Non-Respiratory and Non-Diarrheal Causes of Acute Febrile Illnesses in Children Requiring Hospitalization in a Tertiary Care Hospital in North India: A Prospective Study

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Abstract. Acute febrile illnesses (AFIs) in children from the developing world can have varying etiologies. Awareness of local epidemiology helps in prioritizing investigations and empiric treatment. This prospective study was carried out in a tertiary care center in North India, aiming to determine the burden, etiology, and outcome of AFI other than pneumonia and diarrhea in hospitalized children. A total of 613 consecutive children aged 3 months to 12 years with febrile illness of < 7 days during four selected months of 2014 representing different seasons were screened for eligibility. Those with acute respiratory diseases ($N = 175$, 28.5%) and diarrheal illness ($N = 46$, 7.5%) were excluded and 217 children were enrolled. Mean (standard deviation) age was 4.8 (3.4) years. Nearly half ($N = 91$, 41.9%) presented in post-monsoon season. Diagnosis could be established in 187 (86.2%) children. Acute central nervous system infections were the most common ($N = 54$, 24.8%). Among specific infections, scrub typhus was the most frequent ($N = 23$, 10.5%) followed by malaria ($N = 14$, 6.4%), typhoid ($N = 14$, 6.5%), and viral hepatitis ($N = 13$, 6.0%). Blood culture had a low (6.5%) yield; *Salmonella typhi* ($N = 6$) and *Staphylococcus aureus* ($N = 5$) were the common isolates. Serological tests were helpful in 50 (23%) cases. In multivariate analysis, hepatomegaly and/or splenomegaly independently predicted scrub typhus. Mortality rate was 10.1%. We conclude that AFI other than pneumonia and diarrhea are a significant burden and follow a seasonal trend. Scrub typhus has emerged as an important etiology of childhood AFIs in northern India. Periodic review of regional epidemiology will help in understanding the changing pattern of infectious diseases.

INTRODUCTION

Acute febrile illnesses (AFIs) are among the commonest causes of hospitalization in children from developing countries. Most febrile illnesses in children result from infectious etiologies. Several global estimates have demonstrated lower respiratory tract illness, including pneumonia, and acute diarrhea as the commonest causes of febrile illnesses in children younger than 5 years.^{1,2} Although these diseases still remain the major causes of avoidable deaths accounting for about 22% of all postneonatal deaths in 2015, the mortality trend in past 15 years showed > 30% decline in pneumonia- and diarrhea-related deaths.^{3,4} Therefore, focus on other infectious causes remain equally important, especially, in the developing world and should be the target of child survival efforts in achieving sustainable development goals. In a large and populous country such as India, with varying climate and topography, there can be wide variation in infectious etiology of AFI. Factors such as malnutrition, low immunization coverage, and other comorbidities may increase the susceptibility to infections and affect the outcome adversely.⁵ However, a comprehensive estimation of the burden of febrile illnesses other than pneumonia and diarrhea affecting children is scarce. These estimates are critical in understanding the changing epidemiology of infectious diseases in children, choosing appropriate and early targeted intervention strategies to prevent mortality, and setting up public health preventive initiatives to restrain these diseases. Based on these data, guidelines for investigation and antimicrobial therapy may be developed for physicians to deal with AFI.

We hypothesized that although acute diarrheal and acute respiratory illnesses (pneumonia, bronchiolitis, etc.) constitute the largest disease burden requiring hospitalization in

children, their presentation is often straightforward clinically. Yet, there are several other infectious illnesses affecting Indian children, some of them exhibiting age-specific incidence and seasonal prevalence.⁶ These illnesses often remain undiagnosed in most health facilities in India, for either lack of awareness by the clinician or nonavailability of adequate diagnostic armamentarium. This study was conducted to determine the etiology, clinical profile, and outcomes of AFIs other than pneumonia and diarrhea in children admitted to a tertiary center in North India.

MATERIALS AND METHODS

Site. This was a prospective observational study carried out over a period of 1 year in the Pediatric Emergency Department (ED), Advanced Pediatrics Center, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh. The Advanced Pediatrics Center is a 300-bedded tertiary referral hospital with a stand-alone ED registering about 22,000 patient visits and 12,000 annual admissions. The unit caters to the population of major North Indian states, including Chandigarh, Punjab, Haryana, Himachal Pradesh, Uttar Pradesh, and Jammu.

