Original Articles

Dietary deficiency of vitamin A among rural children: A community-based survey using a food-frequency questionnaire

SHIVALI SURI, DINESH KUMAR, RANJAN DAS

ABSTRACT

Background. Overt vitamin A deficiency has been controlled in most parts of India, but prevalence of subclinical deficiency may still be high, which may enhance susceptibility to infections, reduce growth potential and also lead to higher mortality. We aimed to: (i) assess the consumption pattern of vitamin A-rich foods in children 1–5 years of age in rural Jammu; and (ii) estimate the dietary deficiency of vitamin A leading to risk of subclinical vitamin A deficiency in cluster-villages of the study area.

Methods. In 2011, we conducted a survey of 750 children by selecting 50 from each of the 15 clusters. The Helen Keller International's Food-Frequency Questionnaire (HKI-FFQ) modified to the local context was used to assess past week's intake for 28 food-items, including vitamin A-rich foods.

Results. The study revealed that plant sources such as amaranth, carrots, etc. and animal sources such as eggs and butter were the major sources of vitamin A in the study population. Consumption of amaranth (2.7 days/week) and carrots (1.7 days/week) was moderate but that of animal foods rich in vitamin A was low to negligible (1.1 day/week for eggs and 0.2 day/week for liver and fish combined). The majority (80%) of the cluster-villages manifested inadequate intake of vitamin A-rich foods, thereby making subclinical vitamin A deficiency a public health problem for the whole area. Faulty diets, improper breastfeeding practices, low coverage of vitamin A supplementation and high prevalence of undernutrition could be related to the observed subclinical deficiency.

Conclusion. Dietary diversification by including both plant and animal sources of vitamin A in adequate amounts along with improved breastfeeding, better implementation of mega-dose vitamin A supplementation and minimizing undernutrition may help in lowering subclinical vitamin A deficiency. The HKI-FFQ may be used as a proxy indicator of vitamin A intake/status for identifying pockets at risk of subclinical vitamin A deficiency in resource-constrained settings.

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INTRODUCTION

Clinically manifest vitamin A deficiency (VAD), a major public health problem of young Indian children, has been controlled to a large extent. However, milder forms of deficiency may not present clinically. Research suggests that such milder forms of deficiency may also lead to enhanced susceptibility to infections, reduce growth potential and even increase mortality, quite like its clinically manifest counterpart.[1–3] This milder form of deficiency, detectable by laboratory-based serum assays, is called subclinical VAD.

While not much is known about the prevalence of subclinical VAD, some studies have suggested that up to 62% of preschool children may be suffering from it. Since manifestations of subclinical VAD are less acute, it generally remains hidden from public view.[3–6] We, therefore, (i) assessed the consumption pattern of vitamin A-rich foods in children 1–5 years of age in rural Jammu; and (ii) estimated the dietary deficiency of vitamin A, leading to a risk of subclinical VAD in villages of the study area.

METHODS

Tool used for assessing subclinical VAD

While laboratory-based estimation of vitamin A in serum is the gold standard for assessing VAD, this is often not feasible due to financial and logistic constraints, especially in public health settings.[7–9] The Vitamin A Technical Assistance Program of Helen Keller International has designed a semi-quantitative tool, the Helen Keller International Food-Frequency Questionnaire (HKI-FFQ), which permits estimation of subclinical VAD at the community level. This tool, has been validated and found to correlate well with direct laboratory assessments, and has been used in a number of studies and settings.[10–12] We used the HKI-FFQ tool to assess vitamin A intake and status.

Sampling design

The HKI-FFQ has been validated by WHO using serum retinol levels for specific sample size and type of sample to provide reliable estimates of subclinical VAD. As per the recommended

methodology by Helen Keller International, 750 children (50 drawn from each of 15 cluster-villages) were surveyed to determine the burden of subclinical VAD.

Study participants were selected by multistage random sampling from the RS Pura block of Jammu district with a population of 180 560 (Census 2011).[13] Each of the eight administrative zones of the district formed our first stage units, and selected villages formed our second stage units. Fifteen villages were randomly selected (from 198 villages) and 50 eligible children were again randomly selected from each village cluster as third stage units.

Adaptation of the tool to local conditions

A prerequisite for using the HKI-FFQ is modification of the tool according to local availability/consumption of food items (including foods rich in vitamin A) so as to permit correct estimation of vitamin A intake and status. The original tool consists of 28 food items of which 11 items are permitted to be replaced with locally available and commonly consumed food items.[14]

The tool was locally adapted in three steps.[10] The first step was drawing a list of commonly available items through shop surveys. Five such shop surveys were conducted by visiting two local grocery stores, one vegetable vendor, one milk outlet and one pharmacy store. The purpose of the shop survey was to identify and document locally available foods including those rich in vitamin A including weaning foods, infant formulas, powdered milk, vitamin supplements, etc. The second step was the holding of focus group discussions (FGDs). Two such FGDs were held, each consisting of 7–12 participants represented by lay women, health workers, members of *panchayat*, grassroots women's groups and other village functionaries. The purpose of the FGDs was to find out the acceptability of locally available foods in the community. The third and last step was to check which of the available and acceptable items had vitamin A concentration >100 RE/100 g, and all these items were included in the modified tool.

Analysis and interpretation

The first author assisted by two community health workers conducted the shop surveys and FGDs. Data collection from respondents, i.e. either mother of identified child or a responsible caregiver was the responsibility of the first author. Prior approval was obtained from the ethics committee. Data were collected from January to December 2011 excluding the months of May to August—the months when mango production is at its peak—so as not to overestimate the intake of vitamin A-rich foods, since mangoes are rich in vitamin A and are consumed in abundance.

Intakes were assessed in terms of 'animal' and 'weighted' sources of vitamin A. The former included items such as eggs, fish, meat and poultry, besides milk and milk products, while the latter included both animal and plant sources with an adjustment made for poor bioavailability from plant sources. Subclinical VAD was inferred for a cluster if mean weekly intakes were below 4 for animal sources or below 6 for weighted sources. If more than 70% of the clusters failed to meet the cut-off values for either criteria, then the entire study area was deemed to have subclinical VAD.[10]

Data management

Data were entered in Microsoft Excel using the double-entry technique and analysis was done using weighted frequency, percentages and proportions.

