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Distribution of Eschar in Pediatric Scrub Typhus

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ABSTRACT

Background: Identifying an eschar in scrub typhus is useful for initiation of prompt and appropriate antibiotic therapy.

Methods: The distribution of eschars in all children <15 years of age admitted with confirmed scrub typhus over a 5 year period is described.

Results: Of 431 children admitted with scrub typhus, eschars were present in 176 (40.8%) children with the following distribution: head, face and neck, 33 (19.1%); axillae, 37 (21%); chest and abdomen, 21 (11.9%); genitalia, inguinal region and buttocks, 58 (33%); back, 8 (4.5%); upper extremities, 13 (7.4%); and lower extremities, 5 (2.8%). The commonest sites of eschars were scrotum (27 of 106; 25.5%) and axillae (15 of 106; 14.2%) in males and axillae (22 of 70; 31.4%) and groin (16 of 70; 22.9%) in females. Eschars were seen within skin folds in 100 of 176 (56.8%) children.

Conclusion: Children should be carefully examined for the presence of eschar especially in the skin folds of the genitalia, axillae and groin to make an early diagnosis of scrub typhus.

KEYWORDS: scrub typhus, eschar, pediatric.

INTRODUCTION

An estimated 1 billion people are at risk of scrub typhus and about 1 million cases are estimated to occur annually [1]. Scrub typhus is endemic in the so-called tsutsugamushi triangle. Scrub typhus is becoming wide spread in India [2–4] with distinct seasonality [5–7]. Patients usually present with non-specific symptoms, and an eschar (20–87%) is identified in some patients. The non-specificity of presentation, the low index of suspicion and the poor availability of diagnostic tests lead to delayed diagnosis and significant morbidity and mortality [1, 8]. Effective treatment is documented [9].

Scrub typhus is caused by *Orientia tsutsugamushi* and is transmitted by the chigger of the trombiculid mite (genus *Leptotrombidium*). The mites are small (0.2–0.4 mm size) and have a four-stage lifecycle: egg, larva, nymph (chigger) and adult. Only the bite of an infected chigger transmits disease. The other stages are free living in the soil. The mites act as the primary reservoirs for *O. tsutsugamushi*. Once infected by feeding on the body fluid of mammals, they maintain the infection throughout their life stages by transovarial transmission and transstadial transmission. Chigger mite populations can autonomously maintain their infectivity over long periods [10]. The chigger bite leaves a characteristic black eschar that is useful for diagnosis, when found. The eschars are painless and are often undetected by the patients. The eschar is sometimes similar to a scab that is formed after trauma and may be small, making its detection difficult [11]. The eschar is also the site

where *O. tsutsugamushi* is inoculated by the chigger bite. There is a proliferation of *O. tsutsugamushi* in the eschar site that can be detected by polymerase chain reaction or culture making an early definite diagnosis possible [12].

Finding an eschar provides early diagnosis and opportunity for early initiation of treatment for scrub typhus. Studies describing the distribution of eschars have been published in adults. However, to the best of our knowledge, there is no pediatric data on the distribution of eschars. Hence, we would like to present our data on the distribution of eschars in children <15 years with confirmed scrub typhus.

METHODS

We retrospectively reviewed the records after institutional review board approval of all children who were admitted with a diagnosis of scrub typhus from January 2010 to December 2014 in the Pediatric department at the Christian Medical College, Vellore, India. Diagnosis was based on the detection of IgM in serum to *O. tsutsugamushi*-derived recombinant antigen performed using the InBios Scrub Typhus Detect ^{TM} IgM ELISA kit or a positive Weil Felix test with an OX K titer >80 [4]. Odds ratios and tests of significance were obtained for those with and without an eschar for various demographic characteristics (age and sex); clinical characteristics (fever, headache, vomiting, rash, abdominal pain, loose stool, cough, breathing difficulty, bleeding, palpable liver and palpable spleen); anthropometry classified as stunted (height for age <2 SD), wasted (weight for age <2 SD), obese/overweight (body mass index >1 SD for age) and thinness/severe thinness (body mass index <1 SD for age); investigations (hemoglobin, total white cell count, platelet count, alanine aminotransferase); complications such as acute respiratory distress syndrome (ARDS; diffuse lung infiltrates on chest radiograph with hypoxia) and meningitis (cerebrospinal fluid pleocytosis with >5 leukocytes); mortality and duration of hospitalization.

