (SMSR) Greater Noida, Uttar Pradesh was obtained. Thorough history was taken and examination was carried-out.

As per evaluation protocol, CBC was sent for all patients along with the other relevant investigations. A general blood picture was performed on the same blood sample that was used for CBC in order to corroborate the findings of the automated cell counter. CBC was done by using hydrodynamic focusing on Sysmex automated analyser XT1800i available in the central laboratory of the hospital.

Statistical methods

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and mathematical functions were then applied using the same. Continuous variables were summarised in the form of means and standard deviations and categorical variables were expressed as frequencies and percentages. Graphically the data was presented by bar and pie diagrams. ANOVA test was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A p value of less than 0.05 was considered statistically significant. All p values were two-tailed.

Results

A total of 211 patients were enrolled, of which 125 were mild/moderate cases, admitted to wards (Non-ICU admissions) and 86 were severe/critically ill cases, hence considered for ICU admissions. The mean age of non-ICU patients was 47.1 ± 16.2 years; ICU survivors were aged 57.4 ± 11.4, and ICU non-survivors were aged 57.3 ± 15.2. Patients with mild disease were significantly younger than those with severe disease with a mean age difference of 10.29 years ($p < 0.001$). However, age did not have statistical significance ($p < 0.966$) in the mortality prediction between ICU survivors and non-survivors. Of the 125 non-ICU admissions, 83 were male (66.4%) while 42 were female (33.3%) with no mortality noted. Of the 86 ICU admissions 69 were male of which 27 were non-survivors and 17 were female of whom 5 were non-survivors. There was a significant difference between both genders as to the requirement of ICU admission and mortality. We found that males had an overwhelming higher percentage of ICU admission and mortality than female patients. When the parameters were compared between the three groups it was found that there was a significant difference in all parameters except lymphocyte-monocyte ratio (LMR) and PDW. We did intergroup analysis to find the parameters that could provide a better prognostication of disease severity and mortality.

Table I: Characteristics of the three groups of patients.

Characteristics	Severity			p value
	Non ICU	ICU		
		Survivors	Non-survivors	
Age (years)	47.1 ± 16.2	57.4 ± 11.4	57.3 ± 15.2	< 0.001*
Sex	M = 83 (66.4%) F = 42 (33.6%)	M = 42 (77.7%) F = 12 (22.2%)	M=27 (84.4%) F=5 (15.6%)	
Haemoglobin (g/dl)	12.89 ± 1.61	12.07 ± 2.02	12.5 ± 2.6	0.03*
TLC	6466.4 ± 2051.4	9696.3 ± 4401.7	15560.9 ± 6036.9	< 0.001*
Neutrophils	4093.2 ± 1792.4	7777 ± 3972.7	13372.5 ± 5982.8	< 0.001*
Lymphocytes	1814.1 ± 766.3	1360.6 ± 1418.1	1443.9 ± 781.2	0.009*
Monocytes	449.5 ± 184.1	462.2 ± 314.7	620.1 ± 326.4	0.002*
Platelets	220104 ± 108211	266037 ± 125074.8	207187.5 ± 105968.2	0.02*
RDW	14.59 ± 1.62	14.95 ± 1.82	16.86 ± 2.71	< 0.001*
PDW	16.05 ± 3.27	14.89 ± 3.55	15.60 ± 2.52	0.09
MPV (fl)	11.95 ± 1.35	11.41 ± 1.25	11.29 ± 1.08	0.005*
NLR	2.859 ± 2.35	7.939 ± 5.31	12.161 ± 9.51	< 0.001*
LMR	4.532 ± 2.84	4.091 ± 4.58	3.169 ± 2.85	0.125
PLR	142.79 ± 93.61	266.12 ± 165.53	180.85 ± 147.59	< 0.001*

In the intergroup comparison between non-ICU and the ICU survivor group of patients, we found that there was a significant difference between the two groups when compared for age, haemoglobin, TLC, neutrophils, lymphocytes, platelets, PDW, MPV, NLR and PLR.

In the intergroup comparison between the ICU survivor and non-survivor group of patients we found that there was a significant difference between the two groups when compared for TLC, neutrophils, monocytes, platelets, RDW, NLR and PLR.

In the intergroup comparison between non-survivors and the non-ICU group of patients we found that there was a significant difference between the two groups when compared for age, TLC, neutrophils, lymphocytes, monocytes, RDW, MPV, NLR and LMR.

Table II: Intergroup comparison between the Non-ICU group and ICU survivor group.

Characteristics	Mean difference	p value
Age (years)	10.29	< 0.001*
Haemoglobin (g/dl)	- 0.82	0.01*
Total leucocyte count	3229.89	< 0.001*
Neutrophils	3683.76	< 0.001*
Lymphocytes	- 453.56	0.031*
Monocytes	12.64	0.785
Platelets	45933.04	0.022*
RDW	0.35	0.221
PDW	- 1.16	0.043*
MPV (fl)	- 0.54	0.011*
NLR	5.07	< 0.001*
LMR	- 0.44	0.517
PLR	123.32	< 0.001*

Table III: Intergroup comparison between the ICU survivor group and Non-survivor group.

Characteristics	Mean difference	p value
Age (years)	- 0.13	0.966
Haemoglobin (g/dl)	0.43	0.427
Total leucocyte count	5864.64	< 0.001*
Neutrophils	5595.58	< 0.001*
Lymphocytes	83.36	0.727
Monocytes	157.85	0.032*
Platelets	- 58849.53	0.023*
RDW	1.91	0.001*
PDW	0.71	0.282
MPV (fl)	- 0.11	0.651
NLR	4.22	0.026*
LMR	- 0.92	0.256
PLR	- 85.26	0.016*

Table IV: Intergroup comparison between the Non-Survivors group and Non-ICU group.

Characteristics	Mean difference	p value
Age (years)	-10.16	0.001*
Haemoglobin (g/dl)	0.39	0.424
Total leucocyte count	-9094.53	<0.001*

Neutrophils	-9279.34	<0.001*
Lymphocytes	370.19	0.02*
Monocytes	-170.49	0.007*
Platelets	12916.5	0.543
RDW	-2.27	<0.001*
PDW	0.45	0.403
MPV (fl)	0.66	0.005*
NLR	-9.30	<0.001*
LMR	1.362	0.019*
PLR	-38.06	0.173

The pooled analysis revealed that the NLR at admission was significantly elevated for ICU survivors, when compared to ward patients with the NLR cut-off of > 3.85 associated with severity and prediction for ICU admission with a sensitivity of 77.8% and a specificity of 84.0% (area under the curve (AUC): 0.852, 95% confidence interval (CI) 0.791 to 0.900 (p < 0.001). It had a diagnostic accuracy of predicting severity of 82.12%.

The pooled analysis was similarly elevated for non-survivors, when compared to survivors of ICU (p < 0.001). The NLR of > 5.2857 was associated with mortality, with a sensitivity of 78.1% and a specificity of 77.7% (area under the curve (AUC): 0.811, 95% confidence interval (CI) 0.752 to 0.862, (P < 0.001). The diagnostic accuracy of predicting mortality was 77.25%.

Table V: Receiver operating characteristic curve of NLR for predicting ICU and mortality.

NLR	ICU	Mortality
Area under the ROC curve (AUC)	0.852	0.811
Standard error	0.0334	0.0451
95% confidence interval	0.791 to 0.900	0.752 to 0.862
p value	< 0.0001	< 0.0001
Cut-off	> 3.85	> 5.2857
Sensitivity (95% CI)	77.78% (64.4 - 88.0%)	78.12% (60.0 - 90.7%)
Specificity (95% CI)	84% (76.4 - 89.9%)	77.65% (70.8 - 83.5%)
PPV (95% CI)	67.7% (54.7 - 79.1%)	38.5% (26.7 - 51.4%)
NPV (95% CI)	89.7% (82.8 - 94.6%)	95.2% (90.4 - 98.1%)
Diagnostic accuracy	82.12%	77.25%

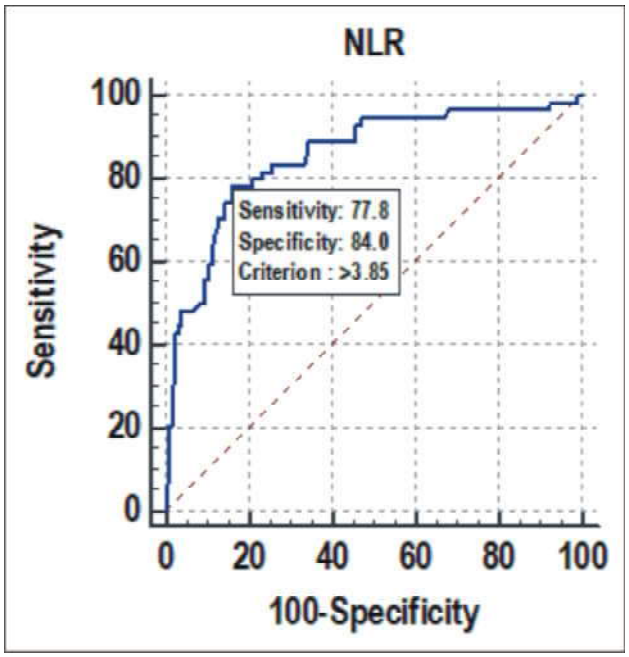

Fig. 1: *Receiver operating characteristic curve of NLR for predicting ICU admission.*

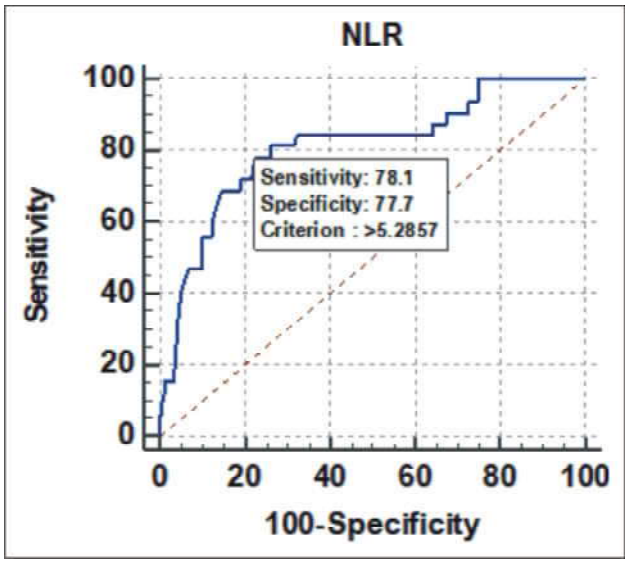

Fig. 1: *Receiver operating characteristic curve of NLR for predicting mortality.*

Discussion

Complete blood count (CBC) is simple, readily obtainable and affordable haematological investigation, that can provide comprehensive yet reliable information regarding disease progression. Haematological parameters, such as white blood cells (WBCs) and their subpopulations like neutrophils and lymphocytes and red cell distribution width, platelet count, mean platelet volume, platelet distribution

width and derived markers such as neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and lymphocyte to monocyte ratio (LMR), are established biomarkers of inflammatory responses[6-9]. There is a pressing need to rely on easily obtainable and cost-effective indicators to simplify the diagnostic process and evaluate the disease severity[13].

In our study, we enrolled 211 patients (Table I), of which 125 were mild/moderate cases, admitted to wards (Non-ICU admissions) and 86 were severe/critically ill cases who were admitted to ICU. Of the 86 patients admitted to ICU 32 expired and were grouped as non-survivors. Younger population, age < 50 years were less prone to develop severe disease. Clinical improvement was predicted by younger age with no associated co-morbidities, female gender and a low NLR. Transfer to ICU was instead forecasted by leucocytosis, lymphopenia, neutrophilia and advanced age along with an increased NLR. Wang *et al*[4], have shown similar association for the factors that predict severity of COVID-19. In their findings, compared with patients who did not receive ICU care (n = 102), patients who required ICU care (n = 36) were significantly older (median age, 66 years [IQR, 57 - 78] vs 51 years [IQR, 37 - 62]; P < .001) and were more likely to have underlying comorbidities. They also found that most patients had marked lymphopenia, and non-survivors developed more severe lymphopenia over time. White blood cell counts and neutrophil counts were higher in non-survivors than those in survivors. In another study, Tao *et al*[13], found that age, leucocytosis, neutrophilia, and lymphopenia were the predictors of worse clinical outcomes in patients. These results corroborate the findings of our study. In our intergroup comparison (3 groups of Non-ICU admissions, ICU survivors and ICU non-survivors), there was no statistically significant relationship noted between the other haematological variables such as haemoglobin, platelet parameters like PLT count, PDW, PLR and also Lymphocyte to monocyte ratio. Hence, these variables alone may not be considered for predicting severity or mortality outcomes in COVID-19 patients (Table II, III, IV).

Neutrophil proliferation and lymphocyte apoptosis are physiological responses of the innate immune system to systemic inflammation. In several previous studies[7-10], NLR has been linked to conditions such as pancreatitis, appendicitis, lung cancer and pneumonias. Elevated NLR is also associated with increased mortality in patients with severe acute respiratory syndrome[11-12].

In our study, the ROC curve of NLR for predicting ICU admission and mortality (Table V) showed AUC of 0.852 and 0.811 to predict the severity and mortality, respectively. Confidence interval (95%) is 0.791 to 0.900 for severity prediction and 0.752 to 0.862 for mortality prediction, which confirms the strength of association between elevated NLR and disease severity. Fig. 1 shows NLR cut of value for predicting severity was > 3.85 (95% confidence interval (0.791 to 0.90), p value < 0.001) with a sensitivity of 77.78% and specificity of 84%. Fig. 2 shows NLR cut-off value for predicting mortality was > 5.29 (95% confidence interval (0.752 to 0.862), p value < 0.0001) with a sensitivity of 78.12% and specificity of 77.65%.

Yang *et al*[14], comparing the NLR, LMR, PLR and CRP amongst severe and non-severe patients of COVID-19, found that WBC count, NLR, LMR, PLR, and CRP of severe patients were significantly higher than those of non-severe patients. These results are similar to ours. In their study, Yang *et al*, also found that the optimal threshold at 3.3 for NLR showed a superior prognostic ablity and had the highest sensitivity and specificity (63.6% and 88%) and the largest AUC (0.841). The AUC is similar to the one found in the present study. However, our optimal cut-off value was slightly higher at 3.85 with a sensitivity and specificity of 77.78% and 84%, respectively.

