Research Article

The role of thrombocytopenia in the clinical course of leptospiral infection

Linda Rose Jose[1], M N Sumana[2*]

[1]Research Scholar, [2]Professor, Department of Microbiology, JSS Medical College and Hospital, Mysore, Karnataka, INDIA.
Email: mnsumana12@gmail.com

Abstract

Aim: This study is aimed to find out the incidence of thrombocytopenia in leptospirosis patients and to correlate thrombocytopenia with other parameters like hepatorenal failure, lung involvement and bleeding manifestations. **Material and Methods**: This study was conducted at Department of Microbiology, JSS Medical College and Hospital, Mysore, India from September 2014 to February 2015. Ethical approval was obtained from the Institutional Ethics Committee. The medical records of all serologically confirmed leptospirosis patients were retrospectively reviewed. Thrombocytopenia was then categorized as mild, moderate and severe and then correlated with renal dysfunction, hepatic dysfunction and haemorrhagic manifestations along with the course of infection. **Results**: A total of 60 patients were serologically positive for leptospirosis during this study period. Thrombocytopenia was observed in 52/60 cases, bleeding manifestations were seen in11, 43 had hepatic failure, 22 had renal failure. **Conclusion**: Thrombocytopenia in patients with Pyrexia of Unknown Origin (PUO) should alert physicians to the differential diagnosis of leptospiral infection and prompt the institution of appropriate therapy. It is important to recognize thrombocytopenia early in the course of leptospirosis so that appropriate steps can be taken to prevent further complications associated with thrombocytopenia in such patients.

Keywords: Leptospirosis, Thrombocytopenia, hepatic dysfunction, renal dysfunction, bleeding manifestations.

[*]**Address for Correspondence:**
Dr. M. N. Sumana, Professor, Department of Microbiology, JSS Medical College and Hospital, Mysore, Karnataka, INDIA.
Email: mnsumana12@gmail.com
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INTRODUCTION

Leptospirosis is a zoonotic disease which is more prevalent in developing countries. It has a wide clinical spectrum ranging from mild febrile illness to severe icteric disease with renal failure (Weil's disease) that can be fatal[1]. Thrombocytopenia is one among the most common haemotological manifestation in leptospirosis. Thrombocytopenia is often observed in connection with hemorrhagicpneumopathy and is considered as a predictor of the development of acute respiratory failure[2]. The potential causes of thrombocytopenia that are taken into consideration include vasculitis, decreased thrombocyte production by bone marrow, increased peripheral destruction of thrombocytes which is immune mediated caused by antiplatelet antibodies and increased peripheral platelet consumption due to wide spread haemorrhages[3]. Thrombocytopenia is often associated with hepatorenal dysfunction. In this regard, the present study was retrospectively carried out to find out the prevalence of thrombocytopenia in serologically positive Leptospira patients and was correlated with other parameters like hepatic dysfunction, renal dysfunction and haemorrhagic manifestations.

MATERIALS AND METHODS

This retrospective study was conducted during September 2014 to February 2015 in a tertiary care center, Mysore, Karnataka. Only those patients who were serologically positive for leptospirosis were included in this study. The protocol of this study was approved by the ethics committee of the institution. All the cases suspected of leptospirosis were screened with IgM ELISA (Panbio, Brisbane, Australia) and ICT which detects both IgG and IgM (Standard Diagnostics, Haryana). Only the

