

Estimation of Serum Albumin Level and its Prognostic Significance in Scrub Typhus Patients in Districts of Lower Assam

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Abstract: *Background & Objectives:* Scrub Typhus, a zoonotic disease caused by a bacteria called *Orientia tsutsugamushi* is a reemerging disease and so this study aims to estimate the serum Albumin Levels in Scrub typhus patients and to determine its prognostic significance in scrub typhus patients in terms of complications, duration of hospital stay, ICU admission, recovery or death. *Method:* A hospital based observational, prospective study with a total no of 175 patients with Scrub typhus diagnosed as IgM positive were included in the study. Patients were divided in to three groups based on serum albumin level; Group I - normal albumin (>3.5mg/dl), Group 2 - mild hypoalbuminemia (2.5 - 3.5mg/dl) and Group 3 - marked hypoalbuminemia (<2.5mg/dl). Patients were monitored daily for complications and outcome during hospital stay and observations of group 3 were compared with group 1 and 2. *Results & Conclusions:* 175 patients were included of which, 21 were categorized in group 1, 98 in 2, and 56 in 3 based on serum albumin level. Patients in group 3 had significantly higher incidence of Pleural effusion, Pneumonia, AKI, ARDS, and Meningoencephalitis compared to that of group 2 and 1. ICU admission was significantly high in group 3. Duration of hospital stay and mortality was significantly longer and higher in group 3 comparatively but not statistically significant. Patients with marked hypoalbuminemia in scrub typhus had higher incidence of complications, ICU admission and longer hospital stay as compared to normal albumin and considered to be a prognostic indicator of scrub typhus.

Keywords: Eschar, *Orientia tsutsugamushi*, hypoalbuminaemia, Acute kidney injury, Vasculitis

1. Introduction

Scrub Typhus, is a zoonotic disease caused by a bacteria called *Orientia tsutsugamushi* considered as reemerging public health problems.¹ Hypoalbuminemia is known to be associated with complications and mortality in patients with acute infectious diseases. Despite the common occurrence of hypoalbuminaemia in patients with scrub typhus, there has been limited information about the relationship between the hypoalbuminemia and severity of disease². Therefore, this study was planned to investigate the significance of serum albumin as a prognostic marker of scrub typhus in this region of Assam. Of the 29 states in India, 23 have reported the presence of scrub typhus. The clinical presentation of scrub typhus ranges from subclinical disease to multiorgan failure and death. The disease usually presents with fever, diffuse lymphadenopathy, myalgia, rash, jaundice, thrombocytopenia, capillary leak syndrome, hepatomegaly, and splenomegaly.³ The pathognomonic feature of scrub typhus is the necrotic eschar at the bite site. The disease can progress to severe complications like acute respiratory distress syndrome (ARDS), hepatitis, acute kidney injury, myocarditis leading to heart failure, and meningoencephalitis in different proportions of the patients.²

2. Materials and Method

This study was conducted at tertiary care hospital at

BARPETA in North east Assam during February 2022 to January 2023 after taking clearance from institutional ethical committee. This is a hospital based prospective study including patients with Scrub typhus infection aged 12 years and above. A total no of 182 patients admitted in Fakhruddin Ali Ahmed Medical College, Barpeta with Scrub typhus diagnosed as IgM positive cases using ELISA technique and 175 were included in the study, who has fulfilled the inclusion criteria. Patients were diagnosed for Scrub typhus by ELISA IgM positive (optical density ≥ 0.5), using ELISA kit manufactured by In Bios International Inc, USA.⁴ After taking written consent, patient data including detailed history, baseline characteristics, clinical findings, hospital management, and outcomes were recorded in a pretested proforma meeting the objectives of the study. All patients underwent thorough systemic examination and laboratory investigations like CBC, LFT, RFT, X - ray chest PA View and USG abdomen.

