How to Cite:
Jaikar, S. K. B., Divya, N. S., Ramesh, B., Vanisri, H. R., & Shashikumara, S. (2022). Assessment of rickettsial diseases presenting as acute undifferentiated febrile illness using clinical tools in a government tertiary care teaching hospital, Chamarajanagar, Karnataka. *International Journal of Health Sciences*, *6*(S2), 12349–12360. https://doi.org/10.53730/ijhs.v6nS2.8274

Assessment of rickettsial diseases presenting as acute undifferentiated febrile illness using clinical tools in a government tertiary care teaching hospital, Chamarajanagar, Karnataka

Dr. Sharat Kumar B. Jaikar
Associate Professor, Department of General Medicine, Chamarajanagara Institute of Medical Sciences, Sy. No:124, Yadapura Village, Kasaba Hobli, Chamarajanagar-571313.Karnataka, India.
Email: sharatjaikar@gmail.com

Dr. Divya N S
Assistant Professor, Department of Pathology, Chamarajanagara Institute of Medical Sciences, Sy.No:124, Yadapura Village, Kasaba Hobli, Chamarajanagar-571313.Karnataka, India.
Corresponding author email: drdivyans@gmail.com

Dr. Ramesh B
Professor and HOD, Department of Medicine, Chamarajanagara Institute of Medical Sciences,Sy.No:124, Yadapura Village, Kasaba Hobli, Chamarajanagar-571313.Karnataka, India.
Email: drrameshsargur@gmail.com

Dr. Vanisri H R
Professor and HOD, Department of Pathology, Chamarajanagara Institute of Medical Sciences, Sy.No:124, Yadapura Village, Kasaba Hobli, Chamarajanagar-571313.Karnataka, India
Email: drvanisri16@gmail.com

Shashikumara
Department of Pharmacology, Chamarajanagara Institute of Medical Sciences, Sy. No:124, Yadapura Village, Kasaba Hobli, Chamarajanagar-571313.Karnataka, India
Email: samsruthia2@gmail.com

***Abstract*---**Background: Rickettsial diseases are re-emerging in India. Acute undifferentiated febrile illness is a difficult case to treat (AUFI). The greatest problem for clinicians is the early diagnosis of these

diseases when antibiotic therapy is most successful.To determine the prevalence of RDs, therapy outcomes, and socio-demographic factors associated with RDs in AUFI. Patients and Methods: Fever and/or clinical signs of Rickettsial infection in patients admitted to the CIMS teaching hospital in Chamarajanagar for four years. Purposive sampling found AUFI in 1638 people. The diagnosis of rickettsial disease relied on clinical features. The Weil-Felix test was one. Then came a 48–72-hour estimate of doxycycline response. Results:Out of 1810 AUFI cases, 198 (10.93%) were rickettsial, with 190 (95.95%) having an RGA score of 14 or more, and 18 (9.09%) having an RGA score of 14 or less. Males aged 30-40 were most affected. Leucopenia, thrombocytopenia, etc. were found. Doxycycline was effective in 151 (89.35%) of cases within one week of onset. The remaining 18 (10.65%) required longer-term doxycycline with other drugs, three had severe complications, and one died. RD prevalence 70.01 % Conclusion: Enteric fever, Dengue fever, Chikungunya fever, and Rickettsial diseases were the most common diseases diagnosed in patients with undifferentiated febrile illness. Clinicians must consider rickettsial diseases as one of the differential diagnoses when treating febrile patients. Highlights: In AUFI, RDs can be diagnosed using the RGA Scoring System in the periphery, and beginning Doxycycline early with clinical suspicion reduces morbidity and mortality.

***Keywords*---**rickettsial diseases, acute undifferentiated febrile illness, doxycycline.

Introduction

In tropical countries such as India, infectious diseases continue to be the leading cause of disability and death. Fever is frequently self-managed or treated with empirical medicine in low-resource settings due to a lack of public health care facilities and limited access to diagnostic tests[1]. Acute undifferentiated febrile illness (AUFI) is characterised by a 14-day fever that lacks evidence of an organ or system-specific etiology[1, 2]. Rickettsial diseases (RDs) are among the most under-recognized emerging and re-emerging diseases in India, according to the Asian Union for Food and Agriculture (AUFI). There is a possibility that it is the only symptom of a minor self-limiting illness or that it is the beginning of an extremely serious infection caused by a bacterial pathogen[3,4.]