RESULTS

Characteristics of population

A total of 750 children were studied of which 312 (41.6%) were girls. The mean (SD) age of the participants was 33.45 (12.7) months (Table I). The majority (84.5%) of children belonged to families of the middle socioeconomic class as per the modified Uday Pareek scale. Undernutrition as assessed by mid upper-arm circumference was present in 28.4% of children. Breastfeeding practices were suboptimal; 30.6% were not breastfed for the

TABLE I. Demographic characteristics of the study population

Characteristic	Boys (*n*=438)	Girls (*n*=312)	Total (*n*=750)
Age (in months)			
12–24	149 (34.0)	102 (32.7)	251 (33.4)
25–36	138 (31.5)	103 (33.0)	241 (32.1)
37–48	106 (24.2)	71 (22.7)	177 (23.6)
49–60	45 (10.3)	36 (11.6)	81 (10.8)
Socioeconomic status			
Upper	40 (9.1)	34 (10.9)	74 (9.8)
Upper middle	116 (26.5)	66 (21.2)	182 (24.3)
Middle	188 (42.9)	143 (45.8)	331 (44.1)
Lower middle	68 (15.5)	53 (16.9)	121 (16.1)
Lower	24 (5.5)	14 (4.5)	38 (5.1)
Below poverty line	2 (0.5)	2 (0.6)	4 (0.6)
Nutritional status by mid upper arm circumference			
Normal	322 (73.5)	215 (68.9)	537 (71.6)
Mild-to-moderate undernutrition	82 (18.7)	62 (19.9)	144 (19.2)
Severe undernutrition	34 (7.8)	35 (11.2)	69 (9.2)
Duration of breastfeeding (in months)			
None	39 (8.9)	20 (6.4)	59 (7.8)
1–6	92 (21.0)	79 (25.3)	171 (22.8)
7–12	81 (18.5)	59 (18.9)	140 (18.7)
13–24	149 (34.0)	113 (36.2)	262 (34.9)
>24	77 (17.6)	41 (13.1)	118 (15.7)
*Vitamin A supplementation in past 6 months**			
Received	60 (16.1)	36 (13.3)	96 (14.9)
Did not receive	312 (83.9)	234 (86.7)	546 (85.1)

**n*=642 children as 108 children did not have documented evidence of receiving vitamin A

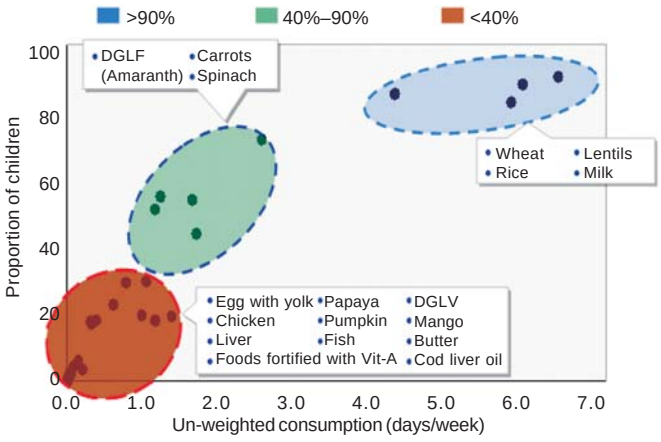

FIG 1. Pattern of consumption (unweighted) of food items included in the HKI-FFQ screening tool DGLF dark green leafy food DGLV dark green leafy vegatables

recommended 6 months, 7.8% did not receive any breastfeeding while 46.4% had been exclusively breastfed till 6 months. Prophylactic dose of vitamin A supplementation was received by only 14.9% in the past 6 months.

Dietary pattern and frequency of consumption of vitamin A-rich foods

Three distinct patterns were noted. High frequency of consumption in high proportion of children was seen for cereals, pulses and milk. Low frequency of consumption in low proportion of children was observed for foods from animal sources and coloured fruits. Intermediate frequency of consumption was seen for foods rich in vitamin A obtained from plant sources (Fig. 1).

Table II shows the mean frequency of consumption of items included in the HKI-FFQ and proportion of children consuming them at least once a week. Of the items included in the analysis of vitamin A intake, amaranth was consumed most frequently (2.7 days/week), while carrots (1.7 days/week) and papaya (0.8 days/week) came next. Among animal sources, eggs (1.1 days/week) and butter (1.0 days/week) were consumed at a higher frequency compared with liver and fish (0.2 day/week). The proportion of children consuming eggs (32.5%) and butter (21.6%) in the past week was higher than that for liver (5.2%) or fish (4.4%), while it was highest for amaranth (79.2%) and carrots (59.3%). Food supplements fortified with vitamin A were also consumed frequently (1.2 days/week). Cod liver oil, an important source of vitamin A, was not consumed by any child.

TABLE II. Semi-quantitative assessment of consumption of food items included in the HKI-FFQ tool

Food item in the HKI-FFQ	Mean frequency of consumption (days/week)	Children consuming the item at least once a week (%)
Staple, wheat	6.8	99.5
Rice*	6.3	97.3
Milk	6.2	91.2
Lentils*	4.6	94.0
DGLF (amaranth)†	2.7	79.2
Peanuts*	1.8	48.1
Carrots†	1.7	59.3
Foods cooked in oil	1.5	21.2
DGLF (mustard leaves) *	1.3	60.4
Spinach*	1.2	56.1
Food fortified in vitamin A*‡	1.2	19.9
Egg with yolk‡	1.1	32.5
Butter‡	1.0	21.6
Papaya‡	0.8	32.4
DGLF (fenugreek)*	0.7	24.9
Chicken*	0.4	19.9
Coconuts*	0.3	18.8
Pumpkin‡	0.3	19.6
Weaning food fortified with vitamin A*‡	0.2	3.9
Apricots*†	0.2	6.7
Liver‡	0.1	5.2
Fish‡	0.1	4.4
Sweet potato†	0.0§	2.1
Pepper	0.0§	2.4
Meat	0.0§	2.3
Mango†	0.0§	0.9
Red palm oil†	0.0§	0.1
Cod liver oil‡	0.0§	0.0§

* Food items that could be replaced with similar locally available foods † Plant sources of vitamin A included in the HKI-FFQ for analysis to identify subclinical VAD ‡ Animal sources of vitamin A included in the HKI-FFQ for analysis to identify subclinical VAD § The actual values were less than 0.1, hence rounded to 0.0 DGLF dark green leafy food