Patients and clinical methods. All consecutive children aged 3 months to 12 years admitted to the ED with AFI in four selected months of 2014 representing different seasons (January: winter, May: summer, July: rainy season, September: post-monsoon) were screened for recruitment. Acute febrile illness was considered in a child when axillary temperature was $\geq 38^{\circ}\text{C}$ (100.4°F) at admission or recorded within 24 hours of admission with the onset of illness in the previous 7 days. We excluded children with isolated acute respiratory tract illness (includes bronchiolitis⁷ and pneumonia⁸ as per standard definitions) or acute watery diarrheal illness (World Health Organization [WHO] definition⁹). Children at risk for recurrent infections (immunodeficiency, malignancy, long-term indwelling devices, and steroid therapy) and those who

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underwent recent surgery or hospitalization were also excluded. Children found eligible were enrolled within 24 hours of hospital admission after obtaining written informed consent from parents.

Data collection. Admission information was recorded on a study-specific clinical record form which included domains such as demographics, brief medical history, and immunization status. Anthropometry, vital parameters, and systemic examination findings at admission were also documented. Enrolled children underwent laboratory investigations according to clinical indications considered appropriate by the treating teams as per standard practices followed in the unit. Essential investigations included complete hemogram, electrolytes, urinalysis, and renal and liver function tests. All children had a blood culture performed using BACTEC-instrumented blood culture systems (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD). Blood culture bottles were incubated aerobically for a period of 5 days before declaring sterile. Species identification of bacteria and fungi from culture media were performed by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry.¹⁰ Urine, stool, and body fluid (pus, pleural/ascetic fluid) cultures were performed wherever appropriate. Specific investigations ranged from point-of-care rapid diagnostic tests (RDTs) to serologies and polymerase chain reaction (PCR)-based assays on the basis of suspected etiologies.

Scrub typhus was diagnosed using IgM enzyme-linked immunosorbent assay (ELISA).¹¹ Peripheral smear was taken as the gold standard for malaria, and RDT card test (SD Bioline Kit; Standard Diagnostics, Kyonggi-do, Korea) was performed in all suspected cases for initial bedside diagnosis.¹² Non-structural protein 1 antigen positivity or suggestive IgM ELISA in laboratory were used to diagnose dengue fever.¹³ In culture-negative children with strong clinical suspicion of typhoid, a Widal test titer more than 1:160 or 4-fold rise in paired serum samples was considered suggestive.¹⁴

All suspected cases of acute CNS infections underwent a lumbar puncture unless contraindicated. Cerebrospinal fluid (CSF) examination included cytology; gram stain; culture; latex agglutination test for *Hemophilus influenza*, *Streptococcus pneumoniae*, and *Neisseria meningitidis* antigens; and IgM ELISA and DNA PCR for human alphaherpesvirus 1 and Japanese encephalitis virus. Other notable investigations included serologies for hepatotropic viruses and neuroimaging for CNS pathologies.¹⁵

Outcome variables, including requirement of pediatric intensive care unit care, positive pressure ventilation, occurrence of multi-organ dysfunction syndrome (defined as per diagnostic criteria of pediatric multi-organ dysfunction syndrome (MODS) based on 2002 International Pediatric Sepsis Consensus Conference) and length of hospital stay were recorded.¹⁶ Hospital outcomes, including discharge, death, or discontinuation of care was also noted. This study was approved by the Institute Ethics Committee, PGIMER, Chandigarh.

Statistical analysis. Baseline demographic features and descriptive clinical data were summarized using means and standard deviations (SDs) or medians with interquartile ranges for continuous variables and percentages for categorical variables. For normally distributed quantitative data, *t* test was applied for comparison of two groups and one-way analysis of variance when there were more than two groups. For skewed data or ordered categorical data, nonparametric Mann-Whitney *U* test and Kruskal-Wallis test were used. For categorical data, comparisons were made by Pearson's χ^2 test or Fisher's exact test as appropriate. Univariate analysis was performed to find predictors of common diagnoses. Factors

with *P* value < 0.05 were considered significant. Factors found to have association in univariate analysis were subjected to multivariable logistic regression. Adjusted odds ratio was calculated for factors which were significant after multivariate analysis. Analysis was performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY).

RESULTS

In the 4-month study period representing different seasons, 613 consecutive children with febrile illnesses admitted to the ED were assessed for eligibility; 396 were excluded because of various reasons (respiratory diseases [*N* = 175], diarrheal disease [*N* = 46], fever > 7 days [*N* = 102], underlying chronic conditions [*N* = 44], and pre-referral hospital stay > 48 hours [*N* = 26]). Cases of acute respiratory diseases were more frequent in winter (57 of 175, 32.5%), whereas diarrheal illnesses presented more commonly during the summer month (17 of 46, 37%).