AUFI can be caused by a wide range of viruses, bacteria, protozoa, and rickettsia, with rickettsioses emerging as significant culprits in recent years[4]. Clinical manifestations of rickettsia infections differ depending on the causative agent and the ill patient; however, common symptoms that typically appear within 1 - 2 weeks of infection include elevated body temperature, headache, malaise, rash, nausea, and vomiting [5]. Establishing the etiologic diagnosis of rickettsiosesis during the acute stage of illness is difficult, and definitive diagnosis usually necessitates the examination of serum samples during the acute and convalescent phases of illness[6]. Previously, Rickettsioses were always considered in the differential diagnosis of exanthematous fever in India; however, with the

widespread use of insecticides and the introduction of Tetracyclines and Chloramphenicol, which have a very good therapeutic response, Rickettsial diseases were forgotten[7].

However, with the subsequent reduction in Tetracyclines and Chloramphenicol, there has been an alarming surge in the incidence of Rickettsioses in India during the previous decade[8,9]. Due to a lack of public health care facilities or access to diagnostic tests, fever is frequently self-managed or treated empirically[10.] For example, knowing the incidence of local infections helps focus the condition, do essential clinical work-ups, and monitor treatment plans[11]. The Indirect Immunoperoxidase (IPA) and Immunofluorescence (IFA) assays are considered the serological gold standard, but are only available in laboratories with advanced facilities and expertise. The gold standard for identifying rickettsial illnesses, the IFA and IP tests, are expensive and unavailable in India[8]. India has minimal PCR-based molecular diagnostic facilities6. The lack of adequate serological or culture diagnostic tests[10] is the main obstacle to early antibiotic therapy.

As a result, Weil-Felix becomes a practical, less expensive, readily available test in establishing the presumptive diagnosis in cases of rickettsial fever[8].In a study by Prakash et al., the Weil-Felix test was found to have a sensitivity of only 43% but a specificity of 98% for titres 1:80 or more[8].Apart from laboratory evidence clinical tools like the Rathi-Goodman-Aghai (RGA) scoring system[11] can be used for early detection of rickettsial disease which would help in early treatment hence preventing mortality and morbidity.[12]RGA score of more than 14 shows a sensitivity of 92% and specificity of 83.3%[12].

Local studies from North Karnataka (Vijayapura and Gadag), the centre of Karnataka (Shivamogga), and the southern part of rural Bangalore have reported rickettsial disease among adults and children [4,13,14,15]. This study was conducted because this region is surrounded by forest and the majority of the population is rural, relying on agriculture and farming for a living. There was a need to establish rickettsial disease as one of the neglected unnoticed endemic causes of Acute Undifferentiated Febrile Illness, so we analyzed clinical symptoms and signs of rickettsial disease among AUFI; the diagnosis was precise with the help of RGA scoring and Weil-Felix test so that treatment is started as soon as possible, which would reduce morbidity, complications, length of stay in the hospital, and mortality as proven by many other similar studies

Furthermore, many studies have shown that beginning doxycycline with a mere suspicion of rickettsial disease made a difference in the clinical picture within 48 hours and the outcome of the disease after treatment. Until recently, doxycycline was the empirical drug of choice for most of these infections[5]. As a result, the current study aims to determine the prevalence of RDs in AUFI, therapeutic outcomes of doxycycline, and any socio-demographic characteristics associated with rickettsial diseases.