In a systematic review and meta-analysis[15] of 19 studies, it was found that the sensitivity, specificity, AUC and cut-off value of NLR for predicting mortality and disease severity varied greatly among the studies. The cut-off value for severity ranged from 3.0 - 13.4, with an average of 5.24. The cut-off value for mortality ranged from 3 - 11.8, with an average of 7.14. In terms of predicting disease severity, the cut-off value in six studies was higher than 4.5 and was termed the "high cut-off value" subgroup. Seven others used a lower cut-off value, which were included in the "low cut-off value" subgroup. The AUC was 0.86 (95% CI 0.83 -0.89) and 0.82 (95% CI 0.78 - 0.85), respectively. Similarly, ten studies reporting the predictive value of NLR on mortality were divided into "high cut-off value" (cut-off e" 6.5) and "low cut-off value" (< 6.5) subgroups, and the AUC was 0.92 (95% CI 0.89 - 0.94) and 0.84 (95% CI 0.80 - 0.87), respectively. These findings were consistent with our findings.

The variability in the optimal cut-off for NLR can be explained by geography and race as most of the studies included in this meta-analysis were carried-out in China. Also, the timing of acquiring the sample from the day of disease onset may play an important role in the variability of NLR. As, in severe or non-survivor patients with COVID-19, the lymphocyte count decreases progressively, while the neutrophils count gradually increases. This may be due to excessive inflammation and immune suppression caused by SARS-CoV-2 infection. On the one hand, neutrophils are generally regarded as pro-inflammatory cells with a range of antimicrobial activities, which can be triggered by virus-related inflammatory factors, such as interleukin-6 and interleukin-8. On the other hand, systenic inflammation

triggered by SARS-CoV-2 significantly depresses cellular immunity, leading to a decrease in CD3 + T cells, CD4+ T cells and CD8+ T cells[16].

Strengths of study

NLR was statistically significantly different ($P < 0.001$) in predicting disease severity and mortality. NLR is an easily attainable early bio-marker of inflammation and also cost-effective when compared to other inflammatory markers.

Limitations of the study

Haematological parameters were not measured dynamically, hence it is unclear whether these parameters exhibit cumulative changes when the patients condition deteriorates. Also, inclusion of the other inflammatory markers would complement the initial test results in elucidating the underlying inflammatory mechanism, which contributes to the disease severity.

Conclusion and summary

In conclusion, advanced age (> 58 years), male gender, haematological variables like leucocytosis, neutrophilia, lymphopenia and NLR are useful in prognosticating the disease severity. NLR was notably associated with increased severity and mortality. We conclude that NLR can be considered as an initial screening test to assess the severity and mortality in patients of COVID-19.

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SHORT ORIGINAL ARTICLE

JIACM 2021; 22(1-2): 47

Discovery of a New Method of Elicitation of the Plantar Reflex (Sainani Method)

*Gurmukh S Sainani**

Abstract

Of the various methods of eliciting a plantar response, the Sainani method gave a good response in patients wih thick and rough soles. In this method, stroke is given on the lateral aspect of the foot (between the dorsum and sole of the foot).

Introduction

With my teaching experience of 60 years in internal medicine for undergraduates (MBBS) and post-graduates (MD, DNB, MRCP), I observed that in patients with thick and rough soles, the Babinski (1896) method of eliciting a plantar response often gives a poor response.

I then discovered a new area on the lateral aspect of the foot (between the dorsum and sole of the foot) where stroke given upwards (Fig. 1) gave a good response comparable to other methods (Oppenheim 1858, Gordon 1874, Schaefer 1852, Gonda 1889, Chaddock 1911).

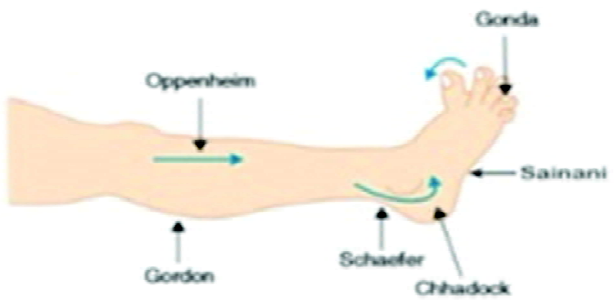

Fig. 1:

I then decided to validate my observation by carrying out the different methods of eliciting a plantar response in patients. In these 40 years (1980 to 2020) I compared personally all the reflexes mentioned above and I have found the following observations.

Observations

1. In all patients with normal soles, response was comparable with all the methods including Sainani.
2. Patients with rough and thick soles had sluggish response to Babinski method, equivocal response with other methods, but good satisfactory response with Sainani method. So, overall Sainani method turns out to be the most reliable of all the methods.

Conclusions

1. Sainani method[1] is easily elicited, relatively less discomforting and overall it turns out to be the most reliable of all the methods in patients as compared to other methods. It is suggested that Sainani method should be used in patients with thick and rough soles.
2. The student appearing for exams must attempt to elicit the plantar response by Sainani method before commenting on its presence or absence. The plantar reflex is a common dilemma for both the student and the examiner.

I wish to thank Dr. Rajesh Sainani and Dr. Ashwin Sainani for abridging and editing this paper.

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REVIEW ARTICLE

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Medical Violence In India

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Abstract

The last decade has witnessed a dramatic rise in cases of violence against medical professionals all over the world, particularly in India. The problem is not simple and needs an in-depth analysis of the reasons for this deteriorating doctor-patient relationship. Poor public health infrastructure, poor tolerance of patients and relatives, together with high cost of treatment in private sector and lack of communication between doctor and patient are the basic reasons for this growing conflict. The time has come to address this issue before it is too late. The government, public, and doctors need to understand that all of them will have to work together in solving this issue for the betterment of public health. This article provides an insight of all the problems associated with rising medical violence.

Key words: Healthcare professionals, medical violence, doctor-patient relationship.

Introduction

Violence against medical profession is not new and can be traced back to many decades[1]. But, over the last few years, it has accelerated at a rather dangerous pace and is making headlines across the world[2]. Medical profession is perhaps going through its worst phase as regards violence against doctors. It is a matter of great concern for healthcare professionals and general public as both of them are adversely affected by it.

The World Health Organisation has defined violence as the intentional use of physical force or power, threatened or actual, against oneself, another person, or against a group or community, which either results in or has a high likelihood of resulting in injury, death, psychological harm, mal-development, or deprivation[3].

Current scenario

Articles on medical violence published in the last decade tell the story of its importance and growing concern. In 2017, it was reported that nearly 75% of doctors in India have faced some form of physical or verbal violence during their lifetime[4]. About 70% doctors feel unsafe while treating a patient[5]. It is not uncommon these days to see newspapers flooded with reports of doctors getting manhandled, threatened and even killed by patient's relatives[6]. The problem is not restricted to India, but extends worldwide to several countries like UK, China, Australia, Germany, Pakistan and Turkey[4]. In Spain, April 20th has been declared as the National Day Against Aggression in Health-care Facilities in memory of the murder of a resident doctor by a patient in 2009[8].

Violence usually occurs in casualty, outside intensive care units and post-surgical wards, where resident doctors managing critical patients become their primary targets[9]. Violence could be in the form of verbal threats, physical assault, extortions, murder, vandalism or arson. As a result, medical professionals work under great stress, leading to problems like depression, insomnia, post-traumatic stress, fear and anxiety[10]. The actual number of attacks of medical violence are much more than the reported figures. Doctors, particularly in government set-ups, are often flooded with patients. This leads to patient dissatisfaction as the doctors are not able to devote adequate time to each patient and their illnesses[11].

Patients, who are already under stress due to illnesses, become further agitated, and a vicious cycle is set in, leading to violence. The situation has reached to an extent that parents have started choosing alternate careers for their children[12].

Due to the poor public health facilities, many patients are forced to seek help in corporate hospitals. High expectations on the patient's part leads to detailed evaluation of rather minor problems. This makes the treatment costlier and it pinches the pockets of the common man, which is perceived as commercialisation of medical profession[13]. The media adds fuel to this deteriorating and delicate doctor-patient relationship and portrays negative images of doctors. The media too needs to have an insight of both sides before portraying doctors as being responsible for all adverse outcomes and also, the doctors should be in regular communication with the media so that wrong

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information is not conveyed to the public.

The doctors retaliate to the violence by wearing black badges, conducting strikes and demonstrations, but they have failed to bring a change in the society's attitude towards this noble profession. The Government of India, in 2019, had asked all states to enact specific legislation for protecting medical professionals from any sort of violence. Since this has become a state subject, different states are making different laws so that doctors discharge their duties in a congenial environment without any fear. However, implementation of these laws is lacking.

Over the past few decades, the outlook of the common man towards medical profession has undoubtedly changed drastically. These acts of violence are a reflection of a deeper systemic failure due to poor public health services, high cost of treatment in private hospitals and lack of confidence in doctors.

Reasons of the common man

- Unrealistically high expectations
- Unacceptability of complications, including death
- Short tempered behaviour, especially of youth
- Ignorance of medical problems, especially among poor population
- Long waiting period before a patient can speak to the doctor
- Lack of adequate health-related infrastructure in government hospitals
- High expenditure in corporate hospitals, particularly in the absence of health insurance
- Perception of medical profession as a business
- Role of media in portraying a negative image of medical profession.

On the contrary, one should not forget the failings of medical professionals

- Lack of communication regarding the nature of disease, its outcome and complications with the patient and relatives
- High targets of corporate hospitals
- Not prescribing generic medications[14]
- Withholding a deceased body until final settlement of bill.

Poor communication between patient and doctors plays a significant role in violence. Patients are dissatisfied when they receive incomplete information regarding their disease, its course and complications. Doctors need to address these issues empathetically. False and unrealistic assurances to the patient or relatives must be avoided. Medical and para-medical staff should undergo proper training which will enable them to develop communication skills, soft skills, refusal skills, remain calm and assertive, and overcome stress and anger. Furthermore, the doctors must protect themselves with a good indemnity insurance[15]. Studies have shown that effective doctor-patient communication is correlated with higher patient satisfaction[5].

A healthy doctor-patient relationship is built on trust but unfortunately, this trust is decreasing day by day. People have forgotten that every complication or death is not due to medical negligence. The term "natural death" seems to be fading from the common man's dictionary. Medicine should not be considered as a black and white subject as diagnosis is based on history narrated by the patient, clinical examination and investigations[16]. Moreover, every patient does not respond to treatment in the same way. So, the outcome is variable for each patient and every disease is not treatable.

According to data, healthcare professionals are four times more likely to be injured (and away from work) as compared to other professionals due to the growing medical violence[17]. So, medical violence should be considered, at least equivalent, to violence on any other on-duty public servant and should be dealt with appropriately by law.

It is never too late to suggest improvements in any sphere of life. The government, general public and healthcare professionals should come together for the betterment of this noble profession. Everybody should understand that the fight is against diseases and not against healthcare professionals. World Health Organisation (WHO) in association with International Labour Office (ILO), International Council of Nurses (ICN) and Public Services International (PSI) developed the "Framework Guidelines for Addressing Workplace Violence in the Health Sector" in 2002 at Geneva. According to these guidelines, workplace violence is not an isolated problem but a structural, strategic problem deep rooted in the social, economic, organisational and cultural factors. Further, these guidelines intended to develop sound policies and practical approaches for the prevention and elimination of violence in the health sector.

Steps for improvement

- Medical curriculum should include communication skills, ethics, and stress management.

- Improvement of health services in public sector.
- Increasing staff and use of technology in hospitals to avoid long waiting periods.
- Hospital security should be strengthened.
- Proper consent and documentation of every intervention.
- Strict law enforcement to ensure that perpetrators of violence do not escape punishment.

Conclusion

Whenever a healthcare professional is a victim of medical violence, it is the duty of the whole medical fraternity to show unity and deal with it appropriately. Also, hospitals should have a standard operating procedure (SOP) to deal with such incidents. There should be zero-tolerance towards medical violence by formulating strict legislations regarding the safety of the healthcare professionals. These laws should be displayed prominently in hospital premises so that people think before committing these heinous acts. Media should be sensitive to reporting of such issues and should give regard to both sides of the story. The government needs to divert more resources towards the health sector than what it is at present.

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REVIEW ARTICLE

JIACM 2021; 22(1-2): 51-56

Ketogenic Diet – Where are we so far?

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Abstract

Ketogenic diet is a normo-caloric diet composed of high fat, low carbohydrates and provides adequate calories. It induces a state of nutritional ketosis in which, under shortage of glucose, there is overproduction of ketone bodies which are used as a source of energy, especially in the Central Nervous System (CNS) as it cannot use fat as an alternative source of energy. Ketogenic diets have been of interest since early 1920s, when they were first tried for resistant epilepsy. Since then the benefits of ketogenic diet have been explored in various other conditions. Many active researches are underway to prove their role in other areas as well. As of our current knowledge, ketogenic diet has proven to be beneficial in: Diabetes, Cardiovascular Diseases, Obesity, Epilepsy. Many other areas have shown promising results as well: improving neurocognitive and motor functions in many Central Nervous System disorders, certain cancers, acne, etc. However, the benefits of ketogenic diet come with certain risks like hypoglycaemia, worsening renal functions, renal stones, gut dysbiosis.

Key words: Ketogenic diet, keto diet, cancer, diabetes, neurological diseases, obesity, cardiovascular diseases, weight loss, insulin resistance.

Introduction

Ketogenic diet (KD) is composed of high fat, adequate protein and low carbohydrates (usually less than 50 g/day)[1]. Despite the change in proportion of its contents, it has a normal calorific value. The carbohydrate content provides less than 10% of total daily calorie requirement. It induces a state of nutritional ketosis in body which has a fasting-like effect in the blood with increased levels of ketone bodies.

KD has been of interest since 1920s when it was used as a therapy for epilepsy by Russel Wilde who also coined the term "ketogenic diet". The novel study by Cahill and colleagues in 1960s showed the metabolic benefits of KD and subsequently the benefits of KD in other areas were explored[2]. KD now have shown to be of proven benefits in obesity and weight loss, diabetes, epilepsy, and cardiovascular disease while there is emerging evidence of it benefits in metabolic syndrome, neuro-motor and neurocognitive functions, cancers, etc.

What makes a ketogenic diet?

KD is a very low carbohydrate diet, rich in fat and provides normal calorific requirement. The carbohydrate component provides < 10 per cent of the daily calorie requirement of a 2,000 kcal diet. This is equivalent to 20 - 50 gms of carbohydrate/day[3].

The high content of fat in KD is kept at a ratio of 4:1 (4 gm of fat for every 1 gm of protein and carbohydrate combined).

There have been a few modifications to the classic KD described above; a summary of different types of diets is given in Fig. 1.

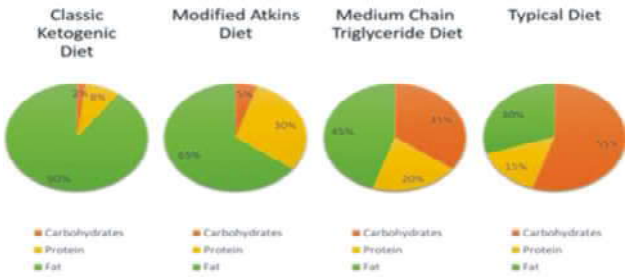

Fig. 1: *Types of very low carbohydrate diet.*

There are a variety of options KD, mostly ones with high fat content. The examples of various food items are:-

1. Nuts and seeds: Almonds, walnuts, cashews, sunflower seeds, chia seeds, pumpkin seeds, flax seeds.
2. Non-starchy vegetables: Green cauliflower, broccoli, tomatoes, mushrooms and peppers.
3. Full-fat dairy: Yogurt, butter and cream.
4. Healthy fats: Coconut oil, olive oil, avocado oil, coconut butter and sesame oil.