A total of 217 children with non-respiratory and non-diarrheal AFIs were enrolled. Non-respiratory and non-diarrheal AFIs were most prevalent during post-monsoon month (September) (*N* = 91, 41.9%), the number being nearly double of what was enrolled in other seasons. Mean (SD) age of study population was 4.8 (3.4) years. Nearly half (45%) were in 5–12 years age group. Boys outnumbered girls with a ratio of 1.3:1. Baseline characteristics of the study population are

TABLE 1
Demographic characteristics, clinical symptoms, and examination findings of patients

Patient characteristics	<i>n</i> (%)
Age group	
3 months to 3 years	73 (33.6)
3–5 years	46 (21.2)
5–12 years	98 (45.2)
Gender	
Male	124 (57.1)
Female	93 (42.8)
Socioeconomic class (Modified Kuppusamy scale)	
Class 1	18 (8.3)
Class 2	115 (53)
Class 3	72 (33.2)
Class 4	12 (5)
Immunization status	
Complete	163 (75)
Incomplete	52 (24)
Not known	2 (0.9)
Anthropometry (WHO classification) ¹⁷	
Normal	160 (73.7)
Moderate under nutrition	38 (17.5)
Severe under nutrition	19 (8.8)
Presenting symptoms	
Altered sensorium	54 (24.9)
Seizures	66 (30.4)
Vomiting	33 (15.2)
Abdominal pain	28 (12.9)
Rash	22 (10.1)
Facial puffiness	13 (5.9)
Examination findings	
Pallor	93 (42.9)
Meningeal signs	36 (16.5)
Lymphadenopathy	17 (7.8)
Rash	29 (13.3)
Hepatomegaly	60 (27.9)
Hepatosplenomegaly	31 (14.4)
Splenomegaly	9 (4.2)

WHO = World Health Organization.

given in Table 1. Mean (SD) duration of fever was 4.9 (1.9) days. Seizures ($N = 66$, 30.4%) and altered sensorium ($N = 54$, 24.9%) were the most prevalent symptoms. Vomiting ($N = 33$, 15.2%), abdominal pain ($N = 28$, 12.9%), and rash ($N = 22$, 10.1%) were other common presenting features.

Of 217 subjects, diagnosis could be established with reasonable certainty in 187 (86.2%) children. Acute CNS infections were the most common group ($N = 54$, 24.8%). Microbiologically confirmed bacterial meningitis ($N = 3$) and viral encephalitis ($N = 10$) constituted about 25% of cases and in the rest, the diagnosis of CNS infection was based on CSF analysis and suggestive neuroimaging. Among other systemic infections, scrub typhus emerged as the single most common etiology diagnosed in 23 (10.5%) patients followed by malaria ($N = 14$, 6.4%), enteric fever ($N = 14$, 6.5%), and viral hepatitis ($N = 13$, 6.0%). Distribution of diagnoses in various age groups is shown in Table 2. On comparing etiological diagnosis in different age groups, scrub typhus was seen significantly more frequently in older children (5–12 years group).

The etiological organism could be identified by laboratory tests in 101 (46.5%) children; methods include blood culture ($N = 14$, 13.8%), serological tests ($N = 50$, 49.5%), peripheral smear ($N = 14$, 13.8%), CSF antigen/antibody detection ($N = 7$, 6.9%), pus culture ($N = 10$, 9.9%), and PCR-based assays ($N = 3$, 2.9%). Blood culture isolates were *Salmonella typhi* ($N = 6$), *Staphylococcus aureus* ($N = 5$), *Klebsiella pneumonia* ($N = 1$), *H. influenza* ($N = 1$), and *Pseudomonas aeruginosa* ($N = 1$).

Laboratory features in common diagnoses. Laboratory features of common diagnoses were as in Table 3. In patients with scrub typhus ($N = 23$), thrombocytopenia (platelet count $< 150 \times 10^3$) was a consistent feature observed in all children. Majority ($N = 18$, 78.2%) had elevated serum transaminases and more than half ($N = 13$, 56.5%) had highly elevated C-reactive protein (CRP) (> 100 mg/dL). Children with malaria also presented with thrombocytopenia ($N = 14$, 100%) and moderate to severe anemia ($N = 10$, 71.4%); mean (SD) hemoglobin was 9.0 (2.0) g/dL. Comparing with other AFI,

children with enteric fever had a lower mean (SD) total leukocyte count. Highly elevated transaminases were a feature of viral hepatitis. Children with meningitis and encephalitis had a higher median platelet count and mean serum albumin as compared with those with systemic infections (scrub typhus, malaria, etc.), and this feature could be useful in distinguishing them at the outset before etiological confirmation is available.