Materials and Methods

The study was carried out at the Department of medicine, Chamarajangar Institute of Medical Sciences, Chamarajangar, and a cross-sectional design. There

were 1810 AUFI cases admitted between June 2015 and May 2020. Details on socio-demographic data like name and age were all included. Approval was obtained from Institutional Ethics Committee bearing reference number CIM/IEC-03/40/2022. Purposive sampling with the aid of Rathi-Goodman-Aghai (RGA) scoring was used to select198 cases. cases, all subjected to a complete blood count, liver function test, blood urea, serum creatinine, serum electrolytes, ECG, ABG, and Weil-Felix serology.

Inclusion and Exclusion criteria

During the trial period, all patients with undifferentiated fever >38°C and no specific localising signs or symptoms were included. Patients who had a fever within 72 hours of being admitted to the hospital were not included in the study. Patients who were febrile and had confirmed pneumonia, skin or soft tissue infections, urinary tract infections, or any other infection confirmed in the lab were also excluded. Following the initial collection of acute specimens, the discharged patients' case sheets were reviewed, and the consulting physician declared them to be treated.

Statistical Analysis

The study's continuous and categorical variables are described in frequency and percentage. The acquired data was entered into a spreadsheet (Microsoft Excel 2016 spreadsheet) and exported to Graph prism pad's data editor (9.23.1). Standard deviations and categorical variables were reported as percentages for continuous variables. To compare categorical variables, either Chi-square or Fisher's exact tests were utilized. At 95% confidence, a P-value of 0.05 was declared statistically significant.

Table 1: RGA (Rathi-Goodman-Aghai) Scoring chart

Clinical features	Score	Laboratory	Score
Rural	1	Hemoglobin < 9gm/dL (%)	1
Pets	1	Platelets < 1,50,000 (cells/L)	1
Tick exposure	2	CRP >50 (mg/dL)	2
Tick bite	3	Serum albumin < 3(gm/Dl)	1
Conjuctival congestion (non-exudative)	2	Urine albumin > 2+	1
Maculopaular rash	1	SGPT > 100 (U/L)	2
Purpura	2	Serum sodium <130 (mEq/L)	1
Palpable purpura / ecchymosis / necrotic rash	3		
Rash appearing 48-96 hrs after fever	2		
Pedal edema	2		

Rash on palms and soles	3	
Hepatomegaly	2	
Lymphadenopathy	1	
Total	25	10

Scoring system for diagnosing spotted fever group (total score = 35)

Results and Discussion

Common endemic infections such as Enteric fever 864 (47.7 %), Dengue 338 (18.7 %), Chikungunya 316 (17.5 %), Malaria 33 (1.8 %), Leptospirosis 18 (1.00 %), Brucellosis 16 (0.9 %), and PUO 27 (1.5 %) were diagnosed based on appropriate clinical and laboratory tests in 1810 AUFI cases (Figure-1). 198 (10.93%) cases with RGA scores of 14 or higher were diagnosed with the rickettsial disease, of which 169 (85.35%) were well-Felix positive with titers greater than 1:160 and the remaining 29 (14.64%) were negative (Graph-1). Males were affected by the rickettsial disease at a higher rate 120 (86.33 %) than females 29 (13.67 %) (Table-2). Age distribution revealed that people aged 30 to 40 years were more 46 (42.59 %) followed by people aged 20 to 30 years, 35(32.40 %), 40 to 50 years, 15(13.88 %), and 50-60 years, 6 (5.55 %). The rural population accounted for 86 (79.62 %) of the cases, while the urban population accounted for 22 (20.37 %) of the cases. According to the Kuppuswamy socioeconomic scale grading-2018 (Table-2&7), the Lower middle class (III) was affected the most (70.81 %), followed by the Upper middle (II) class (27.25 %), and the Upper lower (IV) class (11.18 %). Fever was the most common clinical symptom (Table-3) and (Table-4) followed by headache 142 (72%), myalgia 138 (69.17 %), generalized weakness 129 (65.15 %), joint pain 127 (64.14 %), redness of eyes 131 (66.16 %), rashes over body or skin rashes 122 (66.61 %), nausea 102 (51.51 %), vomiting 99 (49.49 %), breathlessness 71 (35.85 %),Tender hepatomegaly 86 (43.43 %), lymphadenopathy 59 (29.79 %), palpable purpura 57 (29 %), bi-lateral pitting pedal oedema 53 (26.78 %), joint effusion 49 (24.74 %), icterus 38 (19.19 %), lung crepitations 31 (15.65 %), and terminal neck stiffness 28 (14.14 %) were the most common clinical signs (12.03 %).Even though Eschar is a pathognomonic sign of rickettsial disease, it was only seen in 8 (7.40 %) of the cases. Laboratory tests (Table-5**)** revealed thrombocytopenia 156 (78.00 %), hypoalbuminemia 136 (68.68 %), raised levels of liver enzymes 131 (66.16 %), leucopenia 117 (59.00 %), raised serum bilirubin 98 (49.49 %), hyponatremia 89 (44.49 %), urine albumin 77 (38.38 %), anaemia 92(46.46 %), leucocytosis 79 (39.89). Imaging studies revealed mild ascites in 21 (10.60 %), bilateral hilar opacity in 9 (8.33 %), and CT brain was normal in all 4 (4%) of the patients who had seizures.