Patients with scrub typhus were divided into three groups based on serum albumin level, Group I/Normal albumin (Serum Albumin level >3.5gm/dl), Group II/Mild hypoalbuminemia (Serum Albumin level 2.5 - 3.5gm/dl) and Group III/Marked hypoalbuminemia (Serum Albumin level < 2.5gm/dl). Serum albumin level was measured on the day of admission.⁵

Hypoalbuminemia, defined as a first serum albumin level <

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3.5 gm/dl. Acute renal failure was defined as at least 50% reduction in glomerular filtration rate (GFR) using the abbreviated modified diet in renal disease (MDRD) equation, $GFR (ml/min/1.73m^2) = 186 Pcr - 1.154 \times age - 0.203 \times (1.212 \text{ if black}) \times (0.742 \text{ if female})^6$

Acute kidney injury is defined as a rise from baseline of at least 0.3 mg/dl within 48 h or at least 50% higher than baseline within 1 week, or a reduction in urine output to <0.5ml/kg per h for longer than 6 h.⁷

3. Results

A total of 175 patients were included of which, 56 patients (32%) were males and 119 were females (68%) with age group between 14 years to 65years. 21 (12%) patients were categorized in group 1, 98 (56%) patients in group 2, and 56 (32%) in group 3 based on serum albumin level. Patients in group 3 had significantly higher incidence of Pleural effusion (84.6%, p=.031), Pneumonia (81.70%, p=.038), Acute kidney injury (76.90%, p=.044, ARDS (72.60%; p=.017), and Meningoencephalitis (61.50% p=.039) compared to that of group 2 and group 1. ICU admission was significantly high with total number of 46 patients (82.30%, p =0.035) in group 3 compared to that of group 2 (8.30%) and no ICU admission in group 1. Duration of hospital stay was significantly longer with average 8 days (p =0.043) in group 3 patients. Mortality rate was comparatively high in group 3 with 4 death (7.7%; p=0.332) as compared to group 2 and group 1 but not statistically significant.

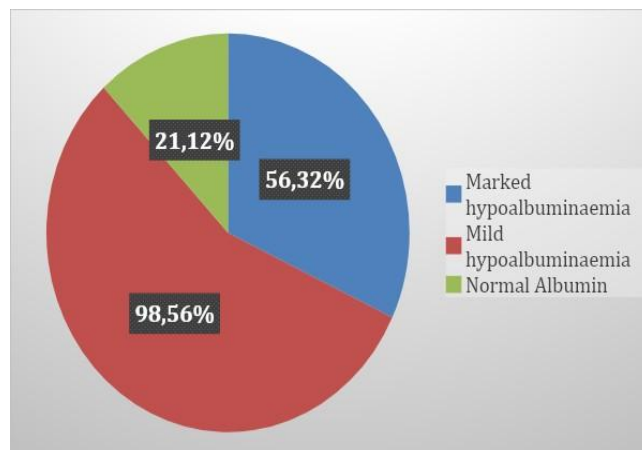


Figure 1: Distribution of patients according to serum albumin levels

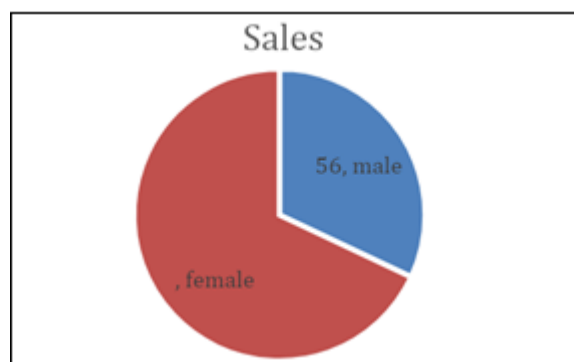


Figure 2: Distribution of patients based on gender

Table 1: Distribution of patients according to serum albumin levels

Groups	Number	%
Marked hypoalbuminaemia	56	32%
Mild hypoalbuminaemia	98	56%
Normal Albumin	21	12%
Grand Total	175	100%

Table 2: Distribution of study participants based on gender and serum albumin level

		Marked hypoalbuminaemia		Mild hypoalbuminaemia		Normal Albumin		p - value
		Number	%	Number	%	Number	%	
Gender	Fema Le	34	61.50%	68	69.60%	17	80.00%	0.786
	MALE	22	38.50%	30	30.40%	4	20.00%	

Table 3: Distribution of study participants according to presence of signs and symptoms with serum albumin level