Initiation of a ketogenit diet

Initiation of KD involves a careful stepwise approach, with consideration towards pre-existing conditions and

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anticipated nutrient deficiency. Initiation of KD has been explained in Table I.

Table I: Initiation of ketogenic diet.

1. Pre-keto diet counselling and evaluation is required. This is followed by implementation of KD, supplementation, follow-up, monitoring and eventually discontinuing KD.
2. Before starting someone on KD, a detailed history and physical examination, nutritional assessment and laboratory investigations including, renal, thyroid, hepatic, lipids should be checked.
3. Patients who have disorders that are absolute contraindications to KD should be excluded *(Liver failure, pancreatitis, carnitine palmitoyltransferase (CPT)deficiency, carnitine translocase deficiency, pyruvate kinase deficiency and porphyrias*).
4. Risk factors like severe dyslipidemia, renal stones, cardiomyopathy, severe gastroesophageal reflux, and chronic metabolic acidosis can prevent initiation of KD.
5. Patients should be supplemented with essential vitamins and minerals like calcium, magnesium, zinc, selenium, phosphorus, etc.

Metabolic changes in ketosis

After being on KD, there is a drastically reduced carbohydrate consumption, hence the glucose reserves in body becomes insufficient for:-

1. Utilisation by CNS
2. Fat oxidation: This occurs by supply of oxaloacetate from the Kreb's cycle, which is dependent on glucose supply.

After 3 - 4 days without carbohydrate consumption, the CNS derives energy from alternative sources by production of acetyl coenzyme A (CoA)[2].

Acetyl coenzyme A (CoA) is first metabolised to 3-hydroxy-3-methylglutaryl–CoA (HMG CoA) which is normally used for the synthesis of cholesterol. However, during ketosis and relative hypoglycaemia, there are low levels of insulin, which diverts this pathway towards production of ketone bodies (acetoacetate, b-hydroxybutyric acid and acetone). This condition leads to ketonaemia and ketonuria. The pathway has been summarised in a simplified diagram in Fig. 2.

When serum ketone levels reach a concentration of about 4 mmol/l, ketone bodies are then used by tissues as a source

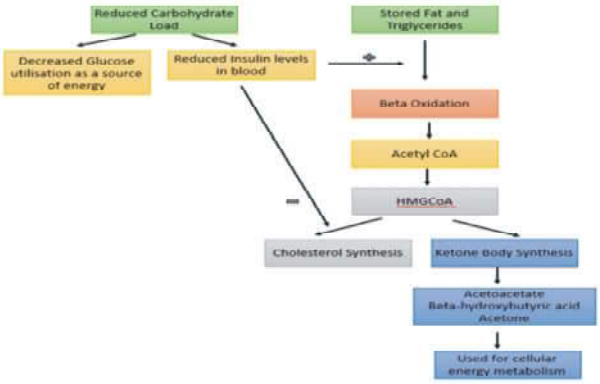

Fig. 2: *Metabolic changes during ketosis.*

of energy.

This state of ketosis can be seen in:-

1. Pathological Ketosis: prolonged fasting, type 1 diabetes mellitus.
2. Physiological Ketosis: while consuming KD.

In physiological ketosis, serum ketone levels reach a maximum of 7 - 8 mmol/l with no change in pH, whereas in uncontrolled diabetic ketoacidosis (i.e., pathological ketosis) it can exceed to more than 20 mmol/l and accompanied lowering of blood pH.

Some unique features to note about this metabolic change are:-

1. Ketone bodies are able to produce more energy than glucose.
2. Although there is a reduction in serum glucose, there is never hypoglycaemia, as glucose is formed from two sources during this time- from glucogenic amino acids and from glycerol liberated via lysis of triglycerides.

Benefits of ketogenic diet

KD has been tried for various conditions in the last century. The first beneficial role of KD was proven in treatment of epilepsy in children in early 1900s. However, it was only after the pioneering work of Cahill and colleagues in 1960s that highlighte the metabolic effects of KD and subsequently the benefits of KD in other area were explored. KD have proven role in certain conditions whereas in others, supportive evidence is there and further studies are being done. These conditions are summarised in Table II.

Table II: Benefits of Ketogenic Diet

Proven Benefit	Emerging Evidence
Epilepsy	Neurological Diseases
Diabetes	Cancer
Weight Reduction	Acne
Cardiovascular Risk	Polycystic Ovarian Syndrome (PCOS)
	Chronic Kidney Disease
	Crohn's Disease
	Respiratory Diseases

1. Weight Loss: There is very strong evidence of the role of KD in weight loss. However, the exact mechanism of weight loss is still not completely understood. There are several proposed mechanisms, the list of which has been ordered below (in order of their supportive evidence):-
   i. Appetite reduction due to satiety effect and also a direct suppressant action on diet[4].
   ii. Reduction in lipogenesis and increased lipolysis[5,6].
   iii. Fat consumption has greater metabolic efficiency by reducing respiratory quotient[7,8].
   iv. Increased metabolic costs of gluconeogenesis and the thermic effect of proteins[9,10]. (Level of evidence, LOE: 3)
2. Cardiovascular benefits: Recent studies have shown clear cardiovascular benefits from KD. The benefit seems to be due to reduction of levels of atherogenic molecules in body. The key metabolic changes that reduce cardiovascular risks are:-
   i. Reduced cholesterol synthesis: Nutritional ketosis decreases the blood Insulin levels, which otherwise on a carbohydrate-rich fed diet, causes cholesterol synthesis (Fig. 2).
   ii. KD increases the levels of high-density lipids[8].
   iii. KD increases the volume of very-low-density- lipid molecules, which reduces the cardiovascular risk, as smaller LDL particles are considered to have more atherogenic potential[11].
   iv. KD also decreases the triglyceride level[12]. (LOE: 3)
3. Insulin Resistance: In conditions with carbohydrate intolerance due to Insulin resistance (e.g., Type-2 Diabetes Mellitus, Metabolic Syndrome, PCOS), the pathophysiology of the disease revolves around hyperinsulinemia. Due to insulin resistance, the skeletal muscles are not able to utilise glucose for their energy needs. High insulin level leads to diversion of this unutilised glucose to liver where it is converted to fatty acids (*de novo* lipogenesis).

   KD, by reducing the carbohydrate load of the body, has shown beneficial effects both in improving biomarkers of risk of disease (i.e., Fasting Plasma Glucose, HbA1c) and also improving insulin sensitivity[13,14]. Several recent studies have confirmed the benefits of KD. In one of the studies, there was reduction of HbA1c levels from pre-treatment 10.5%, to 9.3%, 8.1%, 7.2% and 6.6% over 4 months, solely based on KD without any pharmacological interventions[15]. (LOE: 5)
4. Neurological diseases: KD has shown to be useful in many neurodegenerative and neurocognitive conditions. This is an area of ongoing research and many potential benefits have been proposed from KD. Multiple mechanisms have been proposed which centre around improvement in energy utilisation by cells, and increased mitochondrial biogenesis which then improves synaptic transmission, and improved membrane excitability. Some of the conditions where KD have shown benefits are:-
   i. Epilepsy: KD has been used historically for refractory epilepsies[2]. Based upon the available evidence, a 2018 expert consensus panel recommended that KD therapy should be offered to children with drug-resistant epilepsy after unsuccessful treatment trials of two antiseizure drugs[16]. Several hypotheses have been put forward to explain the mechanism of action of KD: (1) anticonvulsant effect of ketone bodies; (2) a reduced excitability of neurons by ketone bodies[17]; (3) an effect on the mammalian target of rapamycin pathway(mTOR)[18].

      The efficacy of KD was reported in a recent review where studies showed marked reduction (30 - 40%) in seizures, and was also reported that the effects were comparable to modern antiepileptic drugs, atleast in children. (LOE:1)
   ii. Alzheimer's disease: Recent studies have shown that KD has resulted in gain in daily motor activity and also improved cognitive function. It is proposed that KD causes reduction in deposition of amyloid proteins in neurons and improved the neuronal energy utilisation[19]. (LOE: 5)
   iii. Amyotrophic Lateral Sclerosis (ALS): Mitochondrial dysfunction in energy production is the key pathologic mechanism in this disease. KD have shown improvements in energy utilisation and have resulted in longer maintenance of motor function[20]. (LOE:7)

iv. Parkinson's Disease: Although not many studies have been done and benefits remain uncertain early results have shown improvement in motor functions by protection of dopaminergic neurons from degeneration[21,22]. (LOE:7)

v. Others: Apart from the above, KD has also shown benefit in various other conditions, although more data is needed before accepting KD as a treatment alternative. The following diseases where KD have shown potential benefit:-

- Angelman Syndrome
- Mitochondrial myopathy
- Rett Syndrome
- Spinal Cord Injury and Traumatic Brain Injury
- GLUT1 deficiency: Ketogenic diet can be initiated once the diagnosis of GLUT1 deficiency syndrome in paroxysmal exercise-induced dystonia is confirmed[23]. (LOE: 1)

5. Chronic Kidney Disease (CKD): Traditionally, a hypoproteinaemic diet is proposed for CKD. However, recent trials have proved KD are effective in ameliorating metabolic disturbances in CKD, delaying the initiation of dialysis by almost 1 year and slowing down the rate of decline in renal function by 57%[24]. (LOE: 7)

6. Crohn's Disease: Crohn's disease is known to be characterised by a progressive worsening of symptoms. Standard therapies may result in a temporary symptom relief but are accompanied by significant side-effects. In one of the studies, an advanced state of Crohn's disease was treated with KD. It was able to reverse the cluster of symptoms and abnormalities associated with the disease by normalising the intestinal permeability[25]. (LOE:7)

7. Cancers: Preliminary data points towards potential benefits in certain cancers. This is thought to be achieved by inhibition of insulin, which otherwise causes cellular proliferation by Insulin/IGF-1 pathway. KD also results in "glucose starvation" of cancer cells[26].

8. Acne: KD reduces acne by decreasing IGF-1 Levels. This results in reduction in (a) androgen-mediated production of sebum, (b) excessive desquamation of the follicular epithelium, (c) proliferation of basal keratinocytes and (d) *P. acne* colonisation and hence inflammation[27]. (LOE:7)

9. Respiratory functions: KD results in more fat oxidation to meet energy requirements, which leads in turn to reduced respiratory exchange ratio and of metabolic carbon dioxide output, and a decrease in arterial carbon dioxide partial pressure. These effects might be useful in respiratory failure; however, this aspect of KD remains to be investigated.

Risks of ketogenic diet

Much of the risks proposed to be associated with KD have come from the trials on paediatric patients treated for epilepsy. Some of the common problems associated with KD are:-

1. Ketone Flu: The most common short-term side-effects, include nausea, vomiting, dizziness, headache, insomnia, fatigue, referred to as keto flu which resolve in a few days to weeks[28].

2. False-positive breath alcohol test: Due to ketonaemia, acetone in the body can sometimes be reduced by dehydrogenase which can give a false positive alcohol breath test result.

3. Hypoglycaemia: KD can also cause hypoglycaemia in certain patients who have risk factors for the same (older age, previous history, on OHAs)[29].

4. Gastrointestinal system: KD have shown to cause diarrhoea, vomiting, abdominal discomfort in some patients. KD causes gut dysbiosis by reducing the supply of carbohydrate to gut biota, which in turn results in reduced fermentation in the gut leading to decreased butane levels which is thought to decrease inflammation. This may cause many gut inflammatory diseases[30].

5. Bone and calcium metabolism: KD has shown to decrease bone mass and cause frequent fractures. In addition. KD has also shown to increase the incidence of renal stones[31].

6. Cardiovascular: there have been case reports of patients developing cardiomyopathies secondary to nutritional deficiencies (e.g., Selenium and others)[32]. Some reports have even shown development of arrythmias.

7. Haematological: KD has shown to cause bone marrow suppression and anaemia[33].

Conclusion

KD is a low carbohydrate, fat-rich, and adequate calorific value diet. It has proven benefits in weight loss, diabetes, reducing cardiovascular risks, epilepsy. There is emerging evidence of a potential role in – Motor function improvement in ALS; Alzheimer's; Parkinson's Disease, and several other neurological diseases. KD has also shown benefit in cancers, acne, CKD, IBD. However, more study

needs to be done before any conclusive statement. The initiation of KD needs to be supplemented with key essential minerals and vitamins. KD has certain side-effects and should be avoided in at-risk patients.

Annexure 1: Levels of evidence(LOE)

Level of evidence (LOE)	Description
Level I	Evidence from a systematic review or meta-analysis of all relevant RCTs (randomised controlled trial) or evidence-based clinical practice guidelines based on systematic reviews of RCTs or three or more RCTs of good quality that have similar results.
Level II	Evidence obtained from at least one well-designed RCT (e.g., large multi-site RCT).
Level III	Evidence obtained from well-designed controlled trials without randomisation (i.e., quasi-experimental).
Level IV	Evidence from well-designed case-control or cohort studies.
Level V	Evidence from systematic reviews of descriptive and qualitative studies (meta-synthesis).
Level VI	Evidence from a single descriptive or qualitative study.
Level VII	Evidence from the opinion of authorities and/or reports of expert committees.

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CASE REPORT

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Remitting Seronegative Symmetrical Synovitis with Pitting Oedema (RS3PE)

Virendra Kumar Goyal, Jitesh Aggarwal**, Rootik Patel***, Manan Dave****

Key words: Rheumatoid arthritis, RS3PE, synovitis, pitting oedema, inflammatory arthritis.

Introduction

Remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) is a rare form of inflammatory arthritis which was first reported by McCarty *et al* in 1985[1]. It usually affects elderly age group with a clinical presentation of symmetrical polyarthritis with pitting oedema on the dorsum of hands and feet. The pathophysiology of RS3PE is not understood clearly. Several studies consider RS3PE to be a form of polymyalgia rheumatica and even seronegative rheumatoid arthritis, but the clinical presentation and pathophysiologic mechanisms indicate that it can be a separate entity altogether[2]. The joints involved frequently include metacarpophalangeal (MCP), proximal interphalangeal (PIP), wrist, shoulder, knee, ankle, and elbows[3]. This article presents a case of RS3PE, followed by a brief discussion.

Case report

A 65-year-old lady was referred to GBH General Hospital, Udaipur on August 12, 2020 with the history of low-grade fever for 10 days followed by swelling over left knee, right hand and swelling over bilateral feet since 7 days. Patient also had a history of hysterectomy followed by radiotherapy about 20 years back, records of which were not available and nature of the illness was unknown.