Out of 1810 cases, 96 (88.88 %) were admitted within one week of the onset of fever and responded well to doxycycline initiation within 48 to 72 hours. The remaining 12 (11.11 %) who were admitted after 1 week of fever after being treated elsewhere and trying alternate forms of medicine stayed in the hospital for more than 15 days, of which 8 required doxycycline for a more extended period, i.e. more than 10 days, along with other drugs such as azithromycin and rifampicin**.** 4 (3.70%) cases had severe complications such as Multi-Organ Dysfunction Syndrome, Acute Kidney Injury, and respiratory distress, with one (0.92%) dying as a result of Ventilator-Associated Pneumonia (Table- 6).

Table 7 depicts the association between the socio-demographic characteristics of the patients and the prevalence of rickettsial infection. The prevalence of rickettsial disease was found to be 70.01 percent in males and 29.79 percent in females, with the link being statistically insignificant (P-value = 0.3960). Furthermore, the prevalence of rickettsial disease increased with age, but this relationship was not statistically significant (P-value0001). The prevalence of rickettsial disease among rural patients was 83.88 percent, and the link was statistically significant. (The P-value is 0.0256.) However, we identified a statistically significant link between socioeconomic class as measured by the Kuppuswamy socioeconomic scale and the prevalence of rickettsial disease in the examined population(P-value = 0.0072).