	Marked hypoalbuminaemia		Mild hypoalbuminaemia		Normal Albumin		p - value
	Count	Column N %	Count	Column N %	Count	Column N %	
FEVER	56	100.00%	98	100.00%	21	100.00%	0.003
PAIN ABDOMEN	30	53.80%	43	43.50%	8	40.00%	0.789
VOMITING	17	30.80%	26	26.10%	8	40.00%	0.817
RESPIRATORY DISTRESS	26	46.20%	34	34.80%	8	40.00%	0.797
ALTERED SENSORIUM	13	23.10%	13	13.00%	4	20.00%	0.732
ESCHAR	4	7.70%	17	17.40%	4	20.00%	0.685
	30	53.80%	47	47.80%	4	20.00%	
COMORBIDITIES		7.50%		5.40%		2.50%	0.008
DIARRHEA							0.02

Table 5: Distribution Of patients based on complications with serum albumin level

		Marked hypoalbuminaemia		Mild hypoalbuminaemia		Normal Albumin		p - value
		Count	Column N %	Count	Column N %	Count	Column N %	
AKI	Yes	34	76.90%	23	23.50%	4	20.00%	0.044
PE	Yes	47	84.60%	26	26.10%	5	22.00%	0.031
ARDS	Yes	41	72.60%	1	1.00%	0	0.00%	0.017
PNEUMONIA	Yes	46	81.70%	21	21.70%	0	0.00%	0.038
PANCREARTITIS	Yes	7	11.70%	4	4.30%	0	0.00%	0.028
MEINGOENCEPHALITIS	Yes	43	61.50%	13	13.00%	0	0.00%	0.039

Distributions based on duration of hospital stay and serum albumin level

Duration	Marked hypoalbuminaemia		Mild hypoalbuminaemia		Normal serum albumin		P - Value
	N	%	N	%	N	%	
1 - 3 days	7	12.50%	13	13.20%	11	52.30%	0.0001
4 - 7 days	18	32.10%	60	61.20%	7	33.30%	0.0001
>7days	31	55.30%	25	25.50%	3	14.20%	0.0001

Distribution based on ICU admission, discharge and death

		Marked hypoalbuminaemia		Mild hypoalbuminaemia		Normal Albumin		p - value
		Count	Column N %	Count	Column N %	Count	Column N %	
ICUAD M	Yes	46	82.30%	8	8.30%	0	0.00%	0.035
DISCHARGE	Yes	52	92.30%	98	100.00%	21	100.00%	0.332
DEATH	Yes	4	7.70%	0	0.00%	0	0.00%	0.332

4. Discussion

The mechanism of hypoalbuminemia in acute infectious diseases is known to be due to poor oral intake of protein, decreased synthesis of protein from the liver, increased catabolism of proteins and increased metabolism of albumin due to the vascular leakage of serum proteins due to increased vascular permeability.⁸ Pathologic finding in scrub typhus is a focal & disseminated vasculitis due to macrophage activation and the secretion of cytokines leads to destruction of endothelial cell lining of the small vessels which is manifested as perivascular infiltrations of leukocytes.⁹ Pathology of scrub typhus due to affinity of agent to endothelial cells of small blood vessels evoke vascular inflammation which leads to microthrombi and hemorrhage in lymph nodes and spleen. Vasculitis & perivascularitis in scrub typhus may involve multiple organ systems like lung, brain, kidney, gastrointestinal tract, liver, spleen and lymph node.¹⁰

The pulmonary manifestations of scrub typhus vary from mild atypical pneumonia to very serious adult respiratory distress syndrome include varying degrees of bronchitis and interstitial pneumonitis.¹¹ Interstitial pneumonitis frequently occurs in patients with scrub typhus and such patients had higher incidences of hypoxia, hypotension, severe thrombocytopenia and hypoalbuminemia.¹² Interstitial pneumonitis in scrub typhus is closely associated with severity in scrub typhus. Scrub typhus patients with abnormal CXR findings had a higher rate of serious complications including pneumonitis, septic shock, acute respiratory distress syndrome, meningitis/meningoencephalitis, CHF, severe jaundice, acute renal failure, acute pancreatitis and peptic ulcer compared with patients with negative CXR results.¹³