RESULTS

There were 431 children admitted with scrub typhus during the study period with 237 males (55%) and 194 females (45%). The average age was 6.6 years (range: 0.17–15 years). Diagnosis of scrub typhus was made on 120 (27.8%) children based on a positive scrub typhus IgM ELISA and the rest on a Weil Felix test OX K >80. An eschar was present in 176 (40.8%) children with 106 males (44.7% of all males with scrub typhus) and 70 females (36.1% of all females with scrub typhus). The eschars were distributed as shown in the figures among males (Fig. 1) and females (Fig. 2). The commonest sites of eschars were scrotum (27 of 106; 25.5%) and axillae (15 of 106; 14.2%) in males and axillae (22 of 70; 31.4%) and groin (16 of 70; 22.9%) in females. Eschars were seen within skin folds behind the ears, axillae, groin and scrotum in 100 of 176 (56.8%) children. The groin, genitalia and buttock regions had 58 of 176 (33%) eschars. The age distribution of the eschars was 96 (54.5%), 56 (31.9%) and 24 (13.6%) in the <5, 6–10 and 11–15 years' age categories. The eschars were distributed in the head and neck in 25.3%, 14.3% and 4.2%; axilla and groin in 47.4%, 55.4% and 70.8%; trunk in 24.2%, 23.2% and 20.8% and limbs in 3.1%, 7.1% and 4.2% in the <5, 6–10 and 11–15 years' age categories. The distribution of eschars was more often in the head and neck in children aged <5 years compared with children in the 11–15 years' age group [OR: 7.7 (0.99–60.69); $p = 0.051$] and in the 6–10 years' age group [OR: 2.03 (0.841–4.89); $p = 0.115$].

Comparison was made between those with and without eschar with regards to their demographic, clinical and outcome measures (Table 1). The median age of those with an eschar was 5 years compared with a median age of 7 years in those without an eschar [OR: 0.90 (0.85–0.94); $p < 0.001$]. With regards to clinical symptoms, breathing difficulty [OR: 2.92 (1.76–4.86); $p < 0.001$] and hepatomegaly [2.26 (1.24–4.13); $p = 0.007$] were more common in those with an eschar, whereas headache [0.48 (0.26–0.88); $p = 0.016$] and vomiting [OR: 0.54 (0.35–0.81); $p = 0.003$] were less common in those with an eschar. Those with an eschar were also less wasted [OR: 0.50 (0.32–0.79); $p = 0.003$]. ARDS was more common in those with an eschar [OR: 2.92 (1.69–5.05); $p < 0.001$], whereas meningitis was less common in those with an eschar [OR: 0.34 (0.18–0.63); $p < 0.001$]. There was no difference in mortality between the two groups.

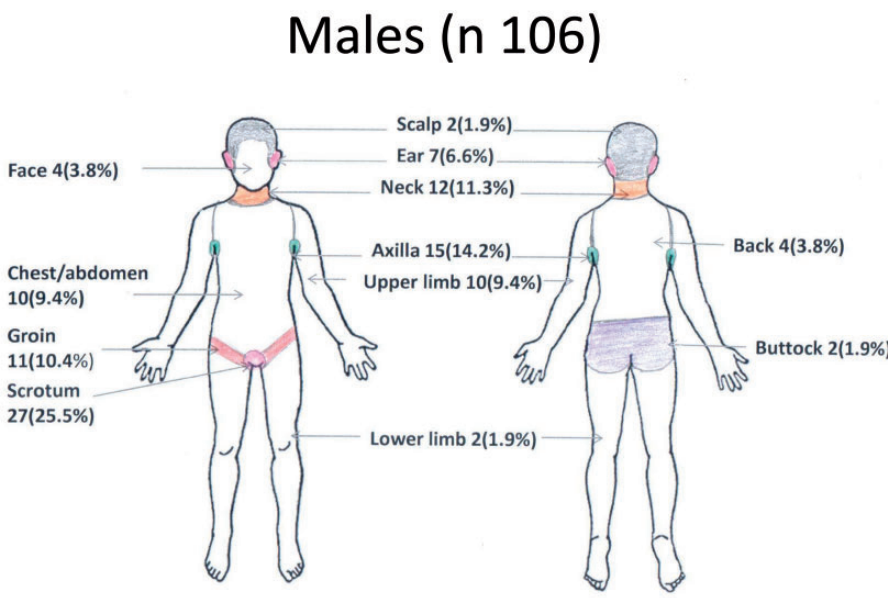

Fig. 1. Distribution of eschar in males.