Graph-1: Flow chart Depicting AUFI cases distribution

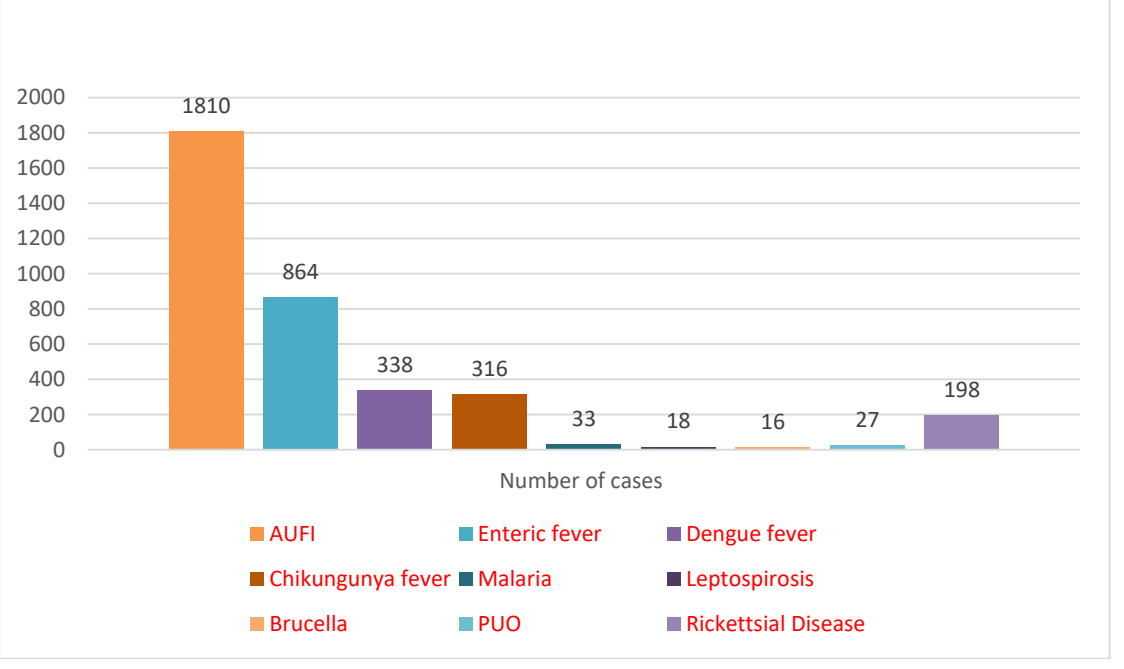

Table 2: Socio-demographic characteristics of the studied patients

Characteristic	Variable	n (%)
Gender	Male	139 (70.20%)
	Female	59 (29.26%)
Age	15-19	7 (3.54%)
	20-29	58 (29.29%)
	30-39	76 (38.38%)s
	40-49	32 (16.16%)
	50-59	16 (8.08%)
	>60%	9 (4.55%)
	Rural	162 (81.82%)

Residence	Urban	36 (16.11%)
Socioeconomic status	Upper middle (II)	38 (19.19%)
	Lower middle (III)	142 (71.72%)
	Upper lower (IV)	18 (9.09%)

Results were expressed in percentage (%)

Table 3: Clinical Profile

General			Hepatobiliary and Abdominal		
	n	(%)		n	(%)
Symptoms			Symptoms		
Fever	189	95.45%	Nausea	102	51.51%
Headache	142	72%	Vomiting	99	49.49%
Myalgia	138	69.17%	Dark-colored urine	47	23.73%
Generalized weakness	129	65.15%	Mouth ulcers	31	15.65%
Joint pain	127	64.14%	Diarrhea	33	16.66%
Redness of eyes	131	66.16%			
Skin rashes	122	61.61%	Signs		
Chills and rigors	57	28.78%	Hepatomegaly	86	43.43%
Rashes over palms and soles	48	24%	Icterus	38	19.19%
			Splenomegaly	22	11.11%
Signs					
Lymphadenopathy	59	29.79%	Imaging	49	20.70%
Palpable purpura	57	29%	Ascitis on USG		
Pedal oedema	53	26.78%			
Joint effusion	49	24.74%			
Eschar	18	9.09%			

Table 4: Clinical Profile

Respiratory			Central nervous system		
	n	(%)		n	(%)
Symptoms			Symptoms		
Breathlessness	64	32.23%	Altered mentation	12	6.06%
Cough	56	28.28%	Seizures	8	4.04%
Signs			Signs		
Lung crepitations	31	15.65%	Terminal neck Stiffness.	28	14.14%
Imaging			Imaging		
Chest x-ray	17	8.58%	Ct brain normal in		
Bilateral hilar opacity			All patients with seizures	8	4%

Table 5: Laboratory profiles

	n	Percentage		n	Percentage
Thrombocytopenia Leucocytopenia	156	78.00%	Low Serum albumin	136	68.68%
Elevated CRP	117	59.00%	Raised levels of liver enzymes	131	66.16%
Anemia	92	46.46%	Elevated bilirubin	98	49.49%
Leucocytosis	79	39.89%	Hyponatremia	89	44.49%
	72	36.36%	Urine albumin	77	38.88%
			Blood urea	46	23.32%
			Serum creatinine	34	17.17%
			Hyperkalemia	27	13.66%

Table -6: Complications and Mortality rate

Total cases	Cases with Complications	Patient died
198	6 (6.06%)	1 (0.50%)

Table-7: Association of Sociodemographic Characteristic and rickettsial disease among studies patients