The renal pathology usually shows characteristic acute diffuse glomerulonephritis, focal interstitial lesions, cloudy swelling of the tubular epithelium and occasional evidence of severe vascular damage.¹⁴ Acute renal failure in patients

with scrub typhus is caused by acute tubular necrosis due to the direct invasion of *Orientia tsutsugamushi*, which is confirmed by renal biopsy with Immunohistochemistry staining and electron microscopy.¹⁵

Gastrointestinal symptoms and signs of scrub typhus were vomiting, diarrhea, jaundice and abdominal pain frequently reported.¹⁶ Scrub typhus induced hepatitis causes mild portal inflammation and intra hepatic sinusoidal endothelial vasculitis which leads to increased serum AST and ALT.¹⁷

CNS involvement is another complication of scrub typhus. It ranges from aseptic meningitis to frank meningoencephalitis.¹⁸ Meningoencephalitis is a constant autopsy finding in fatal cases of scrub typhus Pai et al.¹⁹ Patients with septic shock in scrub typhus had multiple organ failure: respiratory failure²⁰ and DIC²¹ being predominant, followed by renal²² and hepatic involvement.²³

5. Conclusions

Patients with marked hypoalbuminemia in scrub typhus had higher incidence of complications (pleural effusion, pneumonia, Acute kidney injury, ARDS and meningoencephalitis), ICU admission and longer hospital stay as compared to normal albumin and considered to be a prognostic indicator of scrub typhus.

References

- [1] Devasagayam E, Dayanand D, Kundu D, Kamath MS, Kirubakaran R, Varghese GM. The burden of scrub typhus in India: A systematic review. *PLoS Negl Trop Dis.*2021; 15 (7): e0009619. Published 2021 Jul 27. doi: 10.1371/journal.pntd.0009619
- [2] Lee CS, Min IS, Hwang JH, Kwon KS, Lee HB. Clinical significance of hypoalbuminemia in outcome of patients with scrub typhus. *BMC Infect Dis.*2010; 10: 216. Published 2010 Jul 21. doi: 10.1186/1471-2334-10-216

