Original research article

A Study of Hepatic Dysfunction in Children admitted with Fever with Thrombocytopenia

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Abstract

Background: Infections frequently cause the disease known as febrile thrombocytopenia. The goal of the current study is to understand the underlying causes of fever and thrombocytopenia as well as its varied manifestations and its hepatic dysfunctions in children admitted with fever and thrombocytopenia in our tertiary care hospital in south India.

Methods: A Pre structured proforma was used to obtain information from the parents. Clinical features consisting of respiratory distress (tachypnoea, retractions), abdominal distension, tender hepatomegaly, and Jaundice are recorded at the time of admission. Laboratory investigations included CBP, Platelet count, Coagulation profile including INR, PCV, Serum proteins, serum Albumin, Total bilirubin, Aspartate aminotransferase (AST) Alanine aminotransferase (ALT).

Results: The analysis of different liver enzymes and bilirubin levels was studied in the current study. The high AST levels were found in 10% of cases out of which 50% were in group II. The ANOVA analysis between the groups and AST values found p-values were significant. The ALT levels in the study were between the groups and >132 ALT values were found in n=9 cases out of which 77.78% were in group II the p-values were found to be significant. The serum alkaline phosphatase ALP was found in n=2 cases and they were in group II. Similarly, high levels of serum bilirubin were found in n=3 cases and all these cases belonged to group II and p-values were significant.

Conclusion: In this study, we found 28% of the study sample had Dengue without warning signs 26% had dengue with warning signs 30% had Fever with Thrombocytopenia without warning signs and 16% had Fever with Thrombocytopenia with warning signs. It was found in this study that children with high AST values and high ALP values tend to have a poor prognosis and prolonged admission time as compared to those with lesser elevated values. In addition cases with high PT and aPTT, PCV >40 and platelet counts tend to have a severe form of the disease.

Keywords: Fever, Thrombocytopenia, AST (Aspartate Aminotransferase), ALP (Alanine aminotransferase), Alkaline Phosphatase (ALP), Dengue

Introduction

Fever and thrombocytopenia patients are becoming more common these days. The recent rise in infections is mostly to blame for the increase in instances. Patients with severe thrombocytopenia have a higher death rate and a higher risk of bleeding manifestations. [1] Platelets are responsible for maintaining both thrombosis and normal hemostasis. Thrombocytopenia-related bleeding appears as cutaneous and mucous membrane bleeding. Intracranial hemorrhage is a possibility in cases of thrombocytopenia. [2] Many factors can contribute to thrombocytopenia. Certain infections affect the hematopoiesis in general while having a greater impact on platelets. [3] Numerous illnesses, including Rubella, EBV

infection, Hepatitis B and C, Cytomegalovirus, and HIV infection, as well as subacute bacterial infections including Syphilis, leptospirosis, and endocarditis, resulting in immune-mediated death of platelets. Certain viral infections result in the production of autoantibodies, which cause the immune system to destroy platelets. Because of severe thrombocytopenia, ITP manifests in a healthy youngster as mucous membrane and skin bleeding. [3] Due to severe thrombocytopenia, many bacterial and viral infections result in disseminated intravascular coagulation. The most frequent causes of thrombocytopenia include leptospirosis, malaria, typhoid, scrub typhus, chikungunya, and dengue fever. Fever and thrombocytopenia are the wintertime cases that the OPD sees the most frequently. [4, 5] Some individuals with fever and thrombocytopenia go on to develop multiorgan dysfunction; these patients should be considered for admission to the intensive care unit. Their morbidity and death rates are high. The liver is the organ that is most frequently implicated in fever with thrombocytopenia instances. [6] This study was conducted to assess the liver function test's prognostic usefulness in predicting outcomes in patients hospitalized with fever and thrombocytopenia. The current stud aimed to evaluate the outcome of children with fever and thrombocytopenia admitted to our tertiary care hospital.

Material and Methods

This cross-sectional observational study was conducted in the Department of Pediatrics, Meenakshi Medical College Hospital and Research Institute (MMCHRI), Kanchipuram, Tamil Nadu. Institutional Ethical approval was obtained for the study. Written consent was obtained from the parents/guardians of the cases included in the study after explaining the nature of the study in the vernacular language.