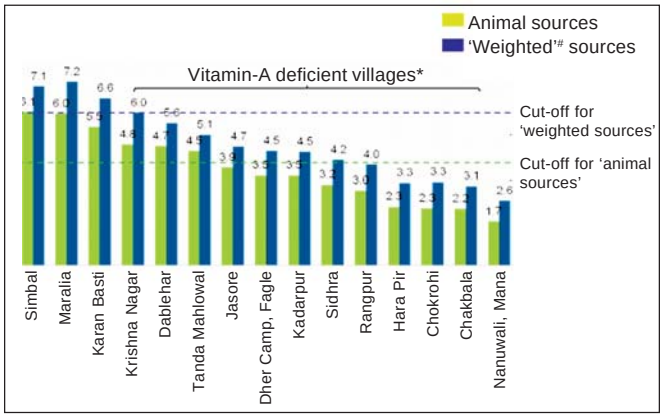

FIG 2. Consumption of vitamin A-rich foods from plant and 'weighted' sources for 15 cluster villages

*Reference period is past seven days
#'Weighted' includes animal and plant sources after adjusting for poor bioavailability of plant sources

Cluster-wise prevalence of subclinical VAD

The mean frequency of consumption ranged from 1.7 to 6.1 days/week for animal sources and it was 2.6–7.2 days/week for the weighted sources. Nine clusters had subclinical VAD on the basis of intakes from animal sources criteria while 12 had VAD by weighted-source criteria. Thus, as per the HKI guidelines, only 3 villages did not have subclinical VAD, while the remaining 12 (80%) had subclinical VAD (Fig. 2). From the public health point of view, the entire survey area was considered to have subclinical VAD.

DISCUSSION

We did this study to understand the prevalent dietary practices, correct subclinical deficiency if any, and also help frame recommendations for its prevention and control.

That fewer girls (41.6%) enrolled in the study could be due to the low child sex ratio of 776 reported for rural Jammu in Census 2011.[13] The high prevalence of undernutrition in our study is similar to that reported in other studies.[15–19] Breastfeeding was suboptimal in the children with an average duration of 16 months compared with 22 months for the state of Jammu and Kashmir and have contributed to subclinical VAD.[15] Suboptimal coverage of vitamin A supplementation has also been reported to be a contributory factor for subclinical VAD in an Ethiopian study.[20] A lower proportion of children (14.9%) had received vitamin A supplementation in the past 6 months in our study compared with that reported by the National Family Health Survey (NFHS)-3 and the National Nutrition Monitoring Bureau (NNMB) where it was 18% and 58%, respectively.[15,21,22]

While plant sources of vitamin A were consumed more frequently with 92.1% children consuming such sources at least once a week and unweighted frequency of consumption being 5.8 days/week, low bioavailability from such foods increased the risk of subclinical VAD. NFHS-3 has also reported low vitamin A intakes with only 29% of the recommended dietary allowance (RDA) being met in children 6–35 months old.[15] Another study also reports that 91% of their subjects consumed less than the

RDA for Indians.[23] Studies by NNMB and Narkhede *et al* have also found, like in our study, that animal sources of vitamin A are consumed less frequently as compared to plant sources.[16,24] NNMB also noted the intake of leafy vegetables to be low and in the range of 16%–21% of RDA.[25] High prevalence of subclinical VAD even in the presence of moderate intake of green leafy vegetables but low animal food intakes has been reported by other studies also, possibly as a result of low bioavailability of vitamin A from plant sources.

According to the National Sample Survey Office (NSSO), 62% of Indian preschool children suffer from subclinical VAD and the high prevalence was attributed to low intake of vitamin A-rich foods with 86% of subjects consuming less than 50% of the RDA.[22] Another study reports that less than one-third of eligible preschool children received vitamin A supplementation.[25] In a recent paper, we have also reported dietary deficiency as a major factor for the high burden of subclinical VAD among children 1–5 years of age.[26]

Limitations

There are two important limitations of this study. The first is the possibility of over-estimation of deficiency because breast and animal milk intakes were not taken into account for analysing VAD even though they contribute considerable amounts in Indian diets, especially among vegetarians. This is an inherent limitation of the tool that we used. The second limitation pertains to non-corroboration of the estimated burden of subclinical VAD with serum retinol levels, which could not be circumvented as our institution did not have the required facilities.

To conclude, subclinical VAD continues to be a public health problem due to suboptimal consumption of green vegetables, low consumption of eggs/butter and negligible consumption of other animal source foods. Besides the low overall intakes of vitamin A-rich foods, subclinical VAD could also be attributed to low bioavailability of vitamin A from plant sources. Dietary diversification through the inclusion of a wider range of plant and animal sources of vitamin A, better implementation of mega-dose vitamin A supplementation, improved breastfeeding practices, coupled with control of undernutrition together could play a major role in reducing subclinical VAD. The HKI-FFQ may be useful as a proxy indicator for assessing vitamin A intake/status to identify pockets of subclinical VAD, especially in resource-constrained settings.

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A study of events between the onset of symptoms and hospital admission in patients with acute abdomen

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ABSTRACT

Background. Acute abdomen is a common surgical emergency. Prompt investigation and treatment, including surgical intervention, is critical in reducing morbidity and mortality.

Methods. We carried out a prospective observational study at a large urban secondary healthcare centre in India. Patients with surgical acute abdomen were consecutively enrolled in the study over a period of 2 years. Data were collected regarding the onset of symptoms, time of presentation to the hospital and events in the intervening period.

Results. Analysis showed that misdiagnosis by medical personnel was significantly associated with delay in admission to the hospital. Unfamiliarity with the medical facilities, ignorance, low education and illiteracy and public holiday were the contributing factors for delayed presentation. Even though we detected some trends, the delay was not significantly associated with age, sex, educational level or socioeconomic status of the patient. The delay resulted in an increased mortality and morbidity especially in patients who needed emergency operative management.

Conclusion. Delayed presentation of acute abdomen is often not due to a single reason. The causes are distributed over various levels starting from the patient, family, medical personnel, administrative deficiencies, socioeconomic and sociocultural status of the country.

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INTRODUCTION

Acute abdomen accounts for 5%–10%[1] of visits to the emergency department and is responsible for most non-trauma-related surgical admissions and about 1% of all hospital admissions. The dictum has been that a majority of severe abdominal pain occurs in patients who have enjoyed fairly good health. This pain usually persists as long as 6 hours and is likely to be caused by a disease requiring surgical intervention.[2]

In the majority of patients, symptoms arise from diseases within the abdominal cavity itself, but occasionally they may originate elsewhere in the body.[3] The range of disease extends from the relatively trivial to the life-threatening. Attempts to reach a diagnosis must sometimes be curtailed in the interests of immediate treatment.