Characteristic	Variables	n	%	Weil -flix positive	Weil flix-negative	Prevalence	p-value
	Male	139	70.2	120 (86.33%)	19 (13.67%)	70.01	0.3906 (ns)
	Female	59	29.8	48 (81.33%)	11 (18.64%)	29.79	
Total		198	100	169	30		
Age (Years)	15-19	7	3.54	2 (1.18%)	5 (17.24%)	3.53	<0.0001****
	20-29	58	29.29	53 (31.36.3%)	5 (17.24%)	29.29	
	30-39	76	38.38	70 (41.42%)	6 (20.69%)	38.38	
	40-49	32	16.16	27 (15.97%)	5 (17.24%)	16.16	
	50-59	16	8.08	13 (7.69%)	3 (10.34%)	8.08	
	>60	9	4.55	4 (2.36%)	5 (17.34%)	4.54	
Total		198	100	169	29		
Residence	Rural	162	81.82	151 (83.88%)	11 (61.11%)	81.81	0.0256*
	Urban	36	18.18	29 (1611%)	7 (38.88%)	18.8	
Total		198	100	180	18		
Socio - Economic status	Upper Middle (II)	38	19.19	26 (15.47%)	12 (40%)	19.19	0.0072*
	Lower middle (III)	142	71.72	126 (75%)	16 (53%)	71.71	
	(Upper lower IV)	18	9.09	16 (16%)	2 (6.67%)	9.09	
Total		198	100	168	30		

P-value <0.05 considered significance at 95% confidence intervals.

Acute undifferentiated febrile fever accounts for a high proportion of cases treated in hospitals. Rickettsial infections are among the oldest and most dangerous

diseases known to humanity. They have repeatedly appeared as a human scourge, flourishing as epidemics during times of conflict and starvation[14].

Since it is challenging to have community-based laboratories to confirm diagnoses, which would require knowledge and expensive gear, varied clinical presentation and lack of suspicion lead to unnecessarily expensive work-up for PUO. As a result, in a country like India with poor health infrastructure and the majority of its population living in rural areas, endemic disease knowledge that is closely associated with socio-cultural practices of rural families, as well as less expensive and easily accessible clinical scoring systems like Rathi-Goodman-Aghai (RGA) scoring that is understood by all health care professionals for early detection of rickettsial disease, is critical. Simply having a clinical suspicion and starting therapy would reduce morbidity and mortality significantly.

A study done by Bhaskar Naik *et al.,* found that RGA scores of more than 14 have a sensitivity of 92 % and a specificity of 83.3 % compared to PCR[11]. We discovered that Weil-Felix has a sensitivity of 90.74 % and a significant positive correlation with a p-value 0.05. (0.02). Similarly, Sharma *et al.,*[15], Kamarasu *et al.,*[16], Bithu et al.,[17], and Prakash et al.,[18] found that 9 %, 33 %, 38 %, 49.1 %, and 44 % of people tested positive for Weil Felix. Many studies, such as Tabeen Mansoor et al.,[9] Bhaskar Naik et al.,.[11], Mallesh *et al.,*[19], Thomas *et al.,*[20], Muruli et al.,[21], Kumar *et al.,*[22], have found that males are affected more than females; in our study, males are affected more than females in a 2:1 ratio. Unlike in the study by Seena Sankar *et al.,*[8], females were affected more than males.

Tabeen Mansoor *et al.,* [8]. Our study found that upper-middle-class people aged 40-59 were more affected than lower-middle-class people aged 30-39. Rural populations constituted the majority of cases, 86 (79.62%) compared to urban populations, consistent with other studies such as Tabeen Mansoor *et al.,*[9], Thomas *et al.,*[20], and Bhaskar Naik *et al.,*[11]. Many studies have found similarities in clinical symptoms and signs because they are non-organ specific and have elaborated on various symptoms and signs (Table-8). The laboratory features of various studies have been compared in (Table-9), with thrombocytopenia being the most common feature.