On examination, the left knee joint was red and swollen with increased local temperature. There was pitting oedema of bilateral lower limbs and over right hand. Ultrasonography of local parts showed effusion of the left knee joint with synovitis of the joint along with soft tissue oedema over bilateral lower limbs and right hand. Arthrocentesis of the knee was done which showed inflammatory arthritis with cytology showing total counts of 6,400/mm^3 with neutrophils 60% , ADA 19.8 U/L, sugar 1.0 mg/dl, protein 4.5 g/dl (AS the joint aspirate report did not have mononuclear cells predominance the possibility of viral arthritis was ruled-out) , serum uric acid 4.0 mg/dl, negative Rheumatoid Factor (RF), normal anti-Cyclic Citrullinated Peptide (anti-CCP) normal Anti-Nuclear Antibody (ANA), normal Thyroid-Stimulating Hormone (TSH), haemoglobin of 7.8 g/dl, WBC (11*10^3/mm^3 N: 85%, L: 20%). elevated erythrocyte sedimentation rate (ESR) 111 mm/hr and elevated C-Reactive Protein (CRP) 137 mg/l. All other viral markers HIV, HBSAG, ANTIHCV were negative. X-ray of the affected joints did not reveal any joint erosion. Ultrasonography of the abdomen showed cholelithiasis of 11 mm and minimal ascites. After ruling-out all other causes, the patient was started on prednisolone 30 mg. During her brief hospital stay the patient started responding to treatment, her swelling started reducing and pain subsided and she was discharged.

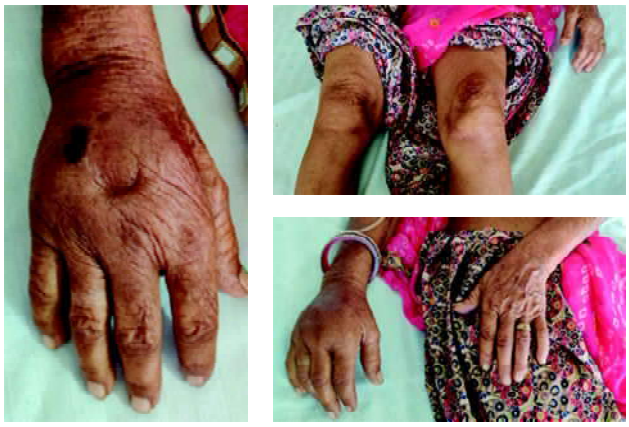

Fig. 1: *Showing pitting oedema of right hand and swelling over left knee.*

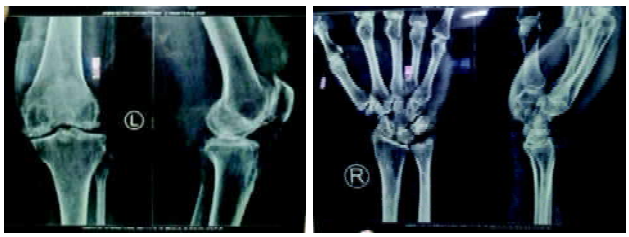

Fig. 2: *X-ray of left knee showing osteoarthritic changes. X-ray of right wrist showing soft-tissue swelling.*

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Discussion

Remitting, seronegative, symmetric synovitis with pitting oedema syndrome is defined as seronegative symmetric polysynovitis and arthritis of the distal limbs, primarily the wrist, MCP, PIP and ankle joints with acute onset, together with pitting oedema on the dorsum of the hands and feet[1]. Olive *et al*[4] evaluated 27 cases with RS3PE retrospectively in 1997 and established the following diagnostic criteria for the disease:

- Clear pitting oedema on both hands.
- Polyarthritis with acute onset.
- Age above 50.
- Negative rheumatoid factor[4].

Non-observation of erosive or degenerative change in joints and dramatic response to low-dose corticosteroid are characteristic[3]. It is thought that pitting oedema, which occurs in distal limbs, develops as a local reaction[1]. RS3PE was diagnosed in the presented case was based on the following: Female gender, age > 50 years, symmetric pitting oedema and sudden-onset polyarthritis, non-observation of erosion on radiographs, and rapid clinical and laboratory response to low-dose corticosteroid treatment within one week.

Associations with HLA[1], parvovirus B-19 infection[5], malignancy[3], rheumatologic and autoimmune diseases[6] and increased vascular endothelial growing factor (VEGF) levels[7] have been cited in the etiopathogenesis.

Low-moderate elevation in sedimentation rate has been determined as a laboratory finding in the disease. RF and antinuclear antibodies (ANA) are negative, while HLA-B7, B22 and B27 tissue antigens may be positive in some patients[8,9]. Sedimentation rate was moderately increased in our case and RF was negative. Response of RS3PE to NSAID treatment is not good[1]. Russell *et al*[10] reported 13 cases that patients responded dramatically to 10 mg/day prednisolone treatment. In this case series it was seen that remission was achieved in an average of 6 - 18 months with low-dose steroid treatment[9,10]. Low degree flexion contractures that developed on wrists and fingers may sometimes be permanent. Recurrence may not occur or may be seen between 18 months and 12 years[1,8].

Despite the clear criteria, differential diagnosis of RS3PE is very difficult. Important differential diagnoses include amyloid arthropathy, psoriatic arthropathy, crystal arthropathy, rheumatoid arthritis (RA), late-onset spondyloarthropathies, Reiter syndrome, and mixed connective tissue disease, (they cause pitting oedema on the hands and feet)[11]. Progressive swelling and non-recovery with treatment in amyloid arthropathy, typical skin findings in psoriatic arthritis, and determination of chondrocalcinosis radiologically and crystals in synovial fluid in crystal arthropathy are useful distinctions. Reiter syndrome is differentiated by asymmetric stiffness with conjunctivitis and urethritis and asymmetric pitting oedema in lower limbs; late-onset spondyloarthropathies are differentiated by asymmetric pitting oedema with sacroiliitis; and mixed connective tissue disease is differentiated by Raynaud's phenomenon and ANA positivity in high titer[1,4,9,11]. These were not seen in our case. Asymmetric pitting oedema may be seen in late-onset RA rarely. While having very similar clinical and symptoms, it is distinguished from RS3PE with RF positivity and bone erosions[9].

Remitting, seronegative, symmetric synovitis with pitting oedema is most frequently confused with polymyalgia rheumatica (PMR) since both are seronegative, are seen in older ages and respond to corticosteroids.

Table I: Comparing three polyarthritides affecting the elderly.

	RA	RS3PE	PMR
Onest	Sudden of gradual	Usually sudden	Sudden
Gender	F > M	M > F	F > M
Age at onset	3rd to 5th decade	7th decade	7th decade
Synovitis	Usually Severe	Severe	Mild
Pitting oedema	Unusual	All (by definition)	None
RF	Positive (80%)	Negative	Negative
HLA Association	DR4	B7	DR3.4
Remission	Unusual	Predictable (3 - 36 mc)	Unusual (2 y or more)
Response to low-dose steroids	Often incomplete	Dramatic	Dramatic

Salvarani *et al*[12] found pitting oedema in 8% of cases in their study examining 245 cases with PMR. Cantini *et al*[8] argued that RS3PE may be a precursor or continuance of PMR since inflammation selects the same anatomic target in extra-articular synovial structures in magnetic resonance imaging in PMR cases with pitting oedema, like RS3PE.

However, PMR is a disease mostly seen in women, requiring long-term steroid treatment and showing relapse and recurrence more frequently[6-10]. In our case, although pain and limitation of motion in the knee and ankle joints were present, dramatic response to corticosteroid treatment in very low-doses in a short time supports the diagnosis of RS3PE.

Cases of as RS3PE are observed to suffer from different

rheumatologic diseases in the future, including RA, Sjögren's syndrome, spondyloarthropathy, and PMR[1,9,12].

In conclusion, although its diagnostic criteria are clear, RS3PE is a syndrome with a benign course, the differential diagnosis of which is very difficult, and it may be associated with rheumatologic and neoplastic diseases. Correct recognition of these cases and patient follow-up after diagnosis are important.

Remitting seronegative symmetrical synovitis with pitting oedema responds to relatively small doses of prednisolone. Nonsteroidal anti-inflammatory drugs (NSAIDS) and hydroxychloroquine may provide an added advantage. There is very little role of the disease-modifying antirheumatic drugs (DMARDs). This remission is usually well-sustained. On the other hand, RS3PE with an underlying malignancy, responds poorly, and treatment of the underlying malignancy is needed as a primary step.

Conclusion

Remitting seronegative symmetrical synovitis with pitting oedema is a disease/syndrome characterised by an acute onset of polyarthritis with pitting oedema, negative rheumatoid factor, absence of joint erosions on radiographs, synovitis suggested by USG/MRI, and a good response to low-dose steroids, with a sustained long-term response. A high degree of suspicion and an early prompt diagnosis is required, as proper treatment results in a dramatic relief to the patient, while misdiagnosis results in prolonged and expensive therapy.

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CASE REPORT

JIACM 2021; 22(1-2): 60-62

Unusual Cause of Intractable Vomiting in A Patient After Open Cholecystectomy

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Abstract

Gossypiboma or textiloma is a rare but very unfortunate event of surgery. It refers to a retained foreign body (mostly gauze piece) at the end of an operation, mostly abdominal, but sometimes in thoracic operation[1]. Gossypiboma is derived from a Latin word "gossypium" (cotton) and the Swahilli "boma" (place of concealment)[2]. Clinical examination and radiological findings may sometimes mislead the physician and these are often mistaken as malignancy or abscess[3]. We present a patient with recurrent vomiting which was non-bilious accompanied with weight loss for the last 30 days. There was no significant past history except an open cholecystectomy 5 months back. Upper gastrointestinal endoscopy revealed a surgical sponge in the duodenum which was retrieved successfully.

Key words: Surgical gauze; gossypiboma; textiloma.

Case report

A 29-year-old lady was admitted with complaints of recurrent vomiting, intermittent with bilious content for the last 30 days which had worsened over the last one week with of increased frequency (5 to 6 times per day), amount and contained more undigested food with less bilious contents compared to earlier vomitus. She had pain in the abdomen which was continuous with intermittent exacerbation, located at epigastrium and right hypochondriac region. Pain used to increase after food and reduced after vomiting, the severity of pain had also increased. She was taking treatment from elsewhere before coming to us and was treated symptomatically with antiemetics, antispasmodics, and proton pump inhibitors without any relief. She only had a chest X-ray with her which it was normal. Her haemoglobin was 13 gm% with total leucocytes count (TLC) of 11,000 per cum/ml, and platelets were normal. The pain and vomiting were worsening gradually. She had lost 6 kg of weight over one month. There was no history of fever, cough, urinary complaints, and had a normal menstrual cycle.

Past history

She had upper abdominal pain five months back which was diagnosed as gall stone disease with thickened gall bladder wall, suggestive of cholecystitis. She was admitted in a government hospital and open cholecystectomy was done but reason for doing open cholecystectomy was not known to the patient. Post-surgery period was uneventful with no history of drain placement. She was discharged after 4 days of admission in a stable condition.

She remained stable for 4 months. She had then vomiting and pain abdomen again and for this she visited the local practitioner. When she did not improve, she consulted us. On examination she was conscious, co-operative, and her vitals were normal. She was mildly dehydrated. General examination was also normal. No icterus, pallor, clubbing, lympadenopathy were seen. Cardio-respiratory examination was also normal. Abdomen was soft and skin over the abdomen was normal with no visible peristalsis. Fullness was present in the epigastrium with mild tenderness in epigastrium and right hypochondrium and succussion splash was present, suggestive of gastric outlet obstruction. No other organ was palpable. Bowel sounds were sluggish in all the four quadrants. Initial assessment was suggestive of gastric outlet obstruction. She was treated with intravenous hydration and supportive care was started.

Investigations revealed: Hb - 12.2 gm%, TLC - 9,500 per cum/ml, platelet count - normal. Blood sugar - 92 mg%,blood urea - 17 mg/dl, creatinine - 1.0 mg/dl, electrolytes - normal, urine routine - normal, total S. bilurubin 1.3 mg/dl, conjugated - 0.8, serum alkaline phosphatase was 2,000 IU/L, SGOT - 260 U/l, SGPT - 265 U/L, amylase - normal. Patient had repeated vomiting and gastric succussion splash could be elicited at the time of examination so X-ray abdomen was done (erect and supine) (Fig. 1): there were no air-fluid levels but there was a linear string like radio-opaque shadow, the nature of which was not clear. Blood culture at the time of admission

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was normal. Ultrasound abdomen was done. It showed mildly dilated CBD with no dilated intrahepatic biliary radicals or any common bile duct stones and a hypoechoic area around the pancreas. The patient had a high alkaline phosphatase and transaminitis so we throught of a retained CBD stone. However, our patient presented with recurrent vomiting as the presenting complaint and the X-ray abdomen which revealed a linear metallic foreign body. Ultrasound abdomen showed no intrahepatic biliary dilatation so a consensus decision was made to go for CECT abdomen rather than MRI and MRCP in this patient.