The diagnoses associated with an acute abdomen vary according to age and gender.[4,5] Acute appendicitis is more common in the young,[6,7] whereas billiary disease, bowel obstruction, intestinal ischaemia and infarction, and diverticulitis are more common in elderly patients. The most common causes of abdominal pain requiring admission are acute appendicitis, non-specific abdominal pain, pain of urological origin, intestinal obstruction and biliary tract disease and vary depending on the population and geographical region.[8] The emotional and psychological trauma following emergency admission can increase significantly if surgical intervention is unduly delayed. Although some surgical emergencies can and often should be dealt with within a few hours or days after admission, there remains a group of conditions for which surgery should be available within hours or even minutes of arrival.[9–11]

In a developing country like India, patients tend to present late in the disease course, which in turn may lead to poor outcome. Limited data are available in the literature on this issue from India. On the other hand, it is commonly experienced by surgeons working in India that there is a substantial delay from onset of symptoms to hospital admission in patients with surgical acute abdomen. We aimed to analyse the time period from clinical onset of acute abdomen to admission to our institute to identify factors that may lead to a delayed presentation. A secondary aim was to assess mortality and morbidity associated with delayed presentation in patients needing emergency surgical management.

METHODS

We did a prospective observational study at a secondary care public sector hospital in Mumbai over a period of 2 years (August 2011 to September 2013). All consecutive patients over 12 years of age, admitted to the department of general surgery with a clinical diagnosis of surgical acute abdomen, were enrolled in the study. The approval of the institutional ethics committee was taken before starting the study. We excluded patients with a history of trauma as well as pregnant women.

Data collected by interviewing patients and their family members, and by extracting information from medical records, were entered in a proforma. The information included demographic details such as name, age, sex, occupation, education, etc. In an attempt to calculate the distance from the hospital, the complete residential address of the patient was noted. Socioeconomic status was assessed using the Modified Kuppuswamy scale 2012.[12]

We defined surgical acute abdomen as pain in the abdomen due to a surgical cause that necessitated admission to the surgical unit. The time of onset was defined as the precise time of occurrence of the first abdominal symptom and the time of presentation as the time of admission to hospital. The pre-hospital interval was the time

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difference between onset and presentation. Delayed presentation was defined as a pre-hospital interval >24 hours. We enquired in detail about the events between onset of the first symptom and admission to our hospital. This included the primary treatment received (any treatment in the pre-hospital interval) and the response to it, nature of provider (family member/self/doctor), place of treatment (general practitioner/nursing home/private hospital/ primary health centre), and form of treatment such as antibiotic, analgesic, antiemetic, antacid, laxative, intravenous fluids, etc. The events during the pre-hospital interval were identified and classified as related to patient and family, to medical personnel, and other reasons such as late referral, public holidays, etc.

The symptoms and signs at presentation were noted and a detailed history was recorded. The provisional diagnosis and clinical decision made by the attending healthcare professional at the time of admission to our hospital were noted. A record of interventions done in the hospital (either conservative or operative management) was kept. Details of intraoperative findings were noted and the final outcome recorded. Information on mortality, morbidity as well as hospital and/or intensive care stay was recorded. Statistical analysis was done to assess factors leading to a delayed presentation to our hospital.

Data were entered in Microsoft Excel and analysed using SPSS version 16. Data are presented as frequency, percentage and cross tables. The chi-square test was used for qualitative data and the Fischer exact test for quantitative data. A p value of <0.05 was considered significant. Logistic regression was used to identify factors that may be related to a delay in presentation to the hospital. Factors that were found to be significantly associated with a delayed presentation were entered into a logistic regression analysis.

RESULTS

A total of 491 patients with a diagnosis of acute abdomen were studied, of whom 208 (42.4%) were women. About two-thirds (328) of patients belonged to the lower socioeconomic strata. The commonest condition was an appendicular pathology (Table I). The maximum pre-hospital interval was 408 hours while the minimum interval was 1.5 hours (mean [SD] 65.45 [72.38]) hours. A majority of patients (326 of 491; 66.4%) were admitted to hospital 24 hours after the onset of their symptoms (group II) while the rest were admitted within 24 hours (group I). Of the 326, 105 (32.2%) presented 24–48 hours after the start of the clinical illness; 66 (20.2%) presented after 48–72 hours, 79 (24.23%) presented in 3–5 days and 76 (23.3%) patients presented more than 5 day after the onset of their symptoms.

The age, sex, education, socioeconomic level and distance from hospital among patients in groups I and II were not significantly different and not associated with the delay in presentation to our hospital.

While 417 (84.9%) patients received primary treatment in the pre-hospital interval, only 100 (60.6%) in group I received it compared to 317 of 326 (97.2%) in group II. The most common primary treatment received was an intramuscular analgesic with an antacid by 73 (17.5%) patients followed by an intramuscular analgesic alone by 51 (12.2%) patients. Receiving primary treatment was associated with a delay in presentation to our hospital (p<0.001; Table II). We found that a larger proportion of patients in group 1 had either no relief or an increase in intensity of symptoms after primary treatment compared with patients in group II (71/100 *v.* 124/317; Table III).

Patients who received treatment from a general practitioner, in nursing homes, from more than one healthcare provider and those who had multiple events in the pre-hospital interval had a significantly delayed presentation (Table IV). Due to late referral from primary health centres, 10 (3.1%) patients presented after 24 hours. On questioning about the reasons for delay, patients and families expressed fear of approaching a healthcare provider, fear of dying and senility, being refused admission to hospital, ignorance of the seriousness of symptoms, lack of awareness of diseases and financial problems.

After admission, 331 of 491 patients (67.4%) underwent an operative procedure. Of these, 198 were emergency procedures (Table V); 133 were elective procedures done at a later date/ subsequent admission. Of the patients who needed emergency surgery and presented to the hospital after 24 hours, 35 (29.2%) had seen a general practitioner and this was significantly associated with a delayed presentation (p=0.03, odds ratio: 2.27). Patients who had seen the casualty medical officer (17; 14.2%), had been treated at a nursing home (13; 10.8%), had visited a surgeon (3; 2.5%), been treated by >1 healthcare provider (11; 9.2%), had delayed coming to our centre due to patient and family related

TABLE I. Causes of surgical acute abdomen in the study group

Condition	*n* (%)
Appendix (acute, perforated or gangrenous appendicitis, appendicular lump)	200 (40.7)
Hepatobilliary (acute cholecystitis, cholangitis, cholelithiasis, cholodocholithiasis, choledochal cyst, empyema gallbladder, liver abscess)	94 (19.1)
Gastrointestinal (intestinal obstruction, bowel perforation, abdominal tuberculosis, infective colitis, diverticulitis, etc.)	124 (25.3)
Acute and chronic pancreatitis	33 (6.7)
Genitourinary (renal and ureteric calculi, urinary tract infection, pelvic inflammatory disease, ovarian cyst)	33 (6.7)
Hernia (strangulation, obstructed) and others	7 (1.4)
Total	491