Inclusion criteria

1. Aged from 1 month to 12 years.
2. Diagnosed with thrombocytopenia.
3. Fever >99.9-degree F
4. Admitted to pediatric wards of the Hospital.
5. Those cases were where voluntary consent of parents was obtained.

Exclusion criteria

1. Positive for HbsAg, HAV, HCV
2. Patients with a history of liver diseases
3. Cases of thrombocytopenia without fever
4. Idiopathic thrombocytopenic purpura
5. Patient on treatment with antiplatelet drugs /other drugs causing thrombocytopenia.

A Pre structured proforma was used to obtain information from the parents. The following parameters at admission are studied to predict the outcome among the study group which includes the demographic profile of the cases in the study. A note was made regarding the warning signs of thrombocytopenia (warning symptoms including abdominal pain, vomiting, hematemesis, reduced urine output, and passing black color stools). Clinical features consisting of respiratory distress (tachypnea, retractions), abdominal distension, tender hepatomegaly, and Jaundice are recorded at the time of admission. Laboratory investigations included CBP, Platelet count, Coagulation profile including INR, PCV, Serum proteins, serum Albumin, Total bilirubin, Aspartate aminotransferase (AST) Alanine aminotransferase (ALT). The outcome was assessed as Dengue without warning signs DWOWS (Group I), Dengue with warning signs DWWS (Group II), Fever with thrombocytopenia with warning

signs FWTWOWS (Group III), Fever with thrombocytopenia without warning signs FWTWWS (Group IV).

Results

A total of n=50 cases were included in the study based on the inclusion and exclusion criteria. Out of n=50 cases n=27(54%) were males and n=23(46%) were females. The distribution of age group showed the minimum age of the case included in the study was 2 months and the maximum age was 12 years. In the maximum number of cases, 36% were in the group aged from 1 – 2 years. The mean age of the cohort was 5.66 ± 2.5 years. Details of age-wise distribution in the study have been depicted in table 1.

Table 1: Distribution of cases based on age.

Age group	*Frequency*	*Percentage*
0 - 1	5	10
1 - 2	18	36
3 - 5	8	16
6 - 8	7	14
9 - 10	7	14
11 - 12	5	10
Total	50	100

In this study based on the residence of the cohort, we found n=20(40%) were rural residents and n=30(60%) were urban residents. Taking cut off of serum bilirubin levels at 1.3 mg/dl we found out of n=50 cases n=47(94%) and n=3(6%) cases ad serum bilirubin levels greater than 1.3mg/dl. It is found that 62 % of the participant's blood samples shows a level of AST less than 40 (U/L) and 20% of the participant's blood samples shows a level of AST of more than 150 (U/L). It is found that 62% of the participant's blood samples shows a level of ALT of less than 32 and 18% of the participant's blood samples shows a level of ALT of more than 132. It is found that 97 % of the participant's blood sample shows a level of ALP less than 420 and only 3% shows an ALP level of more than 420 (U/L) details depicted in table 2.

Table 2: Distribution of the sample population based on the level of Liver enzymes.

	Frequency	*Percent*
AST level (U/L)		
<40	32	62.0
41-80	02	06.0
81-150	06	12.0
>150	10	20.0
Total	50	100.0
Level of ALT (U/L)		
<32	31	62.0
33-66	6	12.0
67-132	4	8.0
> 132	9	18.0
Total	50	100.0
Level of ALP U/L		
< 420	48	95.0
> 420	2	5.0

