

Original Research Article

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STUDY OF PATTERN OF LFT ABNORMALITIES IN PATIENTS PRESENTING WITH ACUTE FEBRILE ILLNESS

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Abstract

Background: Derangements in liver function tests is a common scenario in patients admitted to medical wards. It may be due to various causes. However infectious causes and toxins continue to predominate as the cause for hepatopathy. Derangements in liver function test range from mild transaminitis to fulminant liver failure. Materials and Methods: Total of 40 patients admitted in medical ward with acute febrile illness were included in the study. All necessary investigations including liver function tests were done and studied. Result: Our study recruited 40 patients with acute febrile illness. There was a male predominance of patients. 87.5% of patients had liver function test abnormalities. Ratio of AST to ALT was more than 1 in 67.5% of patients. More than 25 times elevation of transaminases was seen in minority of patients (5%). Dengue and viral fever (32.5% each) were the predominant causes of acute febrile illness in our study. Liver function test derangement was predominantly seen in dengue fever with 96.3% of dengue patients showing liver function test abnormalities. Conclusion: Pattern of liver involvement in patients with acute febrile illness varies from normal to isolated elevation of bilirubin as well as mild to marked elevation in transaminases.

INTRODUCTION

Fever is one of the commonest presentations in patients presenting to the hospitals in tropical countries. Causes of fever may be infectious or noninfectious. However, infections continue to predominate as the cause of fever in tropical countries like India.

Infectious and non-infectious causes of fever can cause hepatopathy. Liver function test abnormalities have been observed in COVID-19 patients, and typically include mild elevations of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), ranging from 14 to 53%.^[1–5] Similarly hepatic involvement was observed in dengue in various studies, the severity of hepatic involvement correlating with disease severity.^[6-8] In addition, liver involvement has also been observed in sepsis, enteric fever, other viral, bacterial and parasitic infections.^[9,10] Noninfectious causes of fever can include drug induced, toxins, autoimmune hepatitis, connective tissue diseases, hematologic malignancies and others.[11-13]

Our study is destined to throw light on the various pattern of LFT abnormalities in patients presenting with acute febrile illness due to infectious or noninfectious causes. These abnormalities tend to regress most often once the underlying etiology is addressed. Therefore, having a knowledge of various patterns of LFT abnormalities in diseases presenting with fever can minimize diagnostic dilemma and reduce unnecessary investigations.

MATERIALS AND METHODS

This study is a cross sectional observational study conducted at S Nijalingappa medical college and HSK hospital. Patients admitted with acute febrile illness from December 2022 to May 2023 were recruited in study.

Inclusion Criteria

- 1. Patients more than 15 years of age admitted with acute febrile illness in medicine ward.
- 2. Patients willing to give consent.

Exclusion Criteria

- 1. Patients admitted to intensive care unit.
- 2. Patients with alcoholic liver disease and preexisting liver disease.
- 3. Patients not willing to give consent.

All patients included in the study underwent detailed clinical examination, necessary fever work up along with LFT. The data was later analyzed to observe the various pattern of LFT abnormalities in patients with acute febrile illness.

RESULTS

Our study recruited 40 patients presenting with acute febrile illness to medicine inpatient department. Out

of 40, 22 (55%) were male patients and the rest were female patients i.e., 18 (45%).

The predominant age group affected was 15 to 30 years followed by 31–45-year age group posing a burden on working class. [Table 1]

Sl. number	Age group of patients in years	Number of patients
1	15-30	15 (37.5%)
2	31-45	9 (22.5%)
3	46-60	8 (20%)
4	More than 60	8 (20%)

Fable 2: Clinical features patients.		
Sl. number	Clinical features	Number of patients
1	Fever	40 (100%)
2	Chills	20 (50%)
3	Headache	15 (37.5%)
4	Retroorbital pain	3 (7.5%)
5	Abdominal pain	6 (15%)
6	Generalized body ache	12 (30%)
7	Abdominal pain	6 (15%)
8	Bleeding manifestations	1 (2.5%)
9	Joint pain	6 (15%)
10	Cough	4 (10%)
11	Nausea and vomiting	1 (2.5%)

Fever was the universal finding. Next common clinical features were chills seen in 50% of patients, headache and generalized body ache observed in 37.5% and 30% of patients respectively.