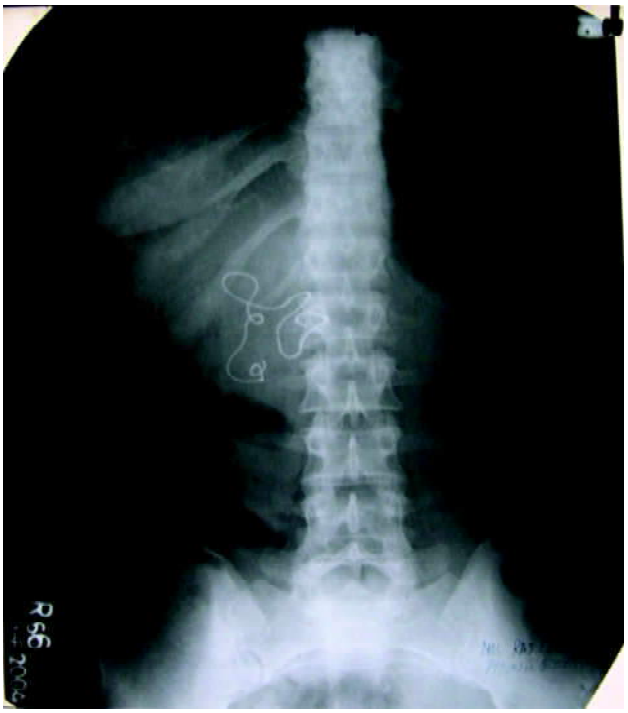

Fig. 1: *X-ray abdomen (erect).*

In view of the above reports, gastroenterologist and surgeon

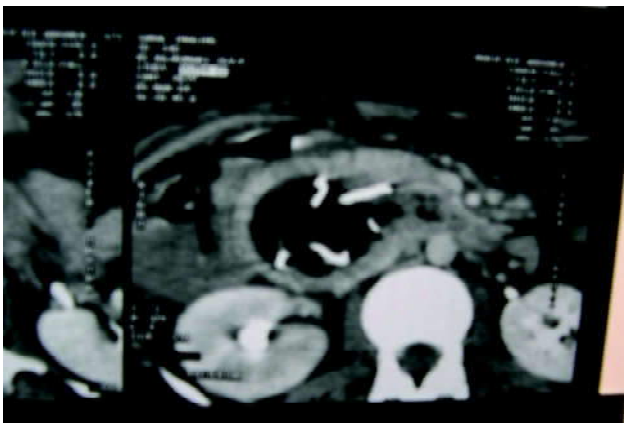

Fig. 2: *CECT abdomen.*

opinion was taken for repeated vomiting and linear shadow in X-ray abdomen. Possibility of some foreign body was considered. It revealed mildly dilated CBD with a normal pancreas. Portal vein was normal in caliber. There was significant dilatation and thickening of 2nd and 3rd part of the duodenum, up to the duodenu-jejunal flexure with presence of food residues and metallic prosthesis, probably clip or wire. There was enhancement of the wall, suggestive of inflammation (Fig. 2). A probable diagnosis of foreign body in stomach and duodenum due to accidental or self ingestion of some chain or clip was considered, though patient denied any such history. The patient was planned for diagnostic UGI Endoscopy. In the presence of surgeon for possible laparotomy if required. UGI Endoscopy showed that the lower end of the oesophagus was hyperaemic with linear ulceration; Stomach showed a few superficial erosions, a piece of cloth was seen protruding from the pyloric opening. The cloth was removed with the help of endoscopic snare (Fig. 3). Duodenal wall at D1-D2 junction was hyperaemic, with ulceration seen, however no visible perforation was appreciated. It was an abdominal sponge complete with loop on its corner soaked with bile. With great difficulty the entire sponge was gradually pulled out. The Gastroenterologist's patience and skills were put to test. The patient withstood the procedure well. She was kept nil orally initially. Liquids followed by soft diet started gradually which she tolerated well and was discharged in good health.

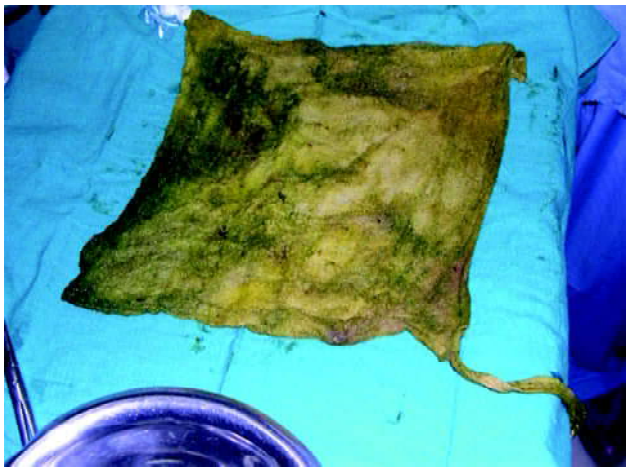

Fig. 3: *Surgical sponge.*

Discussion

This was an interesting case of recurrent vomiting in a young lady – post-cholecystectomy – caused by a foreign body gauze sponge which was removed by endoscopy. The exact incidence of gossypiboma is unknown but may be around one in 3,000 to 5,000 surgeries due to under-reporting of cases due to medico-legal liability[4]. The possibility of a retained foreign body should always be

kept in the differential diagnosis in any post-operative patient who presents with pain, infection, or palpable mass[5]. However, gossypiboma is often missed as the index of suspicion is low due to rarity of the condition and varying time frames of manifestation of symptoms. Such retained objects act as nidus of inflammation and infection and often lead to severe consequences, increased morbidity and mortality. The surgeon too is at risk of medico-legal liability[6].

A forgotten foreign body can have disastrous consequences. The sponges are chemically inert. The patient may be symptom-free or may present with acute or sub-acute symptoms. Patients may present with complaints of abdominal pain, nausea, vomiting, anorexia, weight loss, or a malabsorption type syndrome[7]. They generally have symptoms related to obstruction, adhesions, fistula, abscess formations, intraluminal bacterial overgrowth, or erosion into the gastrointestinal tract[8]. In the abdomen, gut and omentum may also encapsulate the sponge leading to pressure necrosis and resultant partial or complete migration of the sponge into the lumen. The intestinal loop closes after complete migration of sponge. This may lead to fistula or obstruction and the patient may present with symptoms due to them[8,9]. Rarely, patients develop symptoms of peritonitis or have gradual extrusion of sponge via the rectum[6].

Emergency surgery is the most common cause of retained sponge. Other causes are unplanned change in operation and obesity[7]. During the operation, the team must work in coordination and be careful. It is better to avoid small gauzes in large cavities and methodical examination before wound closure should be done to avoid this avoidable complication. The WHO Checklist includes a definite instrument and sponge count at the end of the operative procedure and may help to reduce such complications[7].

It is difficult to pick up the sponge radiologically as they do not use sponge with radio-opaque markers in it. When radiopaque markers are used, the sponges may be picked up easily. Technological advances are now being studied to prevent human error. Radio-frequency tagging and radio-wave detection of impregnated specialised magnetic metal are in an experimental stage[10]. Bar codes can be applied to all sponges, and with the use of a bar code scanner the sponges can be counted on the instrument trolley[2].

In this case, the patient had complications following cholecystectomy, due to a forgotten sponge in the abdomen near the gall bladder fossa which underwent transmural migration and was later extracted under gastroscopy. This is an interesting case where surgical sponge movement was seen upwards and thus blocked the duodenal opening. Moreover, in the past all foreign bodies were either removed through laparotomy or passed through rectum. In this patient, the sponge was removed by gastroscopy. During the procedure there was high-risk of eversion of duodenum, so it was done very slowly and gently, and the surgical team was ready for laparotomy or any eventuality. Gossypiboma is an avoidable complication of surgery. It can remain silent for months to years before manifesting itself with different symptoms. Strict and proper counting of sponges at the end of surgery and adoption of new techniques may help to minimise this.

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CASE REPORT

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A Rare Case of Aluminum Phosphide Poisoning Survival: Role of Early and Aggressive Supportive Therapy

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Abstract

Aluminium phosphide is a cheap, effective and commonly used pesticide but a major cause of suicidal deaths in rural areas. Released phosphine gas causes rapid cell hypoxia due to inhibition of oxidative phosphorylation leading to circulatory failure along with formation of highly reactive hydroxyl radicals. The diagnosis of aluminium phosphide poisoning is based on history, and foul garlicky or decaying fish odor. However, in gastric aspirate or breath, silver nitrate impregnated paper test is done, for confirming the diagnosis. There is no antidote available, so treatment is totally supportive. In our case the patient was treated immediately with all essential measures with close monitoring. The patient survived and was discharged in a stable condition.

Key words: Aluminium phosphide, phosphine gas, KMnO4 gastric lavage, dextrose insulin infusion, glutathione, survival.

Introduction

Aluminium phosphide is a solid fumigant pesticide. In India, it is marketed as tablets of Celphos or Quickphos and used to preserve grains. As a pesticide, it is available as 3 gm tablets or powder and is a leading cause of suicidal poisoning in North India[1].

Aluminium phosphide is highly water soluble and decomposes in the presence of moisture. The reaction between water and aluminium phosphide liberates phosphine gas[2].

$AlP + 3H_2O \rightarrow Al(OH)_3 + \mathbf{PH_3}$

$AlP + 3HCl \rightarrow AlCl_3 + \mathbf{PH_3}$

The deleterious effects of the poison are due to phosphine and the management is directed to sustain life till phosphine is excreted.

Case report

A 16-year-old healthy male was admitted with alleged history of intentional ingestion of 1 tablet of Celphos (3 gms). For that, he was admitted in a local hospital, initially for 12 - 14 hours, and received initial treatment in the form of injection sodium bicarbonate, gastric lavage with potassium permanganate (1: 10,000). On admission to our hospital the patient was restless, his skin was cold and clammy. His vitals were as follows: BP: 80/50 mmHg, pulse: 80/per minute and regular, respiratory rate: 20 per minute, RBS: 154 mg/dl and SpO2 94% on room air. His GCS was: E4V4M6, with APACHE II score of 23 points with predicted mortality of 46%. We admitted the patient to ICU, and all relevant investigations, including ABG and echocardiogram, were done and immediate resuscitative treatment started. As per ABG, patient had severe metabolic acidosis (pH 7.03, pCo2: 30 mmHg, pO2: 185 mmHg, HCO3: 7.9 mmol/ltr, BE: 22.9 mmol/ltr, SpO2: 99%), Also, patient was in shock, so inotropes were started in the form of Noradrenaline (8 mg in 46 ml normal saline at a rate of 10 ml/hr infusion) and Vasopressin (4 mg in 46 ml normal saline at a rate of 2.4 ml/hr infusion) along with normal saline infusion @ 120 ml/hour with hourly monitoring of BP, urine output and other vitals. IV sodium bicarbonate was started as 100 ml bolus followed by 100 ml per hour IV infusion with 3 hourly ABG monitoring. After 12 - 14 hours of admission in ICU, significant correction of metabolic acidosis and shock was achieved. Over the next 24 hours, Vasopressin infusion was gradually weaned off, Noradrenaline and bicarbonate infusion were slowly tapered off according to BP and ABG, and subsequently stopped. Inj Magnesium sulphate, IV 2 gm stat and 2 gm hourly for 3 consecutive hours were given followed by 1 gm, 4 hourly for 5 days with monitoring of serum magnesium levels, (given as a membrane stabilizer to prevent arrhythmias). We also started Inj Human insulin as per GIK regimen: 10 IU regular insulin in 25% dextrose with 10 ml KCL over 3 - 4 hour infusion, three times a day for 5 days as insulin is known to increase cardiac contractility. Tab Trimetazidine 200 mg (sustained release) twice a day was started once patient started accepting orally, as it increases myocardial oxygenation, decreases intracellular acidosis and reduces oxygen consumption. ECG on admission revealed ST elevation in chest leads suggestive of myocarditis. 2D echo was normal with

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ejection fraction of 55% and showed no RWMA. Cardiac enzyme, CPK was also increased which favoured myocardial ischaemia. Cardiologist opinion was obtained. The cardiac condition was monitored with regular ECGs for any worsening of ST-T changes or arrhythmias. Patient had leucocytosis (TLC: 15,000/mm^3) for which Inj Ceftriaxone 1 gm BID was given. On day 3, ECG showed spikes of ill-sustained VT which gradually resolved. A repeat 2D echo on day 3 was normal. Thereafter, patient had severe hypocalcaemia, managed with IV calcium gluconate (10 ml, 10% calcium gluconate in 100 ml saline, IV, TDS). Patient's LFT were also deranged due to oxidative injury caused by phosphine gas, which was managed with hepatoprotectors (Tab Ursodeoxycholic acid, 300 mg, BD) and antioxidant therapy to prevent oxidative injury due to free radicals with IV glutathione (600 mg, IV, BD) given. Due to oxidative injury, kidney function was also affected, which was managed conservatively with IV acetylcysteine (600 mg, IV, BD as antioxidant, replenishing cellular glutathione) and IV fluids to increase renal washout of phosphine. Patient also required NIV support on day 5 for pulmonary oedema and hypoxia. On day 7, patient was haemodynamically stable with no acidosis or oxygen requirement. He was discharged in haemodynamically stable condition on day 12. An informed consent for publishing this case was obtained from his father.

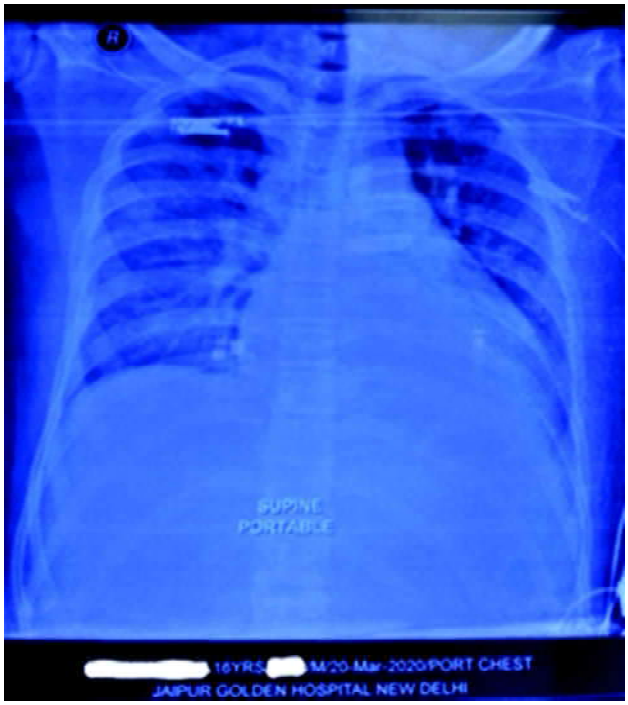

Fig. 1a: *Chest X-ray: (a) Day1: clear X-ray, (b) Day 3: Suggestive of pulmonary oedema (cephalisation of vessels and patchy shadowing of air bronchogram with increased cardiac size).*

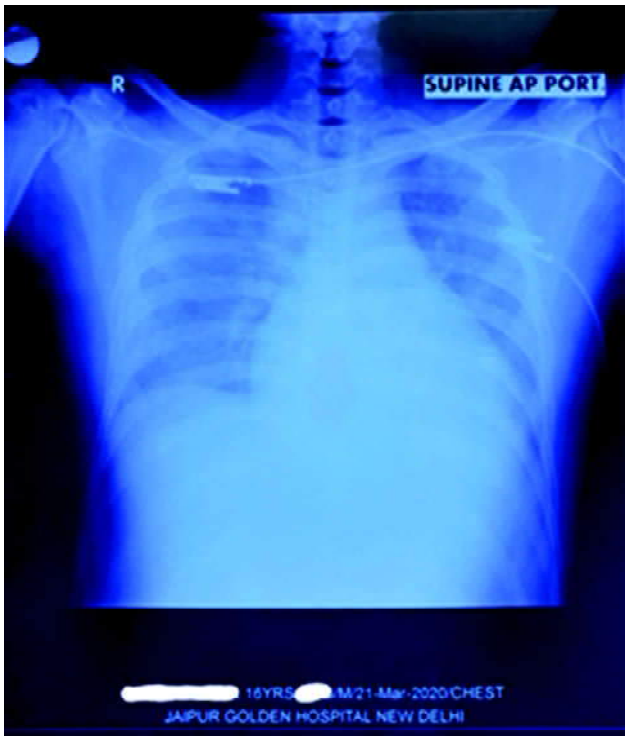

Fig. 1b:

Table I: Serial ABGs of the patients.