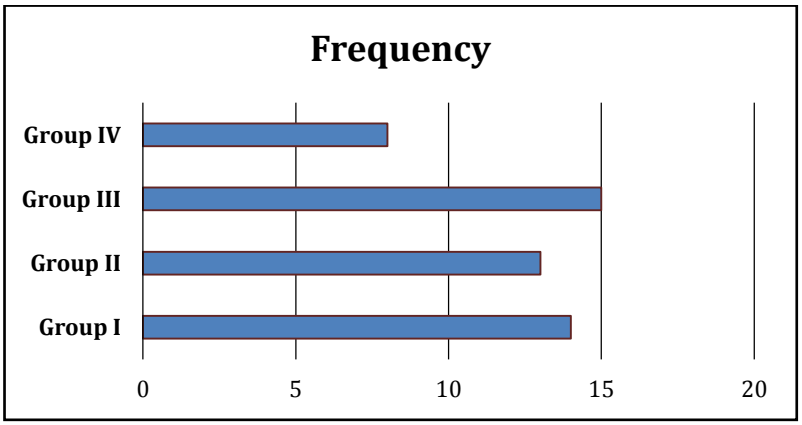
Total	100	100.0

It was found that 18% of the participant's blood samples shows an increased level of PT (APTT). Nearly one-fourth (26 %) of the participants' blood sample shows an increased level of PCV (35 – 40). The platelet counts of the participants showed that nearly three-fourths 70% of the participant's blood sample shows platelet count of 50K - 1.5L the association between Platelet count and the Outcome which is found to be statistically significant (P value = 0.02) and significant (table 3).

Table 3: Distribution of the sample population based on the level of PT APTT

	Frequency	Percent
Level of PT (APTT)		
Increased	9	18.0
Normal	41	82.0
Level of PCV (%)		
<30	13	26.0
30-35	12	24.0
35-40	13	26.0
>40	12	24.0
Level of Platelet /µl		
$<10 \times 10^3$	2	4.0
$10 - 30 \times 10^3$	5	10.0
$30 – 50 \times 10^3$	8	16.0
$50 \times 10^3 - 1.5\ 10^5$	35	70.0

This study observed that 28% of the study sample had Dengue without warning signs (group I), 26% had dengue with warning signs (Group II), 30% had Fever with Thrombocytopenia without warning signs (Group III) and 16% had Fever with Thrombocytopenia with warning signs (Group IV) details depicted in figure 1



The analysis of different liver enzymes and bilirubin levels was studied in the current study. The high AST levels were found in 10% of cases out of which 50% were in group II. The ANOVA analysis between the groups and AST values found p-values were significant. The ALT levels in the study were between the groups and >132 ALT values were found in n=9 cases out of which 77.78% were in group II the p-values were found to be significant. The serum alkaline phosphatase ALP was found in n=2 cases and they were in group II. Similarly, high levels of serum bilirubin were found in n=3 cases and all these cases belonging to group II p-values were significant and the details have been depicted in table 4.

Table 4: Distribution of liver enzymes and parameters with different groups

	Outcome				Total	P-value
	Group I	*Group II*	*Group III*	*Group IV*		
AST levels (U/L)						
<40	14 (43.75)	0 (0.00)	15(46.87)	3(9.37)	32 (100)	0.0014*
41-80	1(50.0)	0 (0.00)	0 (0.00)	1(50.0)	02 (100)	
81-150	1(16.67)	2(33.33)	0(0.00)	3(50.0)	06 (100)	
>150	0(0.00)	8(80.00)	0(0.00)	2(20.00)	10 (100)	
ALT levels (U/L)						
<32	14(45.16)	0(0.00)	15(48.38)	2(6.45)	31 (100)	0.0017*
33-66	1(16.67)	2(33.33)	0(0.00)	3(50.00)	6 (100)	
67-132	0(0.00)	4(100.0)	0(0.00)	0(0.00)	4 (100)	
>132	0(0.00)	7(77.78)	0(0.00)	2(22.22)	9 (100)	
Level of ALP U/L						
<420	14(29.16)	11(22.91)	15 (31.25)	8 (16.67)	48(100)	0.041*
>420	0(0.00)	2(100.0)	0(0.00)	0(0.00)	2(100)	
Serum Total Bilirubin (mg/dl)						
< 1.3	14(29.79)	10(21.27)	15(31.91)	8(17.02)	47(100)	0.0031*
> 1.3	0(0.00)	3(100.0)	0(0.00)	0(0.00)	3 (100)	