Sl. Number	Physical signs	Number of patients
1	Fever	40 (100%)
2	Tachycardia	14 (35%)
3	Bradycardia	10 (25%)
4	Pallor	3 (7.5%)
5	Icterus	7 (17.5%)
6	Edema	2 (5%)
7	Abdominal tenderness	8 (20%)
8	Hepatomegaly	4 (10%)
9	Splenomegaly	2 (5%)
10	Ascites and effusion	2 (5%)
11	Crepitations and rhonchi	3 (7.5%)

On examination tachycardia (35%) and bradycardia (25%) were the findings common next to fever. Abdominal tenderness and icterus were seen in 8 (20%) and 7 (17.5%) cases.

Table 4: The LFT abnormalities			
Sl. number	Pattern of LFT abnormality	Number of patients	
1	Normal LFT	9 (22.5%)	
2	Isolated elevation of bilirubin (>1.2 mg/dl)	4 (10%)	
3	Isolated elevation of transaminases (more than 3 times normal) 16 (40%)		
4	Combined elevation of bilirubin and transaminases (more than 3 times normal)	11 (27.5%)	
5	Decreased albumin	4 (10%)	

When studied for LFT abnormalities isolated elevation of transaminases was the most common finding seen in 40% of patients whereas combined elevation of bilirubin and transaminases was the second most common finding seen in 27.5% of patients. Isolated elevation of bilirubin (>1.2 mg/dl) was seen in 10% of cases.

Table 5: Pattern of AST and ALT elevation.			
Sl. Number	Pattern of AST and ALT involvement	Number of patients	
1	Normal (AST and ALT less than 3 times normal)	12 (30%)	
2	AST>ALT	27 (67.5%)	
3	ALT>AST	1 (2.5%)	

It was noted in our study that AST to ALT ratio more than 1 was the predominant pattern of transaminase abnormality seen. This ratio was reversed in 1 patient which carried a diagnosis of enteric fever.

Table 6: Quantitative depiction of transaminase elevation.		
Sl. number	Degree of elevation of transaminases	Number of patients
1	Normal	12 (30%)

2	Less than 3 times elevation	1 (2.5%)
3	More than 3 times elevation	25 (62.5%)
4	More than 25 times elevation	2 (5%)

Marked elevation of transaminases i.e more than 25 times the normal constituted minority of patients (5%) and were dengue cases. More common abnormality in transaminase was three to twenty-five times elevation which was seen in 62.5% of patients.

Cable 7: Etiology of various causes of acute febrile illness in our study		
Sl. Number	Etiology of fever	Number of patients
1	Viral fever	13 (32.5%)
2	Dengue	13 (32.5%)
3	Rickettsial fever	8 (20%)
4	Pneumonia	3 (7.5%)
5	Urinary tract infection	1 (2.5%)
6	Enteric fever	2 (5%)

Viral fever and dengue fever (32.5% each) continue to predominate as infectious causes of acute febrile illness in our part of World. Rickettsial fever also contributes to good number of infectious causes of fever (20%).

Table 8: LFT abnormalities in various etiologies of fever is shown below.			
SL. Number	Etiology	Patients with LFT abnormalities among various etiologies	
1	Viral fever	10 (76.9%)	
2	Dengue	12 (96.3%)	
3	Rickettsial fever	6 (75%)	
4	Pneumonia	2 (66.6%)	
5	Urinary tract infection	0 (0%)	
6	Enteric fever	1 (50%)	

Among dengue cases 96.3% had some degree of liver function abnormalities whereas 76.9% of viral fever and 75% of rickettsial fever patients had derangements in LFT.