Logistic regression models were created for common diagnoses by univariate and multivariate analysis to find clinical or laboratory predictors (Tables 4 and 5). Facial puffiness, rash, lymphadenopathy, hepatomegaly and/or splenomegaly, thrombocytopenia, elevated transaminases, and hypoalbuminemia were found to have significant association with scrub typhus by univariate analysis. However, only hepatomegaly and/or splenomegaly was a significant independent predictor after multivariate analysis.

Hospital outcomes. The mean (SD) length of hospital stay in the cohort was 9.9 (8.2) days. Multi-organ dysfunction syndrome was noted in 76 (35%) children. Sixty children (27.6%) received positive pressure ventilation. Multi-organ dysfunction syndrome was more frequent in scrub typhus ($N = 16$, 69.5%) compared with other infections. Children with acute CNS infections had significantly longer mean (SD) hospital stay (14.2 [10.3] days). Of the 217 children enrolled, 188 (86.6%) survived to hospital discharge and 22 died with an in-hospital mortality rate of 10.1%. Mortality was highest in group of patients where the etiology was noninfectious or a definitive diagnosis was not established. Disease-specific hospital outcomes were as shown in Table 5.

DISCUSSION

We observed a seasonal trend in the incidence of non-respiratory non-diarrheal AFI with peak in post-monsoon season (91/215, 42%). Similar trend was noted in studies by Chrispal et al.¹⁸ and Ittyachen et al.¹⁹ in Indian adults. This

TABLE 2
Diagnoses in different age groups

Diagnosis	Total ($N = 217$)	3–35 months ($N = 73$)	3–5 years ($N = 46$)	5–12 years ($N = 98$)
1 Scrub typhus	23 (10.5%)	2 (2.7%)	8 (17.4%)	13 (13.2%)
2 Malaria	14 (6.4%)	3 (4.1%)	3 (6.5%)	8 (8.1%)
3 Enteric fever	14 (6.4%)	2 (2.7%)	3 (6.5%)	9 (9.2%)
4 Acute CNS infections	54 (24.8%)	21 (28.7%)	8 (17.4%)	25 (25.5%)
Etiology				
<i>Japanese encephalitis virus</i>	8	1	2	5
<i>Human alphaherpesvirus 1</i>	2	1	0	1
<i>Hemophilus influenza</i>	2	2	0	0
<i>Pseudomonas aeruginosa</i>	1	1	0	0
5 Staphylococcal sepsis	10 (4.6%)	7 (9.5%)	0	3 (3.1%)
6 Viral hepatitis	13 (6.0%)	1 (1.4%)	3 (6.6%)	9 (9.2%)
7 Leptospirosis	2 (0.9%)	0	1 (2.2%)	1 (1.0%)
8 Diphtheria	1 (0.5%)	0	0	1 (1.0%)
9 Infectious mononucleosis	1 (0.5%)	0	0	1 (1.0%)
10 Urinary tract infections	9 (4.1%)	7 (9.5%)	1 (2.2%)	1 (1.0%)
11 Skin and soft tissue infections	13 (6.0%)	7 (9.5%)	4 (8.9%)	2 (2.1%)
12 Deep-seated abscesses/ osteoearticular infections	10 (4.6%)	3 (4.1%)	1 (2.1%)	6 (6.1%)
13 Noninfectious causes*	9 (4.2%)	1 (1.4%)	2 (4.4%)	6 (6.1%)
14 Measles	4 (1.8%)	4 (5.4%)	0	0
14 Others†	10 (4.6%)	4 (5.4%)	2 (4.3%)	4 (4.0%)
15 No definitive diagnosis	30 (13.8%)	11 (15.0%)	10 (21.7%)	9 (9.2%)

* Noninfectious causes included Reyes syndrome ($N = 3$), acute leukemia ($N = 2$), Henoch–Schönlein purpura ($N = 2$), hemolytic uremic syndrome ($N = 1$), and acute disseminated encephalomyelitis ($N = 1$).

† Others included upper respiratory infection with atypical febrile seizures ($N = 7$) and neurocysticercosis ($N = 3$).