TABLE II. Events in the pre-hospital interval

Initial event prior to reporting to our centre	*n* (%)
Treatment at single/multiple private nursing home(s) after which patient went home	37 (7.5)
Treatment by single/multiple general practitioners (GPs) after which patient went home	121 (24.6)
Treatment by casualty medical officer at our centre after which patient went home	67 (13.6)
Treatment by emergency surgical resident at our centre after which patient went home	17 (3.5)
Treatment given by GP/nursing home after which patient went home and came to our centre and went back home or vice versa	35 (7.1)
Visited more than one private clinic (GP and private nursing home)	5 (1.0)
Admission to department other than general surgery	4 (0.8)
Self medication or medication given by family members	51 (10.4)
Sought discharge from private hospital and came to our centre	7 (1.4)
Discharge against medical advice from our centre and reported back	9 (1.8)
No self medication/ no visit to healthcare provider	65 (13.2)
Did not seek any medical advice nor self-medicated	12 (2.4)
Delayed visit to hospital due to public holiday/festival/ hospital workers' strike	2 (0.4)
Treatment taken at primary health centre and referred to us	18 (3.7)
Multiple events	41 (8.4)
Total	491

TABLE III. Response to primary treatment

Response	Group I (≤24 hours)	Group II (>24 hours)	Total
Symptoms decreased initially, appeared again with increased intensity	9 (9)	48 (15.1)	57
Symptoms decreased initially, appeared again with same intensity	5 (5)	64 (20.2)	69
No relief	29 (29)	60 (18.9)	89
Symptoms increased in intensity	42 (42)	64 (20.2)	106
Symptomatic relief followed by reappearance	15 (15)	54 (17.0)	69
Symptomatic relief initially, followed by reappearance of symptoms, which were then refractory to medication	0	27 (8.5)	27
Total	100	317	417

TABLE IV. Factors that contributed to a delayed presentation

Variable	Odds ratio	Confidence interval	p value
Treated by general practitioner	2.682	1.66–4.32	<0.001
Treated at nursing home	3.959	1.68–9.35	0.002
Treated by more than one healthcare provider	6.466	2.45–17.04	<0.001
Multiple events in history	36.947	5.00–272.90	<0.001

TABLE V. Emergency procedures performed

Procedure	*n* (%)
Appendicectomy	152 (76.8)
Primary closure of gastric/duodenal perforation	15 (7.6)
Primary closure of small bowel perforation for abdominal tuberculosis, post-typhoid perforation	6 (3.0)
Resection anastomosis for abdominal tuberculosis, strangulated incisional, inguinal hernia	7 (3.5)
Ileostomy/jejunostomy for abdominal tuberculosis, inflammatory bowel disease or small bowel cancer	13 (6.6)
Sigmoid/transverse colostomy for sigmoid volvulus, iatrogenic perforation	3 (1.5)
Open cholecystectomy	1 (0.5)
Exploration for obstructed hernia	1 (0.5)
Total	198

factors (9; 7.5%) and those that had been admitted to other departments (3 patients were admitted to other departments in our hospital were not associated with a delayed presentation).

The mean (SD) hospital stay was 5.2 (4.9) days; range 1–45 days. Patients who delayed coming to our hospital for >24 hours were more likely to stay for >5 days (p=0.01); 86 (26.4%) patients in group II stayed for >5 days compared with 27 (16.4%) in group I. Even among those who had emergency surgery, patients in group II had a hospital stay of >5 days (p=0.04). The overall mortality in our patients was 0.6% and all those who died were in group II.

DISCUSSION

Acute abdomen presents with rapid onset and progression of symptoms that may indicate a life-threatening intra-abdominal pathology. A definitive diagnosis is often difficult but early presentation to a healthcare provider will lead to appropriate management and a good outcome.[13] The practice of medicine, referral pattern, access to healthcare and awareness about medical emergencies is different in the developing world compared with the developed world.

A few studies from developing countries have explored the factors responsible for mortality and morbidity associated with delayed presentation of acute abdomen. A study from Sudan[14] in 2000 found late presentation to be due to poor awareness about the disease and misdiagnosis at primary healthcare settings. Another study from Lahore in 2006 showed that illiteracy, lack of awareness about medical facilities, and social and cultural values were associated with a delayed presentation.[15] A Nigerian study in 2010 found lack of financial resources to be an important factor in the delay in emergency abdominal surgery.[16] India has its own unique set of sociocultural and behavioural factors that may impact on medical care. Even though acute abdomen is a common surgical emergency, published data about the spectrum of surgical causes of acute abdomen and reasons for delayed presentation are lacking.

We had, for many years, observed delayed presentation of patients with acute abdomen. Most studies from the developing world have focused on complications related to delayed diagnosis in specific abdominal problems such as acute appendicitis. Few studies have assessed factors relating to delay in patients with a surgical acute abdomen.

We focused on the time from the onset of acute abdomen to presentation in an effort to determine factors that led to delayed presentation at our hospital, a secondary public urban health centre in a metropolitan city in India. We divided patients into two groups based on an arbitrary cut-off time of 24 hours as representative of an 'early' or 'late' presentation, as did Salman *et al*.[13] while studying causes for delay in diagnosis and treatment, and the effect on prognosis.

A study by Wig *et al*.[17] in 1978 showed that arrival of patients to hospital was delayed with 45% presenting 24 hours after the onset of symptoms. However, 66.4% of our patients were admitted after 24 hours of onset of symptoms and a substantial number of them needed an emergency operative intervention (40.3%). Wig *et al*. also showed that men were more frequently affected than women in a ratio of 3:1. We had similar findings but with a men:women ratio of 1.4:1. However, gender was not significantly associated with a delay in presentation. Most patients with acute abdomen were in the third and fourth decade of life and age was not associated with a delay in presentation in our study as well as in the study by Chung *et al*.[18] A similar study by Hansson *et al*.[19] observed that delay was not influenced by gender. Women (69.7%) tended to present late as compared to men though the difference was not significant. Akin to other countries in South Asia, in India too women are neglected and their health concerns are not taken seriously.

The level of education contributes to awareness about diseases and its consequences. It is also an important factor in the use of available medical facilities.[20] Due to poor awareness and knowledge about health-related issues, patients tend to present late and this increases morbidity. However, we did not find any relation between the patient's level of education and the delay in presentation (p=0.11), despite a large proportion of our patients as well as those in the delayed group being illiterate or educated up to high school (66.8% and 77.6%, respectively). Doumi and Mohammed[14] in 2007 studied patients admitted to the emergency wards of the University Surgical Unit in El Obeid Teaching Hospital, Western Sudan and observed that late presentation of common diseases such as acute

appendicitis was due to poor awareness of disease and its seriousness despite it being common in the area.