DISCUSSION

Liver involvement is common in various causes of acute febrile illness, the frequency of involvement varying depending on the etiology of fever. Our study showed male predominance of patients presenting with acute febrile illness. In a study conducted by Agarwal R et al. in patients with dengue there was a male predominance with male to female ratio being 1.9:1.^[14] A study performed by Srikanth N et al. also showed predominance of males as the cause of infectious disease involving enteric fever. A study on rickettsial fever by Lledó L et al showed that the studied infection was more common in males.^[15] Similarly, pneumonia in various studies has been shown to be more common in males.^[16]

Predominant age group of afflictions of infection causing fever in our study was 15-30 years. Studies conducted in dengue and enteric fever by Chhina RS et al and Srikanth N et al respectively showed 2nd to 3rd decade as the common age group affected by studied infections.^[6,10]

Fever was the universal presenting feature as patients presenting with acute febrile illness were recruited in the study. Chills, headache and generalized body ache were the second and the third common presenting feature along with fever.

Observation of physical examination findings showed that 35% had tachycardia and 25% had bradycardia. Karjalainen J et al, in their study on cardiac rhythm in febrile patients observed that tachycardia was present during febrile phase in majority of patients18. Whereas various studies showed that relative bradycardia is also a manifestation in patients presenting with dengue fever, viral fever and enteric fever.^[10,19]

In study conducted by Chhina RS et al. in 214 dengue patients Deranged total bilirubin was seen in 19.5% of patients whereas AST and ALT derangements were seen in 97.7% and 93.9% patients respectively6. In 50 patients with enteric fever as studied by Srikanth N et al. normal AST was seen in 28 patients whereas ALT was normal in 29 patients. In the same study bilirubin elevation was seen in 5 patients.^[10] Whereas study in patients with rickettsial fever conducted by ML Hu et al. 30 patients noted that 29 had liver function test derangement.^[20] Whereas in our study of 40 patients involving various etiologies of fever normal LFT was seen in 9 patients and the rest had derangements of various degrees in LFT.

When AST and ALT elevation were studied quantitatively in our study, we noted that 2 patients had enzyme elevation in thousands whereas rest of the patients with transaminitis had lesser degrees of elevation of transaminases. Similarly in a study conducted by Jingar GC et al. in 96 patients with dengue 20 patients had more than 25 times elevation of AST and ALT.^[21]

In our study we noted that viral fever and dengue fever were the most common cause of acute febrile illness in inpatients. Similar results were seen in the study conducted by Guillebaud J et al. It was noted in the study that viral infections and malaria continue to predominate as the etiology of fever in primary health care center in Madagascar.^[22]

In summary in our study, we noted that infections are the predominant cause of acute febrile illness in north Karnataka locality. Among the various etiologies of fever, viral fever including dengue fever predominate the picture. Other noted causes include rickettsial fever, pneumonia, enteric fever and urinary tract infection in decreasing order of number of patients. LFT abnormalities are quite a common feature in patients presenting with acute febrile illness with 31 patients out of 40 having some derangement in LFT. Elevation in transaminases is the most common LFT abnormality noted. Milder elevation of AST and ALT was commoner than elevation of transaminases in thousands. Of the various etiologies of acute febrile illness in inpatients dengue showed highest rate of derangements in LFT. AST elevation more than ALT is more common abnormality in transaminase derangements.

Hence, we conclude that knowledge of various LFT abnormalities and their pattern in acute febrile illness of tropical countries is necessary as a diagnostic dilemma can be prevented as well as advanced investigations, since these liver test abnormalities settle as the underlying infection is treated or settles down.

CONCLUSION

Our study involved a smaller number of patients. A study involving a larger number of patients and following up the patients for the severity of disease and outcome would further highlight the importance of noting down the LFT abnormalities both for diagnosis as well as prognostication of patients presenting with acute febrile illness.

REFERENCES

- Wang Q, Zhao H, Liu LG, Wang YB, Zhang T, Li MH, Xu YL, Gao GJ, Xiong HF, Fan Y, Cao Y. Pattern of liver injury in adult patients with COVID-19: a retrospective analysis of 105 patients. Military Medical Research. 2020 Dec;7(1):1-8.
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DS, Du B. Clinical characteristics of coronavirus disease 2019 in China. New England journal of medicine. 2020 Apr 30;382(18):1708-20.
- Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395:507–13.
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497–506.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. jama. 2020 Mar 17;323(11):1061-9.