* Significant

Discussion

In recent years, one of the most frequent reasons for hospital admissions has been fever and thrombocytopenia. Both mortality and fatal hemorrhage are possible outcomes. Dengue and bacterial sepsis are the most frequent causes of these fatalities. The liver is often impacted in varying degrees of severity, from asymptomatic increases in liver enzymes to severe fulminant hepatitis. [7] Just a few studies have examined the extent of hepatic damage and involvement in fever with thrombocytopenia. This study's objective was to determine the relationship between hepatic dysfunction and treatment outcomes in children who have been hospitalized with fever and thrombocytopenia. Prospectively examined are all the children between the ages of 2 months and 12 years who were hospitalized with fever and thrombocytopenia throughout this time. Out of n=50 cases n=27(54%) were males and n=23(46%) were females. The distribution of age group showed the minimum age of the case included in the study was 2 months and the maximum age was 12 years. In the maximum number of cases, 36% were in the group aged from 1 – 2 years. The mean age of the cohort was 5.66 ± 2.5 years. Of them, 30% had fever and thrombocytopenia without warning indications, 26% had fever and thrombocytopenia with warning signals, and 28% had dengue without warning signs. Most of the children (30%) presented with thrombocytopenia without warning signs. Abdominal discomfort and soreness are the most typical warning signal found in these cases.

The most common clinical symptoms were abdominal pain and abdominal tenderness. In a similar study by Jayaratne S et al., [8] they also found the most common symptom was abdominal pain. The influence of platelet counts at the initial presentation was found to be significant and the p values were found to be (<0.03) n=3(6%) of cases with platelet count less than 10000 developed dengue with warning signs this observation was in concordance with that of Pires RJ et al., [9] where they found low platelet counts as one of the important warning signs. Aspartate transaminase (AST) levels were measured at the time of admission, and we found 62% of cases had AST below 40(U/L) and 12% has AST levels between 81 – 150(U/L) and 20% of cases had AST of > 150 (U/L). This demonstrates that the majority of

kids with probable dengue fever have elevated AST levels similar results were recorded by Roy A et al., [10] in their study. ALT levels in the study recorded at the admission were 62% of the participant's blood samples shows a level of ALT less than 32 and 18% of the participant's blood samples shows a level of ALT more than 132. It is found that 97 % of the participant's blood samples shows a level of ALP less than 420 and only 3% shows an ALP level of more than 420 (U/L). In this study out of n=50 cases, we found IgM dengue ELISA was positive in 54% of cases and IgM negative in 46% of cases.

Final IgM Dengue ELISA testing on 100 research participants revealed that 54% were IgM positive and 46% were IgM negative. Researchers looked at the relationship between the severity of liver enzyme increase and the IgM Dengue ELISA. 80% IgM positive is related to an AST enzyme increase >150(U/L), while 58.3% IgM positivity is associated with values between 81 and 150. IgM positive for dengue is related to an ALT enzyme increase of >132 (U/L) and IgM positivity for 67–132, respectively. We examined the relationship between liver enzyme increase and illness severity. With a significant p-value of <0.05, a link between illness severity and the degree of AST increase was found. This is similar to the research done by Sahana KS et al., [11] With a p-value of 0.05, there is a significant correlation between the ALT elevation's severity and the disease's severity. This is similar to the research by Nguyen TL et al., [12] found a significant p-value of 0.05 indicates a favorable connection between illness severity and thrombocytopenia severity. Comparable research has been done by Narayanan M et al., [13] at the time of admission, ALT levels are also assessed. ALT was below 32 in 62 (62% of cases). 11 (11%) patients had an ALT 33-66 (U/L) range. 18 (18%) of the patients had an ALT >132 (U/L), whereas 9 (9%) had an ALT 67-132 (U/L). This demonstrates that ALT levels are also elevated in addition to AST. an increase in AST that has a large p-value <0.05.

Conclusion

In this study, we found 28% of the study sample had Dengue without warning signs 26% had dengue with warning signs 30% had Fever with Thrombocytopenia without warning signs and 16% had Fever with Thrombocytopenia with warning signs. It was found in this study that children with high AST values and high ALP values tend to have a poor prognosis and prolonged admission time as compared to those with lesser elevated values. In addition cases with high PT and aPTT, PCV >40 and platelet counts tend to have a severe form of the disease.

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