Among the delayed group, 65.3% of patients were from the lower socioeconomic strata. However, we did not find a significant association of this with delayed presentation (p=0.66). Mustafa and Abbas[15] from Lahore highlighted the importance of socio-economic status for early and better utilization of available medical facilities. They showed that 74% of their study population belonged to poor and lower middle class leading to delayed presentation of acute abdomen, which was three times more common than among the more affluent. Another study from a University Hospital in Turkey[21] found that appendiceal perforation was associated with parental delay largely because of low socioeconomic levels. Similarly, Salman and Razzonki[13] found poor socioeconomic status to contribute to a delay in presentation.

Certain sociocultural aspects too could lead to a delay in presentation. We found family issues led to delayed presentation more often in women. The reasons given during the interview were usually the fear of not being available to provide for children and elders of their household. Due to the fact that hospital admission would result in absence of a caregiver for their spouses most of them refused admission on the first visit.

When we interviewed patients in our outpatient department regarding the history of their illness, we found that many patients had received primary treatment in the pre-hospital period. We also observed that delayed presentation was associated significantly with receiving primary treatment during the pre-hospital interval ($p<0.001$). In our study, the spectrum of primary treatment was not influenced by patients' demographic factors such as age, gender, education and socioeconomic status. The primary treatment was often provided by a family member or at times self-medication was resorted to.

The most common treatment received was intramuscular injection of an analgesic. Anand *et al*.[24] studied injection use in a village in northern India and observed that the use of injections in the study area was high—2.46 injections per person per year. This may lead to a delay in appropriate treatment. It is therefore important to triage patients according to the acute abdominal condition.

We found that receiving treatment from healthcare personnel was significantly associated with a delay in presentation. Misdiagnoses and administering analgesics were the main reasons for delay. Similar findings were observed in a study done in Iraq by Salman and Razzouki[13] which showed that in a significant number of cases the physician was responsible for the delay. Our patients were also referred late from primary health centres; this was similar to a study by Doumi and Mohammed[14] from Sudan. Our patients who presented late were more likely to have a prolonged hospital stay. von Titte *et al*.[25] observed that length of hospital stay and postoperative complications were related to a delay in diagnosis at an appropriate healthcare centre.

Compared to patients who were managed conservatively or underwent elective surgery, delay in presentation was more important in patients needing emergency surgery. The 3 patients who died presented after 24 hours and had peritonitis due to a perforation of the bowel.

Our study has a few limitations. Data were collected by interviewing patients and their family members. It is therefore dependent upon the information providers' ability to accurately recall events, their level of education, as well as understanding and awareness of the clinical condition. As the information was being gathered during an illness and in a hospital setting, it is possible that the informant may have responded so as not to upset any healthcare provider. In India, hospital stay is not an accurate indicator of severity of illness as social and economic factors may lead to a longer or shorter stay. Recording the complications would have been more accurate to assess morbidity. However, we believe that our study is representative of the present situation in India as it covers a fairly large number of patients from a public hospital.

We conclude that delayed presentation of patients with acute abdomen is often due to multiple reasons. These include patient, family, healthcare system, socioeconomic and other reasons. Further research needs to be directed towards identifying the contributing factors that play a role in delay in presentation and subsequently policy-making to tackle these issues.

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Scrub typhus: A prospective, observational study during an outbreak in Rajasthan, India

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ABSTRACT

Background. Scrub typhus, a potentially fatal rickettsial infection, is common in India. It usually presents with acute febrile illness along with multi-organ involvement caused by *Orientia tsutsugamushi*. As there was an outbreak of scrub typhus in the Hadoti region of Rajasthan and there is a paucity of data from this region, we studied this entity to describe the diverse epidemiological, clinico-radiological, laboratory parameters and outcome profile of patients with scrub typhus in a tertiary care hospital.

Methods. In this descriptive study, we included all patients with an acute febrile illness diagnosed as scrub typhus by positive IgM antibodies against *O. tsutsugamushi*, over a period of 4 months (July to October 2014). All relevant data were recorded and analysed.

Results. A total of 66 (24 males/42 females) patients were enrolled. Fever was the most common presenting symptom (100%), and in 67% its duration was for 7–14 days. Other symptoms were breathlessness (66.7%), haemoptysis (63.6%), oliguria (51.5%) and altered mental status (39.4%). The pathognomonic features such as eschar (12%) and lymphadenopathy (18%) were not so common. The commonest radiological observation was consistent with acute respiratory distress syndrome. Complications noted were respiratory (69.7%), renal (51.5%) and hepatic dysfunction (48.5%). The overall mortality rate was 21.2%.

Conclusions. Scrub typhus has emerged as an important cause of febrile illness in the Hadoti region and can present with varying clinical manifestations with or without eschar. A high index of suspicion, early diagnosis and prompt intervention may help in reducing the mortality.

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INTRODUCTION

Scrub typhus is a zoonotic infectious disease presenting with acute febrile illness of variable severity. Human beings get infected accidentally when they encroach upon mite-infested rural and suburban areas.[1] It is often acquired during recreational, occupational or agricultural exposure because crop fields are an important reservoir for transmission. It was considered a lethal disease in the pre-antibiotic era and continues to be a public health problem in South Asian and Western Pacific regions.[2]

In India, the first case of scrub typhus was reported in 2009 from Kerala.[3] Though widely prevalent in the Indian subcontinent, specific prevalence data are not available.[4] Apart from this, epidemics of scrub typhus have been reported from north, east and south India.[1] Due to lack of awareness, a low index of suspicion among clinicians, paucity of confirmatory diagnostic facilities and clinical symptoms mimicking other more prevalent diseases such as dengue, malaria and leptospirosis, scrub typhus is under-diagnosed in India, especially in Rajasthan.[5] The overall mortality varies from 7% to 30%, next only to malaria among infectious diseases.[6]

During an outbreak of acute febrile illness in the Hadoti region in the southern part of Rajasthan, investigations revealed the cause to be due to scrub typhus. Such an outbreak has not been reported earlier from this region. We studied the demographic, clinico-radiological and outcome of patients with scrub typhus during this outbreak.

METHODS

We did this prospective, observational study at a tertiary care hospital in the Hadoti region of Rajasthan during an outbreak of scrub typhus from July to October 2014. All clinically suspected patients with an acute febrile illness (in whom malaria, leptospirosis, dengue fever, viral pharyngitis, enteric fever and urinary tract infection were excluded by history, clinical examination and appropriate laboratory investigations) were included in this study. All demographic data, detailed history, past treatment history/any comorbid illnesses were recorded in a proforma. A complete physical examination, vital signs and relevant investigations were also noted.