- Chhina RS, Goyal O, Chhina DK, Goyal P, Kumar R, Puri S. Liver function tests in patients with dengue viral infection.
- Itha S, Kashyap R, Krishnani N, Saraswat VA, Choudhuri G, Aggarwal R. Profile of liver involvement in dengue virus infection. National Medical Journal of India. 2005 May 1;18(3):127.
- 8. Daniel R, Philip AZ. A study of clinical profile of dengue fever in Kollam, Kerala, India.
- Szabo G, Romics L, Frendl G. Liver in sepsis and systemic inflammatory response syndrome. Clinics in liver disease. 2002 Nov 1;6(4):1045-66.
- Srikanth N, Kumar M. Liver function tests abnormalities in enteric fever-A recent update. Journal of Dental and Medical Sciences. 2015;14(3):17-24.
- Steele GM, Franco-Paredes C, Chastain DB. Noninfectious causes of fever in adults. The Nurse Practitioner. 2018 Apr 19;43(4):38-44.
- Shahid Z, Epstein DJ. Noninfectious causes of fever in hematologic malignancies. Are antibiotics still indicated?. Current Opinion in Infectious Diseases. 2023 Aug 1;36(4):209-17.
- DeWitt S, Chavez SA, Perkins J, Long B, Koyfman A. Evaluation of fever in the emergency department. The American Journal of Emergency Medicine. 2017 Nov 1;35(11):1755-8.
- 14. Agarwal R, Kapoor S, Nagar R, Misra A, Tandon R, Mathur A, Misra AK, Srivastava KL, Chaturvedi UC. A clinical study of the patients with dengue hemorrhagic fever during the epidemic of 1996 at Lucknow, India. Southeast Asian journal of tropical medicine and public health. 1999;30(4):735-40.
- Lledó L, González R, Gegúndez MI, Beltrán M, Saz JV. Epidemiological study of rickettsial infections in patients with hypertransaminemia in Madrid (Spain). International Journal of Environmental Research and Public Health. 2009 Oct;6(10):2526-33.
- Corica B, Tartaglia F, D'Amico T, Romiti GF, Cangemi R. Sex and gender differences in community-acquired pneumonia. Internal and Emergency Medicine. 2022 Sep;17(6):1575-88.
- Sun Y, Li H, Pei Z, Wang S, Feng J, Xu L, Gao P, Cao B, Zhan S. Incidence of community-acquired pneumonia in urban China: a national population-based study. Vaccine. 2020 Dec 14;38(52):8362-70.
- Karjalainen J, Viitasalo M. Fever and cardiac rhythm. Archives of internal medicine. 1986 Jun 1;146(6):1169-71.
- Lateef A, Fisher DA, Tambyah PA. Dengue and relative bradycardia. Emerging infectious diseases. 2007 Apr;13(4):650.
- Hu ML, Liu JW, Wu KL, Lu SN, Chiou SS, Kuo CH, Chuah SK, Wang JH, Hu TH, Chiu KW, Lee CM. Abnormal liver function in scrub typhus. The American journal of tropical medicine and hygiene. 2005 Oct 1;73(4):667-8.
- Jingar GC, Parmar D, JainAK, Kamble N, Jakhar R, Sudhir. Liver Dysfunction in Dengue Fever: A Prospective Study.Asian J. Med.Res. 2019;8(3):ME07-ME09.DOI: dx.doi.org/10.21276/ajmr.2019.8.3.ME3
- 22. Guillebaud J, Bernardson B, Randriambolamanantsoa TH, Randrianasolo L, Randriamampionona JL, Marino CA, Rasolofo V, Randrianarivelojosia M, Vigan-Womas I, Stivaktas V, Venter M. Study on causes of fever in primary healthcare center uncovers pathogens of public health concern in Madagascar. PLoS neglected tropical diseases. 2018 Jul 16;12(7):e0006642.