	19/4/2020 Day 1	20/4/2020 Day 2	21/4/2020 Day 3	22/4/2020 Day 4	23/4/2020 Day 5
pH	7.03	7.38	7.45	7.40	7.37
pO2 (mmHg)	185	26	52	99	110
PCO2 (mmHg)	30	61	45	49	28
HCO3 (mmol/l)	7.9	36.6	31.3	26.4	16.2
S. Lactate (mmol/l)	3.2	7.2	2.2	1.8	0.6
SpO2 (%)	99	69	88	94	99
BE(B) (mmol/l)	-22.9	-12.9	-7.3	-5.0	1.0

Discussion

In India, aluminium phosphide (AlP)is marketed as tablets of celphos, alphos, quick phos, phostoxin, etc.[3]. In India, this poisoning was not known before 1980. The first case in India was reported in 1981 from MGM Medical College, Indore[4]. The incidence of this poisoning has been increasing steadily and is now the commonest mode of suicide in the agricultural community in Northern India[5]. Overall, mortality in cases of aluminium phosphide poisoning varies between 70 - 100%. It is higher in those who consume more than two tablets and none of the patients who had ingested more than 3 tablets survived[6-8]. Suicide was the most common cause of death with 94%, followed by accident

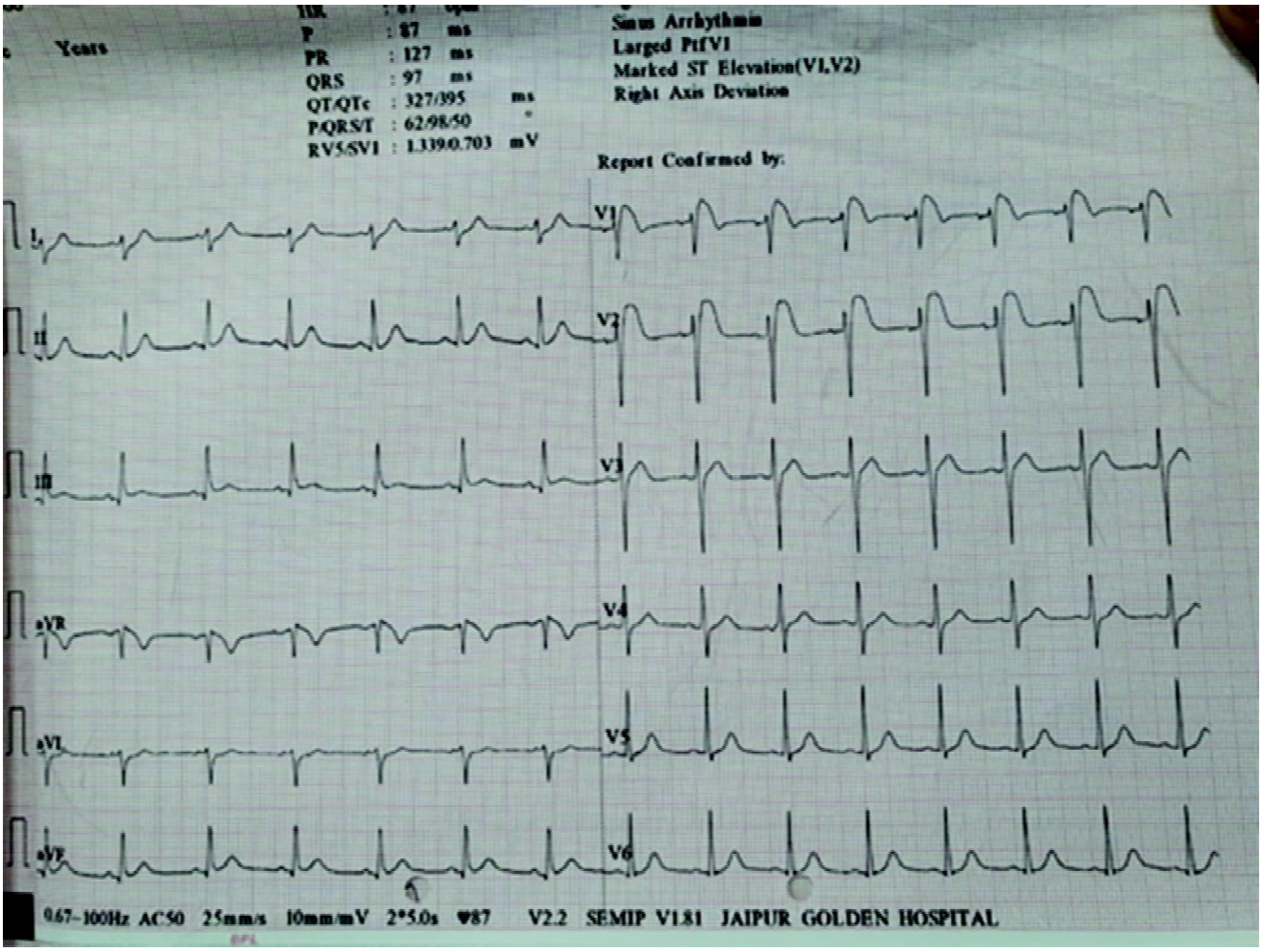

Fig. 3a: *ECG: (a) on day of admission: Showing marked ST elevation in lead V1.*

with 5% of cases, and homicide accounted for 1% of deaths[9].

According to Karamjit *et al* (2003) the pattern of poisoning varied in urban and rural areas, with a higher incidence of poisoning deaths in rural (64%) than in urban areas (36%)[10]. Aluminium phosphide was the most common poison consumed, being responsible for 50% of deaths, followed by insecticides 24%[9]. Poisoning deaths increased from 19% in 1996 to 24% in 2005. The age group most commonly affected was 16 - 25 years (49%). The male to female ratio was 1.9: 1.0 and the rural to urban ratio was 1.5: 1.0[9].

Human toxicity occurs either due to the ingestion of AlP (commonest mode) after exposure and injury from phosphine inhalation (uncommon) or even after absorption through the skin (rare). After ingestion, AlP releases phosphine gas in the presence of HCl in the stomach, which is rapidly absorbed throughout the gastrointestinal tract, leading to systemic toxic effects involving the heart, lung, kidney, and liver – with manifestations of serious cardiac arrhythmias, intractable shock, acidosis, and pulmonary oedema. After absorption, phosphine is oxidised to oxyacids. Phosphine is excreted in the urine as hypophosphite and also through the lung in the unchanged form.

In addition to the corrosive action of phosphine, the mechanism of toxicity includes failure of cellular respiration due to the effect on mitochondria, inhibition of cytochrome-oxidase and formation of highly reactive hydroxyl radicals. Cellular injury due to lipid peroxidation is also suggested. There is a decrease in the level of catalase and increase in the activity of superoxide dismutase in patients of AlP poisoning. The reduction of glutathione concentration in different tissues in AlP poisoning also explains the cellular injury as glutathione is a protection factor against oxidation, by catalysing the reduction of the oxygen peroxide in O_2 and H_2O. Indicators of oxidative stress (reduced glutathione, malonyldialdehyde) reach peak levels within 48 hours of exposure to poison, approaching normalisation by day 5[11].

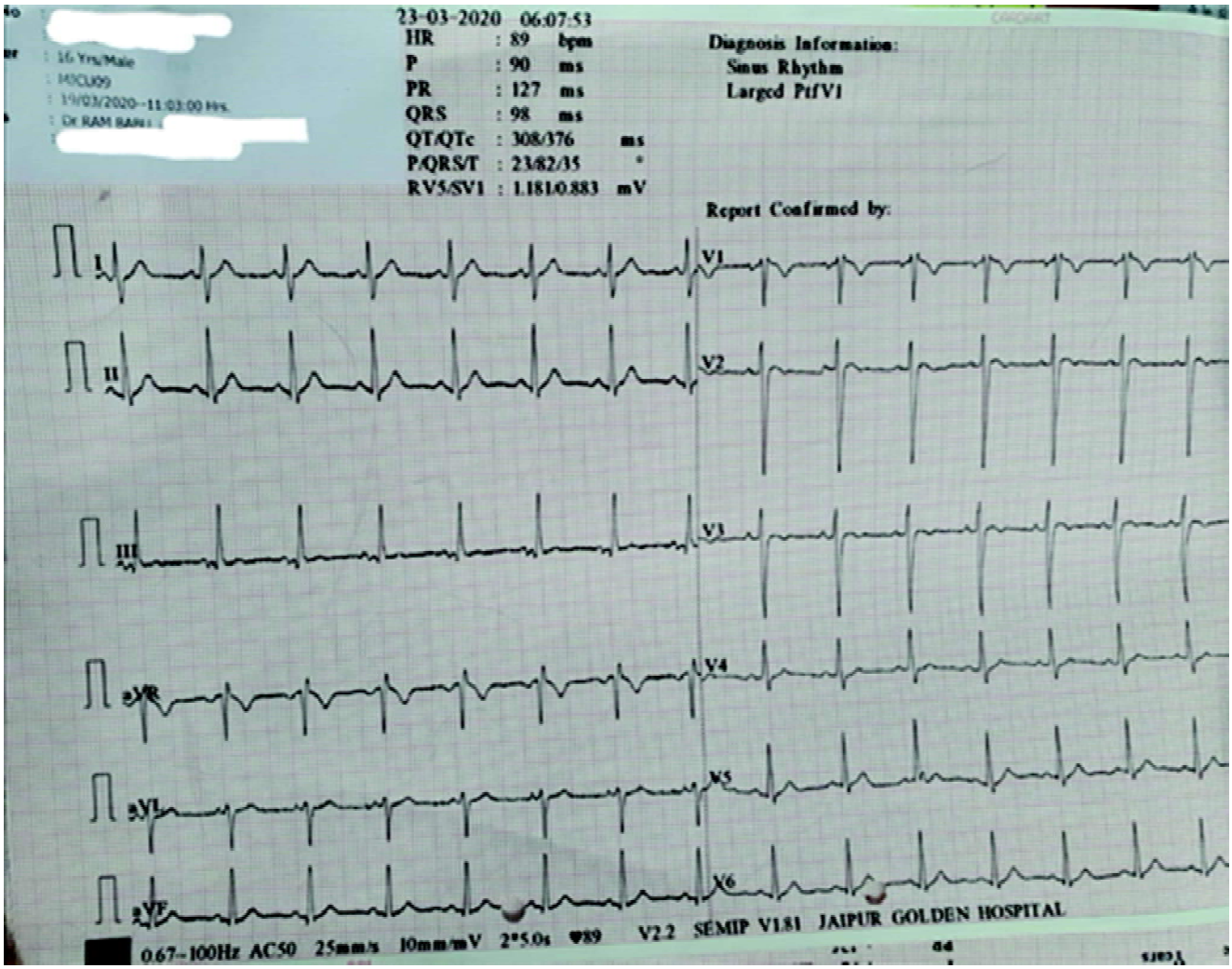

Fig. 3b: *Normalised ECG on day 3.*

Gastric lavage is important in the initial stages. The management principles aim to sustain life with appropriate resuscitation measures until phosphine is excreted from the body. If phosphides have been ingested, ***do not induce emesis***. Gastric lavage with sodium bicarbonate and potassium permanganate (1: 1,000) has also been recommended by earlier studies as KMnO4 solution oxidizes phosphine to non toxic phosphate[12,13]. But recent advances and studies have shown better results of gastric lavage with sodabicarb and vegetable oils.

All patients of severe AlP poisoning require continuous invasive haemodynamic monitoring and early resuscitation with fluid and vasoactive agents. Fluid therapy could be guided by central venous pressure (CVP) or pulmonary artery wedge pressure (PAWP) monitoring. For refractory hypotension, norepinephrine or phenylephrine could be used. Readiness of anti-arrhythmic agents, DC cardioversion and temporary pacemaker should be available at the bedside. Vasoactive agents with more β-receptor agonist action like dopamine and dobutamine should be used cautiously as they are prone to inducing arrhythmias. The reversibility of myocardial injury over few days was objectively assessed by repeated echocardiography[14] Gupta *et al* showed normalisation of the echocardiographic findings in patients who survived AlP poisoning on day 5[14].

Magnesium sulphate acts as a membrane-stabilising agent and also corrects hypomagnesaemia. It also helps in preventing arrhythmias. It may be given in a dose of 2 - 3 gms as a loading dose and then 1 gm every eight hourly. N-acetyl cysteine has been found to be useful by Bogle *et al* in 2006[15].

Intravenous sodium bicarbonate could be considered for mild-to-moderate metabolic acidosis or as a rescue therapy in severe acidosis before dialysis is commenced. In a recent study, using intravenous sodium bicarbonate for the

"aggressive correction of acidosis" protocol resulted in significant improvement in patient outcome (30% vs 55%)[16].

As insulin is known to increase cardiac contractility, GIK regimen was started (100 ml 25% Dextrose + 10 ml KCl + 8 U rapid Insulin)[17]. Numerous reasons exist for the continued interest in GIK despite its variable track record in clinical trials: (1) Substantial laboratory evidence supports a cardioprotective effect in various models of ischaemia/ reperfusion; (2) some clinical trials have demonstrated positive results in specific patient subgroups; (3) the treatment is relatively "nontoxic" and free of major clinical side-effects; and (4) recent evidence suggests that insulin itself, a component of GIK, administered as a strategy to restore normoglycaemia, may be cardioprotective because it has antiinflammatory, antiapoptotic, and provasodilatory properties[18,19].

Trimetazidine is a piperazine derivative. It has been experimentally shown that in ischaemic tissues it improves production of ATP, decreases intracellular acidosis and decreases overproduction of free radicals, this it rectifies most of the metabolic adverse effects of ischaemia[21].

This poisoning has a high mortality (30 - 100%) and survival is unlikely if more than 1.5 g is ingested[22]. Although the lethal dose is 150 - 500 mg for an adult, case reports of survival have been reported even after the ingestion of 9.0 g or more.

In a retrospective analysis of one of the largest series (471 patients) of AlP poisoning, arterial pH, serum bicarbonate level and ECG abnormalities were significantly poor prognostic factors[23]. Other poor prognostic factors were shock, altered mental status, high APACHE II score, acute kidney injury, low prothrombin rate, hyperleucocytosis, requirement of mechanical ventilation, lack of vomiting after ingestion, hyperglycaemia and time lapsed after exposure[24]. As in our case, patients had a low GCS, high APACHE II, with signs suggestive of acute kidney injury with low urine output and deranged kft with maintained renal size and echogenicity on USG, hyperleucocytosis(TLC: 15,000/mm^3).

Conclusion

The case fatality ratio due to A/P poisoning has declined significantly in the last decade due to improved intensive care. Strict implementation of nationwide pesticide regulations, including restricting the availability of this poison, being aware of its toxicity and providing improved medical management in consultation with regional or national poison control centres could further reduce the mortality due to AlP toxicity, as there is no antidote available presently.