TABLE 3
Laboratory features in common five diagnoses

Laboratory parameters*	Scrub typhus (N = 23)	Malaria (N = 14)	Enteric fever (N = 14)	Viral hepatitis (N = 13)	Acute CNS infections (N = 54)
Hb (g/dL)	9.4 (1.5)	9.0 (2.0)	9.8 (1.4)	10.2 (1.9)	10.2 (1.9)
Platelets (/μL)	35,000 (14,000–58,000)	42,500 (22,500–75,000)	150,000 (63,000–183,000)	200,500 (89,500–263,000)	236,000 (149,000–350,500)
TLC (/μL)	11,200 (8,700–18,150)	8,100 (5,500–11,875)	6,800 (5,000–9,350)	8,000 (6,500–16,400)	13,500 (9,850–16,250)
Albumin (g/dL)	2.4 (0.5)	3.0 (0.5)	2.8 (0.5)	2.9 (0.6)	3.2 (0.7)
AST (U/L)	171 (95–267)	40 (34–75)	69 (54–135)	1,134 (300–1,670)	47 (36–62)
ALT (U/L)	98 (68–39)	40 (26–59)	65 (45–101)	1,315 (724–2,148)	38 (31–56)
CRP (mg/L)	112 (66–206)	52 (35–98)	112 (38–139)	4 (2–27)	34 (6–75)

ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRP = C reactive protein; TLC = total leukocyte count.

* Values are expressed either as mean (standard deviation) or median (interquartile range).

post-monsoon surge is attributed to the influence of rainfall on the breeding of vectors and transport and dissemination of infectious agents. This fact points to the need for implementation of preventive steps, public education, and physician awareness during this season. Diagnosis was microbiologically proven in 46.5% (101/217) of patients. This was comparable with the study carried out by Chheng et al. in children from Cambodia where a microbiological confirmation could be established in 50% of AFIs. Noninfectious causes of fever were identified only in nine patients (4.1%), which emphasizes the predominance of infectious illnesses among children with acute fever in developing economies. Blood culture is an essential investigation for any febrile child that offers definitive diagnosis although the yield has been poor in many studies. The low yield (6.5%) seen in this study is comparable with what was reported by Chheng et al.¹ from Cambodia (6.3%) and higher than the report by Mahende et al.² in Tanzanian children (3.2%). Prior antibiotic exposure in many children of our cohort could have contributed to the low blood culture yield seen in study. Another cause of lower sensitivity would be the predominance of infections

such as malaria, scrub typhus, and viral encephalitis where organisms are not usually isolated with routine culture methods.

Proportion of etiologies of AFIs differ between studies in children and adults from different parts of the world.^{18–24} This is due to the variation in epidemiology of different infectious diseases with respect to geographical factors and age groups. There has been a concern regarding recent epidemiological shift in many infections with increasing prevalence noted in younger age groups.^{25,26} To identify this trend, we grouped our cohort into three age groups. We observed that the four common infectious diseases— scrub typhus, malaria, enteric fever, and viral hepatitis together contributed to nearly 40% of AFIs in older age group and 10% of febrile illnesses in 3–35 months age group. High incidence of tropical infections in older age group might be because of the increased outdoor activities and environmental exposure to vectors and pathogens in them.

Acute CNS infections were the leading etiological group, although we could identify the etiological organism only in a fourth of all patients. Exposure to antibiotics before lumbar

TABLE 4
Logistic regression model for scrub typhus

Variable	Scrub typhus (N = 23)	Other AFI (N = 194)	Univariate analysis	Multivariate analysis	
			P value	Adjusted OR	95% CI
Months			< 0.001	–	–
January	0	29 (15%)			
May	0	48 (25%)			
July	3 (13%)	46 (24%)			
September	20 (87%)	71 (36%)			
Age group			0.02		
3–35 months	2 (8.7%)	71 (36.6%)			
3–5 years	8 (34.8%)	38 (19.6%)			
5–12 years	13 (56.5%)	85 (43.8%)			
Facial puffiness	10 (43.5%)	3 (1.5%)	< 0.001		
Lymphadenopathy	11 (61%)	8 (5%)	< 0.001		
Skin rash	13 (56.5%)	15 (8.2)	< 0.001		
AST			< 0.001		
< 40 U/L	0	73 (37.4%)			
41–120 U/L	8 (33.3%)	82 (42.6%)			
21–1,000 U/L	15 (66.7%)	29 (14.8%)			
> 1,000 U/L	0	10 (5.2%)			
ALT			< 0.001		
< 40 U/L	0	95 (49%)			
41–120 U/L	15 (66.7%)	67 (34.5%)			
121–1,000 U/L	8 (33.3%)	18 (9.5%)			
> 1,000 U/L	0	13 (13.6%)			
Hepatomegaly and/or splenomegaly	23 (100%)	77 (39.9%)	< 0.001	8.9	1.0–81.4
Thrombocytopenia	23 (100%)	66 (34.2%)	< 0.001	–	–
MODS	16 (69.6%)	60 (31%)	< 0.001		
Hypoalbuminemia	16 (69.6%)	54 (27.8%)	< 0.001		