- [3] Jain D, Nand N, Giri K, Bhutani J. Scrub typhus infection, not a benign disease: an experience from a tertiary care center in Northern India. *Med Pharm Rep.*2019; 92 (1): 36 - 42. doi: 10.15386/cjmed - 1088
- [4] Kala D, Gupta S, Nagraik R, Verma V, Thakur A, Kaushal A. Diagnosis of scrub typhus: recent advancements and challenges. *Biotech.*2020; 10 (9): 396. doi: 10.1007/s13205 - 020 - 02389 - w
- [5] Kim, DM., Kim, S. W., Choi, SH. *et al.* Clinical and laboratory findings associated with severe scrub typhus. *BMC Infect Dis* **10**, 108 (2010). <https://doi.org/10.1186/1471-2334-10-108>
- [6] Hermann FR, Safran C, Levcoff SE, Minaker KL. Serum albumin level on admission as a predictor of death, length of stay and readmission. *ARCH INTERN MED.*1992; 152 (1): 125 - 130.
- [7] Doi K, Nishida O, Shigematsu T, et al. The Japanese Clinical Practice Guideline for acute kidney injury 2016. *J Intensive Care.*2018; 6: 48. Published 2018 Aug 13. doi: 10.1186/s40560 - 018 - 0308 - 6
- [8] Soong L. Dysregulated Th1 Immune and Vascular Responses in Scrub Typhus Pathogenesis. *J Immunol.*2018; 200 (4): 1233 - 1240. doi: 10.4049/jimmunol.1701219
- [9] Suja L, Krishnamoorthy S, Sathiyam S, Sivanandam S, Koushik AK. Scrub typhus vasculitis causing pan digital gangrene Int J Case Rep Images 2015; 6 (7): 416–421.
- [10] Chang, Po - Hsiung MD*, †; Cheng, Yu - Pin MD‡; Chang, Po - Sheng MD§; Lo, Chiao - Wei MD¶; Lin, Lung - Huang MD¶, †; Lu, Chin - Fang MD**; Chung, Wen - Hung MD††. A Case Report and Literature Review of Scrub Typhus With Acute Abdomen and Septic Shock in a Child—The Role of Leukocytoclastic Vasculitis and Granulysin. *The American Journal of Dermatopathology* 40 (10): p 767 - 771, October 2018. | DOI: 10.1097/DAD.0000000000001167
- [11] Abhilash K, Mannam PR, Rajendran K, John RA, Ramasami P. Chest radiographic manifestations of scrub typhus. *J Postgrad Med.*2016; 62 (4): 235 - 238. doi: 10.4103/0022 - 3859.184662
- [12] Tsay RW, Chang FY. Serious complications in scrub typhus. *J Microbiol Immunol Infect.*1998 Dec; 31 (4): 240 - 4. PMID: 10496165
- [13] Yun, Ji Hyun MDa, b; Hwang, Hye Jeon MDc; Jung, Jiwon MDdb; Kim, Min Jae MDdb; Chong, Yong Pil MDdb; Lee, Sang - Oh MDdb; Choi, Sang - Ho MDdb; Kim, Yang Soo MDdb; Woo, Jun Hee MDdb; Kim, Mi Young MDc, *; Kim, Sung - Han MDdb, *. Comparison of chest radiographic findings between severe fever with thrombocytopenia syndrome and scrub typhus: Single center observational cross - sectional study in South Korea. *Medicine* 98 (46): p e17701, November 2019. | DOI: 10.1097/MD.00000000000017701
- [14] Sedhain A, Bhattarai GR. Renal Manifestation in Scrub Typhus during a Major Outbreak in Central Nepal. *Indian J Nephrol.*2017; 27 (6): 440 - 445. doi: 10.4103/ijn. IJN_133_17
- [15] Sedhain A, Bhattarai GR. Renal Manifestation in Scrub Typhus during a Major Outbreak in Central Nepal. *Indian J Nephrol.*2017; 27 (6): 440 - 445. doi: 10.4103/ijn. IJN_133_17
- [16] Aung - Thu, Supanaranond W, Phumiratanaprapin W, Phonrat B, Chinprasatsak S, Ratanajaratroj N. Gastrointestinal manifestations of septic patients with scrub typhus in Maharat Nakhon Ratchasima Hospital. *Southeast Asian J Trop Med Public Health.*2004; 35 (4): 845 - 851.
- [17] Lee CH, Lee JH, Yoon KJ, Hwang JH, Lee CS. Peritonitis in patients with scrub typhus. *Am J Trop Med Hyg.*2012; 86 (6): 1046 - 1048. doi: 10.4269/ajtmh.2012.11 - 0586
- [18] Boorugu H, Chrispal A, Gopinath KG, et al. Central nervous system involvement in scrub typhus. *Trop Doct.*2014; 44 (1): 36 - 37. doi: 10.1177/0049475513512646
- [19] Mahajan SK, Mahajan SK. Neuropsychiatric Manifestations of Scrub Typhus. *J Neurosci Rural Pract.*2017; 8 (3): 421 - 426. doi: 10.4103/jnrp. jnrp_44_17
- [20] Sankuratri S, Kalagara P, Samala KB, Veledandi PK, Atiketi SB. Scrub Typhus with Acute Respiratory Distress Syndrome (ARDS) and its Management in Intensive Care Unit: A Case Report. *J Clin Diagn Res.*2015; 9 (5): OD10 - OD11. doi: 10.7860/JCDR/2015/13692.5924
- [21] Ono Y, Ikegami Y, Tasaki K, Abe M, Tase C. Case of scrub typhus complicated by severe disseminated intravascular coagulation and death. *Emerg Med Australas.*2012; 24 (5): 577 - 580. doi: 10.1111/j.1742 - 6723.2012.01600. x
- [22] Kim Yo, Yoon SA, Ku YM, Yang CW, Kim YS, KIM SY, Choi EJ, Chang YS, Bang BK: serum albumin level correlates with disease severity in patients with hemorrhagic fever with renal syndrome. *J KOREAN MED SCI*2003, 18: 696 - 700.
- [23] Gaba S, Gaba N, Gupta M, Sharma S. Hepatic and Renal Profile of Scrub Typhus Patients at a Tertiary Care Center in India. *Cureus.*2020; 12 (5): e7925. Published 2020 May 2. doi: 10.7759/cureus.7925