All patients were subjected to investigations to establish the cause of fever. These included a peripheral blood smear for malarial parasites, complete blood count, serology for dengue, leptospirosis, scrub typhus, enteric fever and retroviral infections; blood, urine, sputum and/or endotracheal cultures and a smear for acid-fact bacilli using the Ziehl–Neelson's method. A Mantoux test, X-ray chest, ultrasound abdomen, contrast-enhanced computed tomography (CECT) scan of the thorax and abdomen were ordered as and when required. A CT of the brain and cerebrospinal fluid (CSF) analysis were done, if clinically indicated. Biochemical investigations including fasting blood sugar, renal function and liver function tests were done and recorded.

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Scrub typhus serology was tested in batches for IgM antibodies to *Orientia tsutsugamushi* using commercial enzyme-linked immunosorbent assay (ELISA) kits (Panbio Ltd, Brisbane, Australia). The kit uses a specific 56 kDa recombinant antigen of *O. tsutsugamushi* and has a sensitivity and specificity of >90% when compared with recommended gold standard tests, namely the immunofluorescent antibody (IFA) and indirect immunoperoxidase tests. The test was performed as per manufacturer's instructions. The study protocol was approved by the institutional ethics committee and informed consent was obtained from the patients. A diagnosis of scrub typhus was confirmed when a patient with an AFI had a positive serology for scrub typhus, further strengthened by either the presence of eschar or exclusion of other causes of fever.

Initially, all patients with AFI were treated with empirical antibiotics (intravenous pipericillin–tazobactam and azithromycin) and symptomatic treatment. After confirmation of the diagnosis of scrub typhus, piperacilli–tazobactam was stopped and doxycycline 200 mg per day was started while azithromycin was continued for 7–10 days.

Patients with multi-organ dysfunction (e.g. acute respiratory distress syndrome [ARDS] with or without shock, renal failure, elevated transaminase levels, leucocytosis and thrombocytopenia) were managed with organ support measures as appropriate such as invasive or non-invasive ventilation, inotropic support, renal replacement therapy and blood and blood products.

The presence of organ dysfunction at the time of hospitalization was assessed by using the sequential organ failure assessment (SOFA) score. Organ dysfunction was said to be present if the organ-specific SOFA score was ≥1 and organ failure if the SOFA score was ≥3.[7]

Outcome measures

The primary outcome was in-hospital mortality and the secondary outcomes included length of stay in the intensive care unit (ICU) and hospital, the need for and duration of mechanical ventilation, type of ventilatory support (invasive or non-invasive) and need for dialysis.

RESULTS

During the study period, 290 patients were admitted to our hospital with AFI. Of these 66 (22.8%) patients (24 males and 42 females) were diagnosed to have scrub typhus (Table I). Fever was the commonest presenting symptom followed by haemoptysis and cough. The common clinical signs were pedal oedema, jaundice and hepatosplenomegaly. Eschar (8 patients) and lymphadenopathy (12 patients) were seen less commonly.

Low platelet counts and abnormal renal functions were frequently abnormal (Table II). Nearly half our patients (48.5%) had involvement of three or more organ systems. Respiratory dysfunction was the commonest (46; 69.7%), followed by renal (51.5%) and hepatic dysfunction (48.5%) (Table III). Twenty patients (30.3%) had dysfunction of all five organ systems during the course of hospitalization. Among the 46 patients with respiratory dysfunction, ARDS (34, 73.9%) was the commonest, followed by pleural effusion (30, 65.2%) and pulmonary infiltrates on chest X-ray (12, 26.1%).

Forty-six of the patients required ventilation (Table IV), 18 required dialysis and the overall mortality was 14 (21.2%).

DISCUSSION

Scrub typhus is a potentially fatal infection that affects about one

TABLE I. Demographic and clinical profile of patients with scrub typhus (*n*=66)

Characteristic	*n* (%)
Age (years)	
≥20	4 (6.1)
20–50	48 (72.7)
≤50	14 (21.2)
Sex	
Male	24 (36.4)
Female	42 (63.6)
Duration of symptoms (days)	
<7	10 (15.2)
7–14	44 (66.7)
>14	12 (18.2)
Residence	
Rural	53 (80.3)
Urban	13 (19.7)
Occupation	
Farmer/agricultural work	53 (80.3)
Others	13 (19.7)
Symptoms	
Fever	66 (100)
Breathlessness	44 (66.7)
Decreased urine output	34 (51.5)
Altered sensorium	26 (39.4)
Rash	10 (15.2)
Nausea/vomiting	18 (27.3)
Myalgia	20 (30.3)
Cough	32 (48.5)
Haemoptysis	42 (63.6)
Headache	22 (33.3)
Generalized weakness	34 (51.5)
Other	16 (24.2)
Signs	
Icterus	33 (50.0)
Lymphadenopathy	12 (18.2)
Pedal oedema	42 (63.6)
Hypotension/shock	20 (30.3)
Hepatosplenomegaly	23 (34.8)
Eschar	8 (12.1)
Abdomen/leg/other	4 (6)/2 (3)/2 (3)

TABLE II. Laboratory investigations

Investigation	*n* (%)
Total leucocyte count <4000/cmm	10 (15.1)
Total leucocyte count >11 000/cmm	20 (30.3)
Anaemia (haemoglobin <10 g/dl)	32 (48.5)
Platelet count <100 000/cmm	52 (78.8)
Elevated transaminase levels (normal 40/56 i.u.)	32 (48.5)
Increased bilirubin (normal 0.3–0.8 mg/dl)	12 (18.2)
Increased urea/creatinine (normal 60/0.6–1.2 mg/dl)	34 (51.5)

TABLE III. Organ system dysfunction during the stay in hospital

Organ/system	Frequency of dysfunction (%)
Respiratory	46 (69.7)
Cardiovascular	20 (30.3)
Renal	34 (51.5)
Central nervous system	26 (39.4)*
Liver	32 (48.5)

* 2/26 (7.7%) had evidence of meningitis, the rest had non-specific symptoms

TABLE IV. Outcomes of the study patients

Variable	n (%)
Mechanical ventilation required	46 (69.7)
Type of mechanical ventilation	
Non-invasive	12 (26.1)
Invasive	34 (73.9)
Both	10 (21.7)
Average duration of non-invasive ventilation	3.5 days
Average duration of invasive ventilation	6.2 days
Need for dialysis	18 (27.3)
Average duration of ICU stay	7.5 days
Average duration of hospital stay	13.8 days
Mortality	14 (21.2)

ICU intensive care unit

million people every year worldwide.[8] It is a common cause of multi-organ dysfunction and an important cause of admission in ICUs of patients with AFI.