AFI = acute febrile illnesses; ALT = alanine aminotransferase; AST = aspartate aminotransferase; CI = confidence interval; MODS = multi-organ dysfunction syndrome; OR = odds ratio.

TABLE 5
Hospital outcomes in common diagnoses

Hospital outcome	CNS infections (N = 54)	Scrub typhus (N = 23)	Malaria (N = 14)	Enteric fever (N = 14)	Noninfectious diseases (N = 9)	No definitive diagnosis (N = 30)
Length of hospital stay (days)	14.2 (10.3)	7.7 (2.9)	6.8 (4.7)	6.1 (2.0)	12.3 (6.9)	8.6 (9.8)
Need for PICU care	27 (50.0%)	11 (47.8%)	4 (28.5%)	0	4 (44.4%)	11 (36.6%)
MODS	20 (37.0%)	16 (69.5%)	4 (28.5%)	2 (14.2%)	5 (55.5%)	18 (60.0%)
Positive pressure ventilation	26 (48.1%)	6 (26.0%)	2 (14.2%)	0	5 (55.5%)	15 (50%)
Mortality	7 (12.9%)	2 (8.6%)	0	0	3 (33.3%)	9 (30.0%)

MODS = multi-organ dysfunction syndrome; PICU = pediatric intensive care unit. Values are expressed as mean (standard deviation) or numbers (%).

puncture and lack of laboratory support to identify all possible viral etiologies were important reasons for the low yield.

Scrub typhus was the single most common infection seen in our cohort. Except for three patients, all other scrub typhus cases presented in post-rainy season. This clustering of cases in monsoon months have been observed in different studies in Indian children.^{27,28} Patients presented from four different states and the distribution was equal among hills and plains. These data are in concordance with the recent observations that suggest the endemicity of scrub typhus in northern India.²⁹ In comparison with other AFIs, children with scrub typhus had significantly lower platelets and albumin levels and elevated transaminases and CRP levels. Adding empirical doxycycline at the outset to children presenting with fever and multisystem involvement during post-rainy months can be lifesaving.

Children with malaria presented in all seasons with a definite peak in post-monsoon month, which is similar to the observation by Verma et al.³⁰ in their study in Indian children. Rapid diagnostic test by SD Bioline kit was positive in all smear-positive malaria cases, and this goes with the WHO recommendation of using RDTs in resource-limited settings for diagnosis and initiation of treatment.³¹ Cases of enteric fever were distributed uniformly among all seasons. Majority of the cases belonged to 5- to 12-year age group, which was similar to the report by Walia et al. and Ganesh et al.

It is also interesting to note that definitive diagnosis could not be established in 30 (13.8%) cases and this group had high case fatality rate, which shows the importance of striving to reach a diagnosis which will help in targeted therapy to improve outcomes.

To our surprise, no case of dengue fever was diagnosed during our study period despite North India being endemic for dengue.³² The cyclic epidemic pattern known with dengue virus infection might be the reason for the absence of cases in the months of our enrolment. This highlights the importance of longitudinal data collection and periodically repeating it in the same area to understand the changing trends of etiology of AFI.

Our study is the first in Indian children conducted to identify non-respiratory non-diarrheal etiology of AFIs. Reasonable sample size and enrolment of patients from four different seasons were important strengths. However, restriction of patient enrolment to 4 months in a year and nonavailability of investigations to diagnose viral etiologies in CNS infections could have limited the robustness of our data. A multicenter study carried out over a longer period with additional diagnostic methods can give further information reflecting the national trends.

CONCLUSIONS

Acute febrile illnesses other than pneumonia and diarrhea are a significant burden and follow a seasonal trend. Scrub typhus is an emerging hitherto under-recognized etiology of childhood AFIs. Regional epidemiological database of AFIs needs to be generated and updated periodically to understand the changing pattern of infectious diseases.

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