Table 8: Clinical profile comparison of different studies

Clinical features	Present study	Satish Talikoti *et al.,*[12]	Seena Sankar *et al.,*[9]	Mallesh K *et al.,*[19]
Symptoms				
Fever	95.37%	88%	100%	100%
Headache	75%	5%	53.5%	34.7%
Skin rashes	57.40%	44%	28.3%	57.10%
Breathlessness	31.48%	46%	23.2%	26.5%
Conjunctivitis	59.25%	29%	33.8%	-
Cough	29.62%	78%	29.3%	-
Signs				
Hepatomegaly	34.25%	1%	14%	91.8%
Splenomegaly	9.25%	-	9%	22.4%

Lymphadenopathy	22.22%	0	20.3%	28.6%
Pedal oedema	19.44%	12%	14.9%	51%
Eschar	7.40%	44%	2.7%	10.2%
Altered sensorium	5.55%	71%	2.7%	32.7%
Seizures	3.70%	42%	4%	26.5%

Table 9: Comparison of Laboratory features among different studies

Laboratory parameters	Present study	Satish Talikoti *et al.,*[12]	Seena Sankar et al., [7]	Mallesh K *et al.,*[19]
Thrombocytopenia	75.92%	47.6%	70.77%	91.8%
Leucocytopenia	55.55%	22%	15%	
Anemia	39.81%	65.1%	46.4%	51.1%
Leucocytosis	33.33%	44.7%	11%	34.6%
Low Serum albumin	67.59%	-	78.8%	89.8%
Raised levels of liver enzymes	64.81%	68%	-	-
Elevated bilirubin	45.37%	-	32%	-
Hyponatremia	45.37%	56%	-	87.7%
Serum creatinine	15.74%	12%	25.2%	-

The response to doxycycline is dramatic, and fever that lasts longer than 48 hours after starting doxycycline should prompt consideration of an alternative or additional diagnosis, such as coinfection. Mallesh K *et al.,*[19] recorded a response to doxycycline within 48 hours of starting it. Our study found that 96 (88.88 %) of cases admitted within one week of the onset of fever responded well within 48 to 72 hours after doxycycline was started. Mahajan *et al.,*[15]. recorded Complications in cases admitted after one week of fever onset, and we discovered four (3.70 %) cases had severe complications such as Multi-Organ Dysfunction Syndrome, Acute Kidney Injury and respiratory distress, one of which died as a result of Ventilator-Associated Pneumonia.

Conclusion

Rickettsial disease, which is zoonotic, is inextricably linked to most rural populations' socio-cultural practices. Due to a lack of health care facilities and skilled physicians, diagnosing rickettsial disease in AUFI cases in a rural Indian population is difficult. Only a high level of suspicion can save money on unnecessary PUO work-ups. Early diagnosis in the acute phase is aided by using clinical scoring systems such as RGA. The Weil-Felix test is a low-cost, widely available diagnostic tool. Furthermore, therapy should begin as soon as clinical suspicion of something wrong exists. Morbidity and mortality are reduced.