Rickettsial infections have been documented from various parts of India.[9] There have been reports of sporadic outbreaks of scrub typhus mainly in the eastern and southern Indian states with serological evidence of widespread prevalence of spotted fevers and scrub typhus,[10,11] particularly during the monsoon and post-monsoon months.[1,11–13] The outbreak that we studied also occurred during the same period.

During our study, 22.8% (66/290) of patients with AFI presenting to us had scrub typhus, an observation (24.7%) similar to the study from an adjoining region by Sinha *et al*.[14]

Age, sex, residential area and occupation are known to influence the occurrence of scrub typhus. People working outdoors tend to be afflicted more often. Most of our patients were 20–50 years of age, an observation similar to Sinha *et al*.[14] and Madi *et al*.[15] However, while more women were affected in our series, Rajoor *et al*. reported more men to be affected.[4] This could probably be because men in the Hadoti region tend to migrate to cities for work and women look after the agricultural work.

The clinical manifestations of this disease vary from minimal disease to severe fatal illness with multi-organ dysfunction. Our patients too presented with similar clinical manifestations and these have been reported in another study from the Indian subcontinent.[16]

We considered the duration of symptoms from the time of onset of fever as this was the first symptom in most patients. Two-thirds of the patients were diagnosed in the second week and had manifestations akin to those reported in previous studies.[1,14,15,17]

Eschar at the site of attachment of the larval mite/chigger is considered highly suggestive of scrub typhus, but occurs in a variable proportion of patients in different studies.[18] It is a blackish necrotic lesion resembling a cigarette burn generally found in areas where the skin is thin, moist or wrinkled, and where the clothing is tight such as over the abdomen, groin and on the legs.[4] Its presence is considered pathognomonic of the disease but its absence does not exclude the possibility of scrub typhus. However, it is relatively difficult to detect on dark-skinned patients.[19] In our study, eschar was present in 8 (12.1%) patients and the most common site was the lower abdomen. While similar rates (4%–12%) have been reported by some Indian studies,[4,9,12] Vivekanandan *et al*.[1] (46%), Chrispal *et al*.[16] (45.5%) and studies from Vietnam,[20] Taiwan,[21] and Korea[22] reported slightly higher incidences of eschar probably due to fair-skinned population of these studies, which increases the chances of finding eschar. Premaratna *et al*. also postulated that in dark-skinned patients early/very small eschar could be easily overlooked.[10] This difference in incidence of eschar may also be due to variation in serotypes/endemic strain among the regions.[1,14,23] One study found that not a single patient presented with eschar.[14] Our findings were similar to those by Razak *et al*. who concluded that the occurrence of eschar is less frequent among patients from Southeast Asia.[17] Studies have also found a significant difference in the gender distribution of eschars, but the gender distribution was not significantly different in our study.[24]

Eschar is more often than not associated with regional lymphadenopathy. Only 18% of our patients had lymphadenopathy. A wide range (22%–53%) of lymphadenopathy has been reported in different studies.[1,4,9,14] and some have suggested that the presence of generalized lymphadenopathy suggests a late presentation and a worse outcome.[9]

The abnormalities in cell counts, and liver and renal functions in our patients were consistent with those reported in other studies. [1,4,12,15]

Among our patients who presented with any central nervous system manifestations, 26 required CSF examination and only 2 had confirmed meningitis. However, Viswanathan *et al*. had 17 patients with meningitis among 65 of their patients.[25] This is possibly because they specifically searched for patients with scrub typhus and meningitis. Scrub typhus should be considered in the differential diagnosis of 'subacute' meningitis, especially when accompanied by renal failure or jaundice.[26] Previous studies from India have reported meningoencephalitis in 9.5%–23.3% of patients.[1,11,13]

Scrub typhus is a cause of multi-organ dysfunction. Nearly half of our patients (48.5%) had three or more organ systems involved while 20 patients (30%) had evidence of dysfunction of five organs during the course of their hospital stay. Complications in scrub typhus develop after the first week of illness. Narvencar *et al*. found hepatic dysfunction to be the most common followed by ARDS, circulatory collapse and acute renal failure.[27] We found respiratory dysfunction in over two-thirds of patients, followed by renal dysfunction in over half the patients.

As the main organ dysfunction in our study was respiratory failure, 46 of our patients (69.7%) required mechanical ventilation. Of these, 12 were managed with only non-invasive ventilation, 10 required non-invasive ventilation to be changed to invasive mechanical ventilation and 34 patients were managed at the outset with invasive mechanical ventilation. A study from southern India also showed involvement of the respiratory system in 76.9% of patients and requirement of ventilatory support in 68.9% of patients.[11]

The mortality in patients with scrub typhus has wide variations and depends on the circulatory load of *O. tsutsugamushi*, early or late presentation and treatment modality. Deaths are attributable to delayed presentation or diagnosis, and drug resistance. Complications such as ARDS, renal failure and hepatic involvement are independent predictors of mortality; most of these were present in our patients.[28]

The case fatality rate for scrub typhus has been 7%–30%,[29] including 10% in Korea[23] to 30% in Taiwan.[30] The mortality rate of 21.2% in our study was slightly higher compared to other studies from India by Mahajan *et al*. (mortality 14.2%),[13] Kumar *et al*. (mortality 17.2%)[31] and Rungta *et al*.[32] while somewhat low as compared to that reported by Lai *et al*. (mortality 15%–30%)[30] and Griffith *et al*.[33] Studies have shown inter-strain variability in virulence[23] and since we did not do serotyping and genotyping,

it is possible that the strain type present in our region was a more virulent one causing higher case fatality.

The main strength of our study is that we included confirmed cases of scrub typhus who had IgM antibodies against *O. tsutsugamushi*.

Diagnosis of scrub typhus is difficult in India because of its varied clinical presentation, absence of eschar in many patients, and lack of availability of specific tests (ELISA/serological tests). In developing countries with limited resources such as India, we suggest that the diagnosis of scrub typhus should be based largely on a high index of suspicion and careful clinical, laboratory and epidemiological evaluation. It is prudent to recommend empirical antibiotic therapy in patients with acute febrile illness with evidence of multi-organ involvement.

Conclusion

Scrub typhus is prevalent in many states of southern and eastern India, but outbreaks have been occurring in other parts too, including in Rajasthan. Mortality in these patients is most often due to multi-organ dysfunction.

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