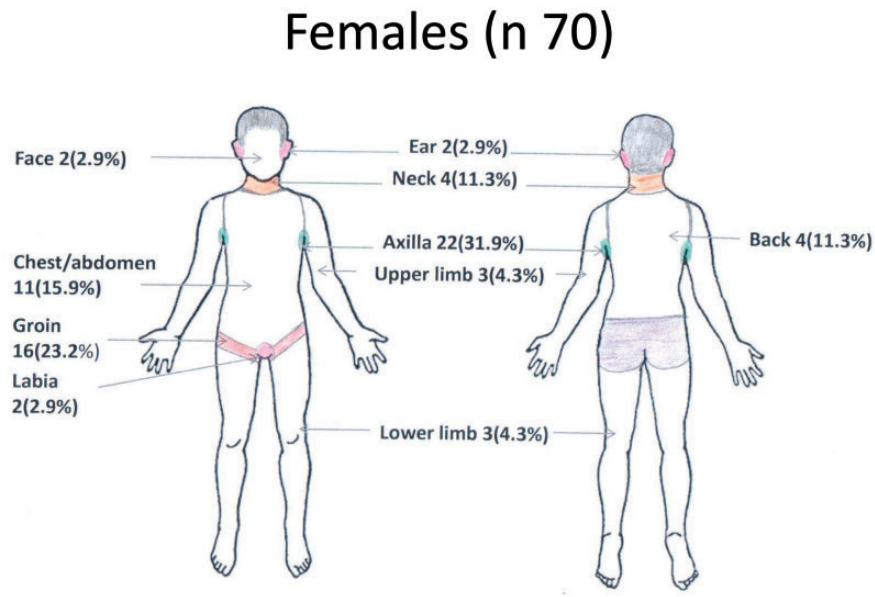

Fig. 2. Distribution of eschar in females.

DISCUSSION

This is the first study that describes the distribution of eschars in pediatric scrub typhus. In our study, 40.8% of our patients with scrub typhus had an eschar enabling early diagnosis and initiation of appropriate therapy in two-fifths of the patients. The distribution of eschar in our study is within skin folds in 56.8% of children and in the groin, genitalia and buttocks in 33% of patients. Being painless and patients being unaware, if children are not examined carefully within skin folds and beneath their

Table 1. Comparison of demographic, clinical and outcome measures in those with or without eschar in children diagnosed with scrub typhus

Demographic, clinical and outcome parameters	Eschar ($n = 176$)	No eschar ($n = 255$)	p	OR (95% CI)
Age in years: Median (IQR)	5 (6)	7 (6)	<0.001[a]	0.90 (0.85–0.94)
Male: *n* (%)	106 (60.2)	131 (51.4)	0.069[b]	1.44 (0.97–2.12)
Duration of fever in days: Median (IQR)	9 (3)	10 (3)	0.730[a]	0.97 (0.93–1.02)
Headache: *n* (%)	16 (9.1)	44 (17.3)	0.016[b]	0.48 (0.26–0.88)
Vomiting: *n* (%)	48 (27.3)	105 (41.2)	0.003[b]	0.54 (0.35–0.81)
Rash: *n* (%)	12 (6.8)	20 (7.8)	0.690[b]	0.86 (0.41–1.81)
Abdominal pain: *n* (%)	36 (20.5)	54 (21.2)	0.856[b]	0.96 (0.60–1.54)
Loose stool: *n* (%)	8 (4.6)	10 (3.9)	0.750[b]	1.17 (0.45–3.02)
Cough: *n* (%)	39 (22.2)	50 (19.6)	0.520[b]	1.17 (0.73–1.87)
Difficult breathing: *n* (%)	48 (27.3)	29 (11.4)	<0.001[b]	2.92 (1.76–4.86)
Bleeding: *n* (%)	1 (0.6)	1 (0.4)	1.000[c]	1.45 (0.09–23.36)
Liver palpable: *n* (%)	160 (90.9)	208 (81.6)	0.007[b]	2.26 (1.24–4.13)
Spleen palpable: *n* (%)	88 (50)	113 (44.3)	0.245[b]	1.26 (0.85–1.85)
Stunted: *n* (%)	40 (26.7)	74 (32.7)	0.209[b]	0.75 (0.47–1.18)
Wasted: *n* (%)	44 (30.6)	87 (46.8)	0.003	0.50 (0.32–0.79)
BMI: *n* (%)				
Obese/overweight	12 (8)	13 (5.6)	0.048[b]	1.16 (0.51–2.63)
Normal	102 (68)	132 (58.4)		1[d]
Thinness/severe thinness	36 (24)	81 (35.8)		0.56 (0.35–0.88)
Hb%: Mean (SD)	9.4 (1.6)	9.5 (1.8)	0.440[e]	0.96 (0.86–1.07)
WBC TC: Median (IQR)	10 250 (7900)	9700 (6700)	0.263[a]	1.02 (0.99–1.06)[f]
Platelet: Median (IQR)	34 500 (69500)	65 000 (12500)	<0.001	0.94 (0.91–0.97)[g]
ALT: Median (IQR)	55 (59.5)	57 (65)	0.732[a]	0.999 (0.998–1.000)
Meningitis (%)	14 (7.9)	52 (20.4)	<0.001[b]	0.34 (0.18–0.63)
ARDS: *n* (%)	41 (23.3)	24 (9.4)	<0.001[b]	2.92 (1.69–5.05)
Child died: *n* (%)	8 (4.6)	5 (2)	0.123[b]	2.38 (0.77–7.40)
Duration of hospitalization in days: Median (IQR)	4 (4)	5 (3)	0.612[a]	1.00 (0.94–1.06)