References

1. Daniel. H. Paris, Nicholas P.J.DAY: Tropical Rickettsial Infections. Manson's Tropical Diseases. 23rd edi. Jeremy Farrar, Peter J Hotez, Thomas Jughanss, Gagandeep Kang. Elsevier Saunders; 2014:273-274.
2. Brezina R, Murray E S, Tarizzo M L, Bogel K: Rickettsiae and rickettsial diseases, Bull Wld Hlth Org; 1973,49:433-442. https://apps.who.int/iris/handle/10665/263630.
3. R.K.Srivastava, D.Bhattacharya, Veena Mittal, Naveen Gupta., et al.,.: Scrub Typhus & other Rickettsioses. CD Alert, National Centre for Disease Control, Directorate General of Health Services, Govt. of India;2019,13(1):01-8.
4. Sophia G de Vries, Louise E van Eekeren, Hans Van der Linden, etal.: Searching and finding the Hidden Treasure: A Retrospective Analysis of Rickettsial Diseases Among Dutch International Travelers. Clinical Infectious Diseases;2021,72(7):1171-1178.
5. Blewitt B: Fever of the Typhus group in the BhimTal area, Kumaon Hills,UP, India. J of Royal Army Medical Corps; 1938:241-245.
6. Rajeev Raiana: Rickettsial Infections. API Textbook of Medicine.11th edi., Vol.1: Sandhya A Kamath, Siddharth N Shah, Millind Y Nadkar. The Association of Physicians of India, CBS; 2019:229-232.
7. Seena Sankar, Shruthi Kulkarni & Kurian Thomas: A Study on Clinical Profile and Complications of Rickettsial Diseases in a Tertiary Care Hospital: Prospective Observational Study: International Journal of current Medical and Applied sciences; 2017, 14(1),20-25.
8. Tabeen Mansoor, Bashir Ahmad Fomda, Ajaz Nabi Koul, et al.,.: Rickettsial Infections among the Undifferentiated Febrile Patients attending a Tertiary Care Teaching Hospital of Northern India: A Longitudinal Study. Infect Chemother; 2021,53(1):96-106.
9. Manisha Biswal, Sivanantham Krishnamoorthi, Kamesh Bisht, et al.,.:Rickettsial Diseases: Not Uncommon Causes of Acute Febrile Illness in India. Trop. Med. Infect. Dis; 2020,5(59):1-10.
10. Rathi M, Gupte MD, Bhargava A, Varghese GM, Arora R. DHR-ICMR guidelines for diagnosis and management of Rickettsial diseases in India. Indian J Med Res. 2015;141:417-22.
11. Bhaskar Naik, A Sailaja, T anusha, et al.,.: A prospective study of the effectiveness of clinical RGA (Rathi Goodman Aghai) Score in relation with PCR in the diagnosis of Scrub Typhus. International J of Paediatrics & Geriatrics; 2019,2(2):01-05
12. Satish Talikoti, Nijora Deka: Clinical profile of Rickettsial Infection in Vijayapur, North Karnataka- A Retrospective Study. J.Evid.Based Med.Health C;2019,16(22):1563-1566.
13. Vasantha Kamath, Sheryashi Ganguly, Jasmine Kaur Bhatia, R Himabindhu: Rickettsial Infections: Past and Present Perpectives.APIK J of Int Med;2020,8:4-10.
14. P Saravanan, M V Nagaraj, C Somashekar: Rickettsial fever in tertiary care hospital in rural Bengaluru: Clinical profile and complications. Indian J Child Health;2020,7(9):385-387.
15. Sharma A, Mahajan S, Gupta ML, Kanga A, Sharma V. Investigation of an outbreak of scrub typhus in the Himalayan region of India. Jpn J Infect Dis 2005;58:208-10.

16. Kamarasu K, Malathi M, Rajagopal V, Subramani K, Jagadeeshramasamy D, Mathai E. Serological evidence for wide distribution of spotted fevers and typhus fever in Tamil Nadu. Indian J Med Res 2007;126:128-30.
17. Bithu R, Kanodia V, Maheshwari RK. Possibility of scrub typhus in fever of unknown origin (FUO) cases: An experience from Rajasthan. Indian J Med Microbiol 2014;32:387-90.
18. Prakash JA, Abraham OC, Mathai E. Evaluation of tests for serological diagnosis of scrub typhus. Trop Doct 2006;36:212-3.
19. Mallesh K, Sarala Sabapathy, Rashmi Patil, Nikarika Shettty: Clinicopathological profile of rickettsial fever in tertiary healthcare centre: a prospective case study. Int J of Contemp Pediatr; 2020,7(5):1003-1007.
20. Thomas R, Puranik P, Kalam B, Britto C, Savita K, Rego S, et al.,. Five-year analysis of rickettsial fever in children in south India: Clinical manifestations and complications. J Infect Dev Ctries. 2016;10(6):657-661.
21. Murali N, Pillai S, Cherian T, Raghupathy P, Padmini V, Mathai E. Rickettsial infections in south India-how to spot the spotted fever. Indian Pediatr. 2001;38:1393-6.
22. Kumar M, Krishnamurthy S, Delhikumar CG, Narayanan P, Biswal N, Srinivasan S. Scrub typhus in children at a tertiary hospital in southern India: clinical profile and complications. J Infect Public Health. 2012;5:82-8.