serologically positive subjects were retrospectively analyzed and incidence of thrombocytopenia was assessed. Thrombocytopenia was categorized into severe $\leq 20\times 10^9$ /L, moderate between 20 to 50 $\times 10^9$/L andmild between 50 to 100 $\times 10^9$/L. It was then clinically correlated with other parameters like renal dysfunction, hepatic dysfunction and hemorrhagic manifestations. Renal dysfunction was defined as the degree of increase in the levels of blood urea nitrogen or serum creatinine or both above normal range. Normal reference range - BUN: 10-15 mg%, Creatinine: 0.8 – 1.4 mg/dl or associated oliguria or anuria. Hepatic dysfunction was defined as any degree of increase in the level of bilirubin or liver enzymes. Normal reference range of bilirubin: up to 1 mg/dl,SGOT -up to 40 U/L and SGPT- upto 37U/L. Hemorrhagic manifestations were categorized as major and minor. Adult respiratory distress syndrome, gastrointestinal bleeding, hematuria and intracranial bleeding were included under major manifestations and rash, conjunctival hemorrhages, petechial hemorrhages and epistaxis were included under minor. Sepsis was determined by clinical evidence of infection, plus a systemic inflammatory response to the infection, which included two or more of the following conditions: (i) Temperature > 38ºC or < 36ºC; (ii) Heart rate > 90 beats/min; (iii) White blood cell count > 12000 cells/ mm^3, < 4000 cells/mm^3 or > 10% immature forms.

RESULTS

A total of 60 patients were serologically positive for leptospirosis during this study period. Out of which 41 were males and 19 were females. The mean age was 41.2 (range 30-72). The total number of patients with thrombocytopenia was 52. Out of which 7 had severe thrombocytopenia, 24 had moderate thrombocytopenia and the rest had mild thrombocytopenia.Haemorrhagic manifestations were seen in 18% (11) of patients among which 2 had major haemorrhagic manifestations and 9 had minor manifestations. In this group thrombocytopenia was seen in all 11 patients. Total number of patients with renal dysfunction was 22 (36.6%) out of which 20 (33.3%) had thrombocytopenia and 2 had normal platelet counts. Total number of patients with hepatic dysfunction was 43(71.6%) out of which 36 had thrombocytopenia and 7 had normal platelet counts. Table: 1 shows the clinical characteristics and laboratory findings of 60 serologically positive patients with leptospirosis with or without thrombocytopenia

Table 1: Clinical characteristics and laboratory findings of 60 serologically positive patients with leptospirosis with or without thrombocytopenia

Characteristics	Mean Values	
	Thrombocytopenic patients (n=52)	Non-thrombocytopenic patients (n=8)
Age(years)	41.2	28.6
Haemoglobin(g/dl)	11.52	13.8
White Blood cells($\times 10^3$ mm^3)	10.8	10.1
Thrombocytopenia($\times 10^9$/L)	52	321
BUN(mg/dl)	88	28.7
Creatinine(mg/dl)	3.13	1.28
Oliguria /Anuria(n)	9	0
Alanine amino Transferase/SGPT(IU/L)	157.1	367.3
Aspartate Amino Transferase/SGOT(IU/L)	159.3	201.6
Creatine phosphokinase (IU/L)	794	195.3
Total/Direct Bilirubin(mg/dl)	19/18	28.6/20.3
Bleeding(n)	11	0
Hepatic dysfunction(n)	36	7
Renal Failure(n)	20	2
Duration of Jaundice(days)	5.1	-
Sepsis(n)	46	2

DISCUSSION

Leptospirosis is one among the many infectious diseases of global importance and also one of the many medical conditions responsible for undifferentiated febrile illness especially, in tropical and subtropical regions. Leptospirosis is commonly seen in regions with poor socioeconomic conditions. The increased incidence of leptospirosis in males which was 68.3% during this study period might be because leptospirosis is considered as an occupational hazard. This is similar to the studies done by Sumana *et al*. (2014), Turgut *et al.* (2002) and Parimal *et al*. (2014) in which incidence in males were 77.7%, 80.5% and 81.6% respectively. Leptospirosis is characterized by a broad spectrum of symptoms[6]. Even in the subjects included in this study showed a similar spectrum of clinical manifestations with fever being the