The authors wish to acknowledge the important contribution of Dr Pradeep Mukhi (Mukhi hospital, Sonipat), Jaipur Golden Hospital medical ICU team and nursing staff for successful outcome of this case.

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CASE REPORT

JIACM 2021; 22(1-2): 69-72

Neuropsychiatric Systemic Lupus Erythematosus (NPSLE)

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Key words: Neuropsychiatric Systemic Lupus Erythematosus, Central Nervous System, Anti Neuclear Antibody.

Introduction

Systemic lupus erythematosus (SLE) is a complex autoimmune disease with variable clinical features[1]. Involvement of the nervous system has been recognised ever since the disease was first reported, and may involve both the central and peripheral nervous systems[2]. Neuropsychiatric symptoms affect up to 90% of patients with SLE, with cognitive impairment, headache and mood disorder being the most commonly recognised syndromes[2].

However, findings of neuropsychiatric symptoms in male patients subsequently diagnosed to have SLE is uncommon. Here, we report a case who presented with seizures and behavioural problems and was diagnosed to have SLE. The patient responded to cyclophosphamide and corticosteroid treatment adequately.

Case report

A 29-year-old male presented to emergency department in our hospital with complaints of fever for 10 days, two seizure episodes since evening, followed by altered sensorium.

In the emergency room, the patient was in altered sensorium. He had a 3rd episode of seizure (GTCS) in the emergency room and was managed with appropriate anti-epileptic medication. There was no history of nausea, vomiting, headache, diarrhoea, shortness of breath, chest pain, head trauma or ear discharge.

Patient had history of prolonged fever about 8 months ago and was found to have bilateral pleural effusion which was drained with bilateral inter-costal drainage tube but the exact cause was not ascertained and patient was managed with antibiotics at a tertiary care hospital in New Delhi. His fever reappeared again after 2 months. He had abdominal distention at that time and exploratory laparotomy was done in view of SAIO which was inconclusive (CB-NAAT was also negative). He was managed on antibiotics and discharged from that hospital. He also had inguinal lymphadenopathy in the 2 months, for which biopsy was done but was inconclusive. Serum ANA was also negative at that time.

There was a history of significant weight loss. There was no history of tuberculosis, hypertension or diabetes. He did not have a history of joint pains, oral ulcers, alopecia, or Raynaud's phenomenon.

His vitals were: Pulse rate - 86/min, blood pressure - 116/68 mmHg, respiratory rate - 16/min, SpO2 of 99% at room air and temperature of 103.8° F. General physical examination showed pallor and presence of erythematous rash on bilateral cheeks. On the day of admission, mini-mental state examination (MMSE) was 16/30. There was no sensory involvement in any limb. Cerebellar and meningeal signs were absent. The abdominal examination revealed a midline scar of 11 cm. The respiratory and cardiovascular systems examination was unremarkable.

According to American College of Rheumatology/European League Against Rheumatism classification criteria for SLE, the patient had a score of 25/51[3]. A diagnosis of neuropsychiatric SLE (NPSLE) was thus made.

Table: Laboratory investigations.

Haemoglobin	6.3 g/dl
White cell count	1,280/mm^3
Neutrophils	68%
Lymphocytes	22%
Platelet Count	1,18,000/mm^3
Albumin	2.5 g/dl
Globulin	3.9 g/dl
Alanine aminotransferase	750 U/L
Aspartate aminotransferase	320 U/L
Alkaline phosphatase	239 U/L
Bilirubin (total)	0.41 mg/dl
Creatinine	0.8 mg/dl
Urea	36 mg/dl
Uric acid	6.6 mg/dl
S. electrolytes (Na, K Cl, Ca, Mg, P)	WNL
Thyroid profile	WNL
RBS at presentation	116 mg/dl

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Peripheral blood film	Pancytopenia with microcytic hypochromic anaemia
Bone marrow aspiration	Pancytopenia with myeloid hyperplasia
Bone marrow biopsy	Mild increase in myeloid and megakacytic precursors. Mild decrease in erythroid precursors.
HIV 1,2 , Hepatitis B surface antigen Anti-hepatitis C virus	All non-reactive
Urine Routine and microscopy	Within normal limits
Blood culture and senstivity	No growth after 72 hrs
ESR	85 mm/hr
CRP	Negative
Rapid malaria antigen test	Negative
Dengue IgM, IgG and NS1Ag	All negative
ECG	Sinus tachycardia
COVID-19 RT-PCR (Nasopharyngeal Swab)	Negative
Rectic, count	0.5%
PT/INR	15.9 sec/1.21
USG whole abdomen	Minimal ascites
Mantoux test	Negative
Chest X-ray, HRCT chest, NCCT Head, MRI brain, 2-D Echo	WNL
S. ANA by EIA (positive > 1.2, Equivocal 1 - 1.2, negative < 1)	Positive 4.13
Anti-dsDNA by EIA (positive > 1.1, Equivocal 0.9 - 1.1, negative < 0.9)	Positive 6.1
Urine creatinine/albumin ratio (normal < 30 mg/g)	602.48 mg/g
C3, C4	WNL
APLA IgM, APLA IgG	Negative

The patient was manged with intravenous methylprednisolone 1,000 mg OD for 3 consecutive days. Subsequently we started oral methylprednisolone, in tapering doses, and Cyclophosphamide pulse of 1 gm IV with Mesna 600 mg, hydroxychloroquine, anti-psychotics, anti-epileptics, haematinics, proton pump inhibitor, calcium and vitamin D. His neuropsychiatric symptoms subsided, fever settled over next 3 days and MMSE improved significantly from 16/30 to 24/30 at discharge.

On follow-up at 1st, 2nd and 3rd month, the patient was asymptomatic. He was given his 2nd,3rd and 4th doses of Cyclophosphamide. His haemoglobin improved to 10.9 gm/dl, TLC count of 9,700/mm^3, platelet count of 1,72,000/mm^3 with normal LFT, RFT and no albuminuria. He is still on regular follow-up.

Discussion

According to numerous studies, NPSLE was found to develop before or during the diagnosis of SLE in nearly 28% to 40% of adult SLE patients, and NPSLE developed in nearly 63% patients within one year after the diagnosis of SLE[4]. However, it may be seen as late as 15 years after the initial diagnosis of SLE[5].

SLE tends to be more severe in men and in paediatric patients[6]. Here, we report an uncommon case of male SLE with neuropsychiatric features which responded to cyclophosphamide and corticosteroid treatment along with anti-psychotics and anti-epileptics. The cognitive functions improvement was remarkable during follow-up and his anti-psychotics were reduced, accordingly.

Cognitive dysfunction can occur in the early stages of disease process but is rare[7]. While cognitive function can deteriorate throughout the disease course, it often fluctuates or improves over time[8]. The profile of cognitive deficits seen in SLE is varied but the most frequently affected domains are attention, memory, visuospatial processing, language, problem solving, speed of information processing and executive function[9].

Serum ANA is now taken as the compulsory entry criterion for diagnosing SLE with new ACR/EVLAR 2019 criteria[3].

MRI is the preferred imaging modality in patients with suspected NPSLE[6]. The most commonly noted abnormalities are small, hyperintense, T2-weighted, focal white matter lesions located in the periventricular and subcortical white matter of the frontoparietal regions of brain[6]. Nevertheless, these findings are nonspecific and can be observed in other disease processes, such as atherosclerotic vascular disease and multiple sclerosis (MS)[6]. Other common MRI findings include cortical atrophy, ventricular dilation, cerebral oedema, diffuse white matter abnormalities, gray matter abnormalities, infarction, leukoencephalopathy, and haemorrhage[6]. However, MRI in the present case was reported as normal. A study of 74 patients with new-onset neuropsychiatric lupus found normal MRI results in 42% of patients[10].

In severe cases, in addition to glucocorticoids and hydroxychloroquine, cyclophosphamide or rituximab (if refractory) should be added[6]. In thrombotic aetiology, with anti-phospholipid antibody (aPL), anti-coagulants are given while aPL negative patients are given anti-platelets[6]. In primary NPSLE, adjuvant therapy like anti-depressants, anti-psychotics, anti-convulsants, anxiolytics can be added[6]. In secondary NPSLE, treatment of underlying pathology is main-stream[6].

The present case could be classified as a case of SLE rather late in the course; it appears that it began as a case of undifferentiated connective tissue disease which later evolved as SLE. During early course of the disease serum

Entry criterion

Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test (ever)

↓

If absent, do not classify as SLE
If present, apply additive criteria

↓

Additive criteria

Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score§.

Clinical domains and criteria	Weight
Constitutional	
Fever	2
Hematologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
Acute cutaneous lupus	6
Serosal	
Pleural or pericardial effusion	5
Acute pericarditis	6
Musculoskeletal	
Joint involvement	6
Renal	
Proteinuria >0.5g/24h	4
Renal biopsy Class II or V lupus nephritis	8
Renal biopsy Class III or IV lupus nephritis	10

Immunology domains and criteria	Weight
Antiphospholipid antibodies	
Anti-cardiolipin antibodies OR	
Anti-β2GP1 antibodies OR	
Lupus anticoagulant	2
Complement proteins	
Low C3 OR low C4	3
Low C3 AND low C4	4
SLE-specific antibodies	
Anti-dsDNA antibody* OR	
Anti-Smith antibody	6

Total score: 25/51

↓

Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

ANA was reported as negative.

Abbreviations

NPSLE, Neuropsychiatric Systemic Lupus Erythematosus; SLE, systemic lupus erythematosus; ANA, antinuclear antibody; MMSE, Mini-Mental State Examination; TLC, total leucocyte count; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; UACR, Urine Albumin-to-Creatinine Ratio.

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PICTORIAL CME

JIACM 2021; 22(1-2):73-75

Some Chest Imaging Findings in COVID-19

Kunal Som, Rudrajit Paul**, Dipanjan Bandyopadhyay****

The COVID-19 pandemic has changed the rhythm of human life all over the planet. This respiratory virus causes sudden, rapidly progressive pneumonia, leading to acute lung injury, along with other systemic manifestations. Chest imaging findings, or more specifically high resolution CT scan (HRCT) of the chest, gives significant insights into the pathophysiology and pathology of the infection. RT-PCR is the gold standard for the diagnosis of COVID-19. But there are many shortcomings of the test, including faulty sample collection (which can give false negative results), cost and delay in getting the results. CT scan, on the other hand, is a quick imaging modality (taking less than 5 minutes) and is quite sensitive in picking up early pulmonary changes of COVID-19[1]. Thus, in cases where the RT-PCR test is inaccessible, HRCT of the thorax can be a valuable tool for diagnosis. In fact, in some countries, early CT scan of the thorax is proposed as a viable diagnostic test for COVID-19 infection in the proper epidemiological setting[2].

This pictorial essay is aimed to sensitize clinicians in India about the common CT findings of the lung in COVID-19. This will help the internist in suspecting a diagnosis of COVID-19 even before the RT-PCR report is available and thus, proper treatment may be started.

Scientific publications over the last ten months have documented a variety of radiological findings in the COVID-19 lung.

Ground-glass opacity (GGO): Fig. 1

GGO is defined as hazy areas in the parenchyma through which underlying vascular structures can be seen[1]. GGO is the most commonly described radiological abnormality in the COVID-19 lung[3]. This was found to be present at an early stage (2 - 3 days), is usually peripheral and multi-lobar.

Consolidation: Fig. 2

Consolidation, the complete replacement of alveolar air with fluids/cells/exudate, is not specific for COVID-19. Radiologically, this is seen as opaque shadows which obscure the underlying vascular structures or septal lines completely. In COVID-19, especially in the late stages, the consolidation tends to be multi-lobar or segmental with peripheral distribution[4]. This is more common in the elderly. Consolidation may progress for up to 2 weeks after disease onset[5]. Areas of GGO and consolidation may overlap.

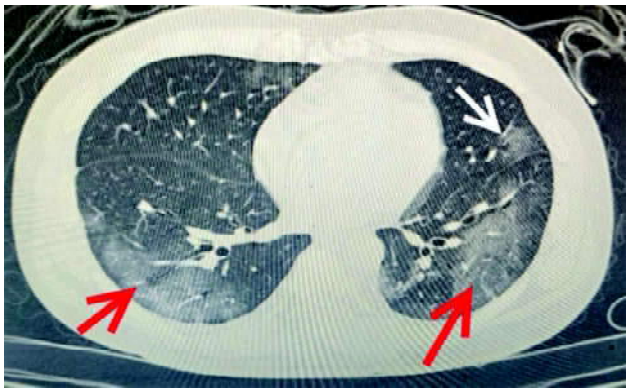

Fig. 1: *Ground glass opacity in both posterior lobes (red arrow) and left middle lobe (white arrow).*

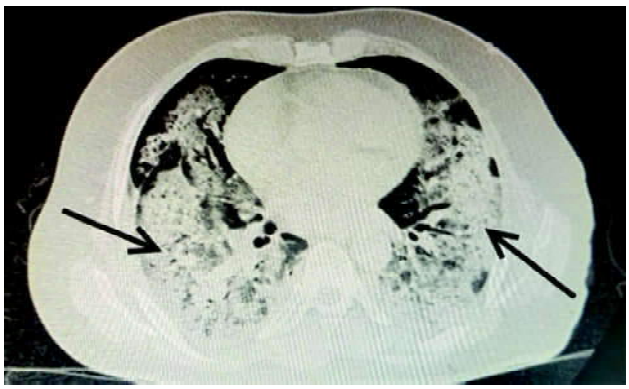

Fig. 2: *CT Massive multi-lobar consolidation (black arrows) with air bronchogram.*

Air bubble sign: Fig. 3

This is a new radiological sign described in the COVID-19 lung. It is an air-filled space surrounded by areas of consolidation or GGO. Different authors have called this "cystic changes", "vacuolar sign", "cavity sign" or "sieve-hole sign". Its exact pathophysiology is unclear as of now; the "air bubbles" are thought to be areas of resolved consolidation or pathological dilatation of airspaces[6]. This is a comparatively rare finding in COVID-19 lung.

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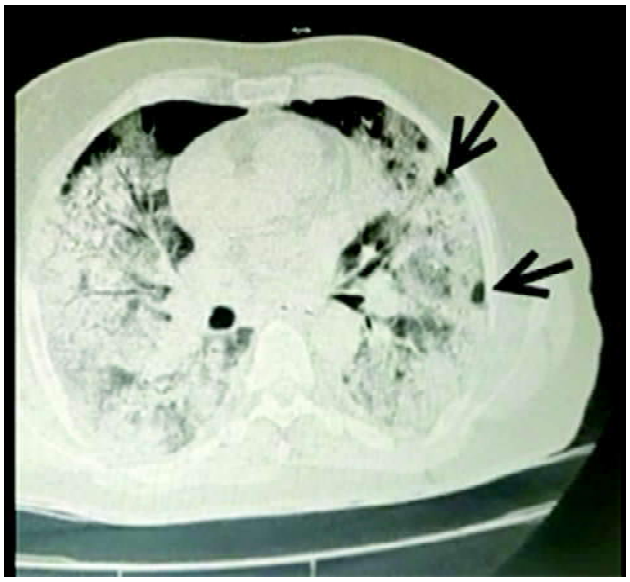

Fig. 3: *Bilateral consolidation with air bubble sign (black arrows).*

Reticular patterns: Fig. 4

Reticular pattern is defined as thickened lung septa giving rise to multiple closely spaced lines in the parenchyma image[1]. There are many causes of reticular pattern in lung imaging, but in cases of COVID-19, this pattern is thought to be due to lymphocytic infiltration of interlobar septa. This imaging appearance may be found in the later stages of the disease[6,7]. The prevalence of this radiological finding varies in different studies, but some studies have found rates as high as 80%[6].