Notes. BMI = body mass index; Hb = hemoglobin; WBC TC = white blood cell total count; ALT = alanine aminotransferase; ARDS = acute respiratory distress syndrome; IQR = interquartile range.
[a]Mann Whitney U-test.
[b]Chi square test.
[c]Fisher's exact test.
[d]Reference category.
[e]Student *t*-test
[f]OR per 1000 WBCs.
[g]OR per 10 000 platelets.

undergarments, a large proportion of eschars will get missed.

In our study, a bigger proportion of males (44.7%) had eschars compared with females (36.1%). This is in contrast to the data on adults where there was female preponderance [11, 13]. It is possible that because of the retrospective nature of our data, the detail to physical examination may have been differential between male and female children contributing to this gender difference in the eschar distribution. As shown

Table 2. Comparison of distribution of eschars in children and adults with scrub typhus

Distribution of eschars	Our study (age < 15 years) $N = 176$	Kundavaram *et al.* [13] (age 45 ± 14 years) $N = 426$	Dong-Min Kim *et al.* [11] (age >18 years) $N = 160$
Head, face and neck	33 (19.1%)	4.2%	5%
Axillae	37 (21%)	13.6%	34.4%
Chest/abdomen	21 (11.9%)	32.5%	
Genitalia, inguinal region and buttocks	58 (33%)	30.4%	28.1%
Back	8 (4.5%)	4.2%	11.3%
Upper extremities	13 (7.4%)	4.2%	9.4%
Lower extremities	5 (2.8%)	10.2%	12.5%

in Table 2, children seem to have a bigger proportion of eschars in the head, face and neck as compared with adults. In our study, higher proportion of younger children have eschars in the head, face and neck compared with the older children. Adults have more eschars in the lower limbs compared with children. Distribution in other parts of the body seem similar in adults and children [11, 13].

In our study, there was strong evidence of association between the presence of an eschar and breathing difficulty, ARDS and thrombocytopenia, whereas absence of eschar was associated with meningitis. In contrast to our results, Kim *et al.* [14] found significant association between severe scrub typhus and the absence of an eschar. Their criteria for severe scrub typhus included breathing difficulty, parenchymal lung lesions and meningitis and their mean age was 68.56 years. Zhang *et al.* [15] in their study where their mean age of cases was 57.33 years and controls 53.35 years, did not find any association between severe scrub typhus and the presence or absence of an eschar. We could not find a similar comparison in the pediatric age group.

The major limitation of our study is that our data are retrospective. Despite that, eschars were found in 40.8% of the patients. The retrospective nature is likely to have underestimated the presence of an eschar. The distribution described, still provides clinical value for physicians to know where to look for eschars. Another limitation is that our diagnosis is based on Weil Felix test OX K > 80 in >70% of the patients, which may not be considered as a good diagnostic test. The cutoff of OX K > 80 provides 30% sensitivity but 100% specificity and positive predictive value [5]. Hence, we believe the diagnosis of scrub typhus is true with the Weil Felix test with a cutoff of OX K > 80.

In conclusion, our study emphasizes the need for clinicians to make a complete skin examination including skin creases and beneath undergarments while looking for an eschar. Finding an eschar will enable early diagnosis of scrub typhus and institute appropriate antimicrobial therapy when children present with acute febrile illness.

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