predominant one followed by head ache and myalgia. This is similar to the studies by Daher *et al* (2003) and Nicodemo *et al* (1990).Thrombocytopenia can occur during leptospiral infection, particularly when sepsis is present[3]. In this study sepsis occurred in 88.4% of subjects with thrombocytopenia which proves this. Thrombocytopenia is a common finding in leptospirosis, occurring in 40.0 – 86.6% of infections. Few studies, however, have focused on thrombocytopenia and its relationship to other clinical and laboratory findings. The exact pathogenesis of thrombocytopenia in leptospirosis is unknown[9,10].Further investigations on this matter might throw light into several of the anomalies regarding the association of thrombocytopenia and its impact on patients with leptospirosis. Edwards *et al* (1982) in their study have reported renal failure up to 72.2% in thrombocytopenic patients and 21.4% in patients with normal platelet counts. This is in contradiction to our study where renal dysfunction was seen in 38.4% of patients with thrombocytopenia. Study by Yang *et al*. (2005) reported hepatic failure in 63.6% of patients with leptospirosis. Similar higher incidence was observed during the course of this study. Thrombocytopenia in leptospirosis is associated with worse prognosis. In some studies, mortality has been correlated with thrombocyte count especially when it progresses to Weil's disease[13]. However during this study period, no mortality was reported. The results of our study suggest that thrombocytopenia is associated with various complications of leptospirosis and appropriate treatment modality should be adopted at the earliest to prevent these.

CONCLUSION

Thrombocytopenia should be considered as an important contributing factor in the pathogenesis of leptospirosis. It might also become a reason for increased mortality and morbidity in this disease. So it becomes mandatory to anticipate and diagnose thrombocytopenia early in the course of leptospirosis. Platelet transfusion can be recommended as and when required which will help in preventing further complications.

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REFERENCES

1. Vinetz JM. Leptospirosis. CurrOpin Infect Dis.2001; 14(5): 527-38.
2. Nicodemo AC, Del Negro G, Amato NV, Thrombocytopenia and leptospirosis. Rev Inst Med Trop Sao Paulo. 1989; 31:71-79.
3. Turgut M, Sunbul M, Bayirli D, Bilge A, LeblebicigluH, Thrombocytopenia Complicating the clinical course of leptospiral infection, The Journal of International Medical Research.2002;30:535-540.
4. Sumana MN, Linda RJ, Tabasum BM, Seroprevalence of Dengue and Leptospira co-infection in Mysore, Karnataka: A study in children at a tertiary care hospital Int.J.Inv.Pharm.Sci.2014;2(3):774-778.
5. Parimal P, Alka N, Grishma T, Serological correlation of clinically suspected cases of Leptospirosis in Valsad, South Gujarat, NJIRM. 2014; 5(4):22-24.
6. Jayashree S, Moushumi S, Thrombocytopenia in leptospirosis and role of platelet transfusion. Asian J Transfus Science. 2007; 1(2):52-55.
7. Dahler E F, Brunetta DM, de Silva Junior GB, Puster RA, Patrocinio RM, Pancreatic involvement in fatal human leptospirosis. Clinical and Histopathological features, Rev Inst Med Trop Sao Paulo. 2003; 45:307-13.
8. Nicodemo AC, Del Negro G, Amato Neto V, Thrombocytopenia and leptospirosis, Rev Ins Med Trop Sao Paulo.1990;32:252-9.
9. Kirchner GI, Krug N, Bleck JS, Fliser D, Manns MP, Wagner S, Fulminant course of leptospirosis complicated by multiple organ failure. Z Gastroenterol.2001; 39:587-592.
10. Higgin R, Coustneau G, The pathogenesis of leptospirosis Hemorrhages in experimental leptospirosis in guinea pigs.Can J Comp Med. 1977;41:174-181.
11. Edwards CN, Nicholson GD, Everard CO, Thrombocytopenia in leptospirosis. Am J Trop Med Hyg. 1982; 31(4):827-829.
12. Yang HY, Hsu PY, Pam MJ, Wu MS, Lee CH, Yu CC *et al*. Clinical distinction and evaluation of leptospirosis in Taiwan: A case control study, J Mephrology. 2005; 18:45-53.
13. Tantitanawat S, TanjathamS, Prognosticfactors associated with leptospirosis, J Med Assoc Thai.2003; 86(10):925-931.

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