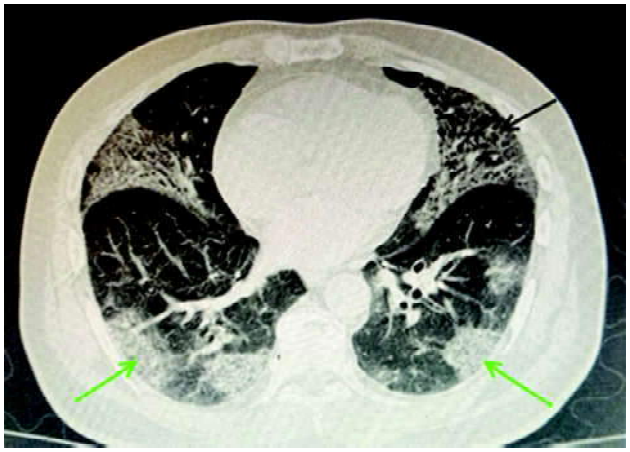

Fig. 4: *Reticular pattern (black arrow) in left lingular lobe with areas of rounded consolidation (green arrows) in both lungs.*

Spider web sign: Fig. 5

This is a comparatively rare sign, described only in a handful of publications[8,9]. It is provisionally defined as angular or triangular shaped peripheral GGO with septal thickening, giving the appearance of a spider web hung with web-strings. Li *et al* described this finding in a substantial number of their patients[9]. However, other authors have not described this imaging appearance separately. This finding has not been described from India till now.

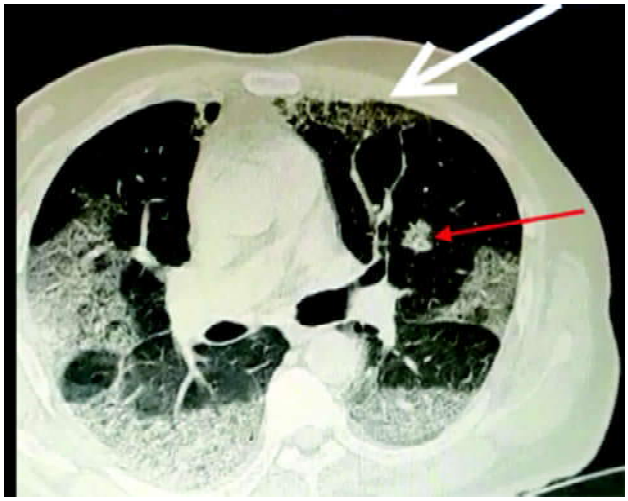

Fig. 5: *Spider web sign in left lung (white arrow). Incidentally seen: nodule (red arrow) in left lung.*

Nodule: Fig. 6; also see Fig. 5

Nodules are small (< 3 cm) opacities in the lung parenchyma. These are not specific for COVID-19 infection and are found in a variety of other infections too. Some authors have also documented a *halo sign* associated with lung nodules in COVID-19[9]. However, these are rare findings. In general, any viral pneumonia may be associated with lung nodules[10].

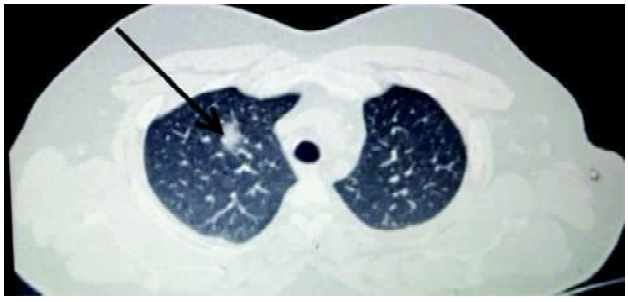

Fig. 6: *A lung nodule in right upper lobe (black arrow).*

Reverse Halo sign: Fig. 7

Reverse Halo sign or the Atoll sign is a GGO surrounded by consolidation. This was earlier thought to be a radiological sign linked to cryptogenic organising pneumonia[11]. But now, many cases of COVID-19 with Atoll sign have been

reported[12]. This may represent progressive disease where a patch of GGO is replaced with consolidation from the periphery.

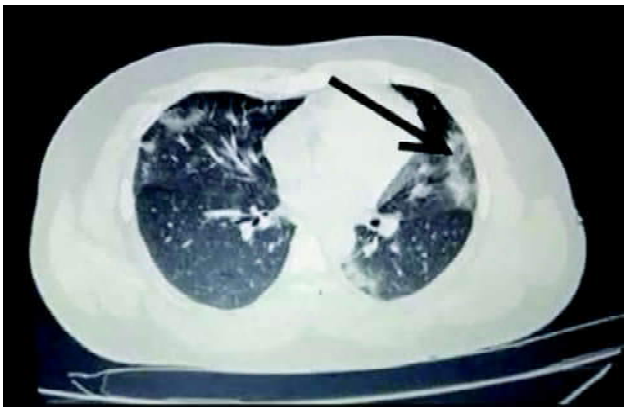

Fig. 7: *Reverse Halo sign in left lung (black arrow).*

There are many other HRCT findings in COVID-19 patients, some of which are demonstrated in Fig. 8.

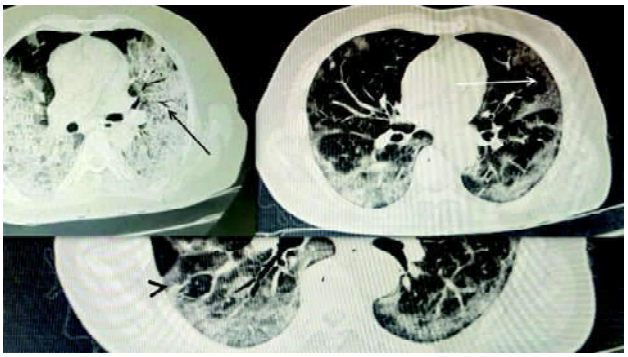

Fig. 8: *Some non-specific CT findings of COVID-19: air bronchogram (black arrow), peripheral based infiltrations (white arrow) and crazy paving appearance (black arrowhead) (GGO with superimposed thickened septal lines).*

These images are presented here to sensitize clinicians to the various HRCT appearances during this pandemic. Even in the absence of an RT-PCR report, these imaging findings, in conjunction with proper clinical presentation, can be diagnostic of COVID-19 infection.

Acknowledgement: The patients, who very kindly permitted academic use of their clinical material. All images are from patients who were treated by the authors.

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PICTORIAL CME

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PET-CT Scan Appearance of Disseminated Tuberculosis

Rudrajit Paul, Dipanjan Bandyopadhyay***

Disseminated tuberculosis (DT) is defined as spread of the infection to "two or more non-contiguous sites resulting from lympho-haematogenous dissemination of *Mycobacterium tuberculosis*"[1]. This is a devastating illness with high mortality and morbidity. Although immunocompromised persons are more prone to be affected, there are ample reports of otherwise healthy immune-competent persons also getting DT. The infection may present with non-specific symptoms at first and elude diagnosis for a long time. The internist (especially in India) has to be ever-vigilant about this disease.

Here, we present the PET-CT scan picture of a patient with DT. As such advanced imaging modalities are becoming available all over India, the new-age internist must also be familiar with the imaging appearance of diseases like DT. As mentioned earlier, DT can be a great masquerader and often, is mistaken for disseminated malignancy. In such cases, PET-CT scan would be done and the imaging appearance can differentiate between malignancy and disseminated TB.

This was a 56-year-old woman with rapidly developing right-sided pleural effusion. The pleural fluid was aspirated for diagnostic testing. It showed 1,250 cells/cmm with 98% mononuclear cells. ADA was 25 U/L. Protein concentration was 5.3 g/dl. Malignant cells were negative and Bactec culture did not grow M.Tb at 6 weeks. However, the patient was started on 4-Drug ATT but she had acute hepatitis for which the ATT had to be temporarily stopped. Meanwhile, the patient developed progressive abdominal pain and gradual loss of weight. USG of abdomen showed lymphadenopathy in peri-portal and para-aortic regions. FNAC from those nodes showed only reactive hyperplasia. Thus, one possibility was disseminated malignancy and before restarting the patient on further modified ATT, a PET-CT scan was done.

This showed FDG-avid Supra and infra-clavicular lymph nodes (Fig. 1), FDG-avid pleural thickening bilaterally (Fig. 2), FDG-avid nodules in the lung (Fig. 3), FDG-avid mediastinal nodes (Fig. 4) and FDG-avid peritoneal thickening, encysted fluid collection and multiple lymph nodes of various sizes in the abdomen and pelvis (Fig. 5). Few of the nodes were necrotic. The overall appearance was suggestive of disseminated tuberculosis. There was no discrete mass anywhere in the body.

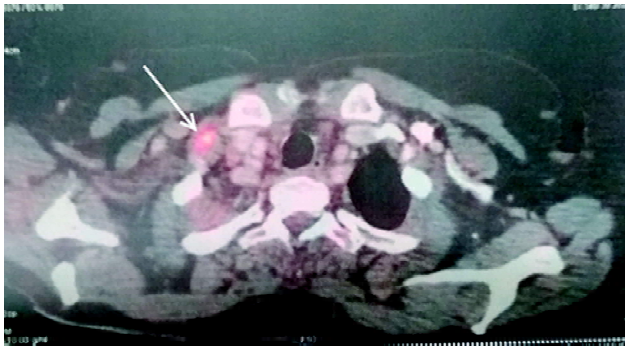

Fig. 1: *PET-CT showing FDG-avid (SUV max = 5) right supra-clavicular lymph node (White arrow).*

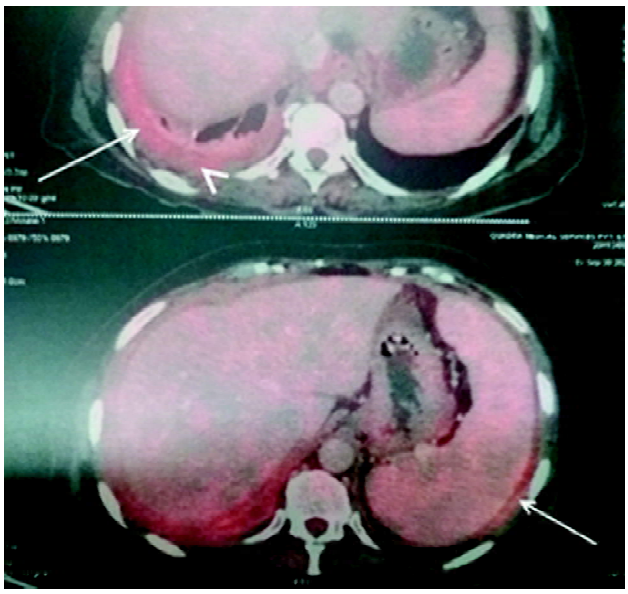

Fig. 2: *Bilateral FDG-avid pleural thickening (white arrow); (SUV max = 3, maximum pleural thickening 6.8 mm); right-sided pleural effusion also seen (white arrow head).*

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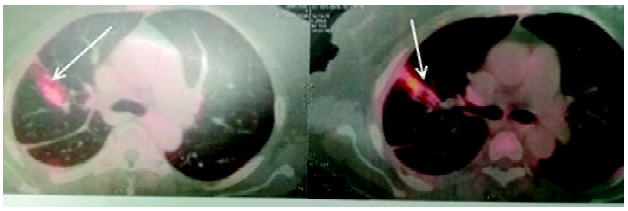

Fig. 3: *FDG-avid nodules with fibrotic strands (white arrows) in right lung upper lobe (SUV max = 5.4).*

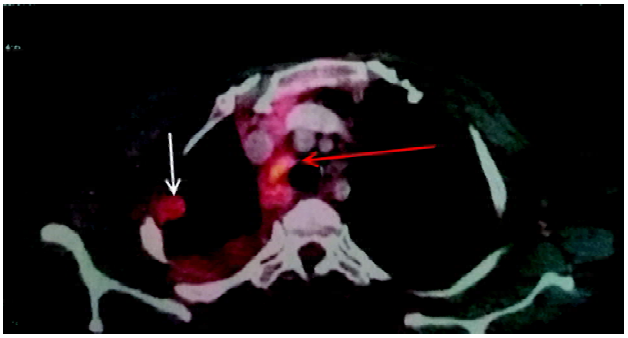

Fig. 4: *Mediastinal nodes (red arrow) SUV max = 5.5 and pleural based nodules (white arrow; SUV max = 3.1).*

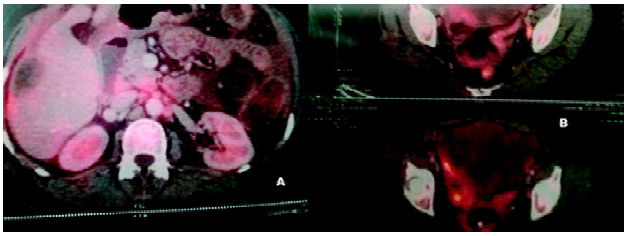

Fig. 5: *FDG avid peritoneal thickening (SUV max = 6; thickening = 9.5 mm) (A) and obdurator nodes (B) SUV max = 4.8.*

Thus, the patient was again started on modified ATT and gradually, the symptoms resolved. In cases like this, where pleural fluid assay or lymph node cytology cannot definitely diagnose TB, a PET-CT scan can be helpful in reaching a conclusion.

Harkirat *et al*, from the Army Hospital, New Delhi also reported on PET-CT scan appearances of Disseminated TB[2]. They commented that it is often difficult to differentiate between malignancy and TB, even after PET scan. High SUV values (> 2.5) are considered to be indicative of malignancy but TB lesions can also have high SUV, as found in the present case. So, often, the clinical acumen and experience of the internist is needed during interpretation of such reports. Features like diffuse pleural thickening, lung lesions with fibrotic strands and absence of any well-defined mass are in favour of disseminated TB (although definite mass may be absent in carcinoma of unknown primary). However, sometimes, the dilemma remains and then, further invasive procedures like pleural biopsy may be needed for diagnosis[3]. But such procedures require skilled operators and the patients may decline (as in our case).

We present this case to sensitize internists to the isotope imaging appearance of disseminated TB.

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