Original Research Article

A Study of Predictors in Outcome of Fever with Thrombocytopenia in Children upto 12 Years

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Abstract:

Background: Fever with thrombocytopenia is one of the leading cause of mortality and morbidity in children <12 yrs. There are various infectious causes for fever with thrombocytopenia including deadly dengue fever and bacterial sepsis. Various studies have showed that there are many prognostic factors which are very useful in predicting the outcome. These factors also alert the treating paediatrician in taking many crucial decisions like whether to treat the case as opd or to admit and treat aggressively. Based on this aim of our study is to evaluate the clinical and laboratory parameters in predicting the outcome of children with fever with thrombocytopenia below 12 years.

Material and Methods: All the patients between 1month to 12 years presenting with the complaints of fever (>99.9degree F) with thrombocytopenia (less than 1,50,000/μL) were included in the study . Pre structured proforma was used to obtain information from the parents which includes general characteristics and blood parameters, after getting consent, detailed history, clinical details and investigations were collected and entered in the proforma. Blood investigations, Ultrasonogram abdomen and chest findings was recorded. Outcome was assessed as morbidity in the form of only fever, fever with bleeding and fever with shock.

Results: Among 100 cases taken in our study, 62% children had only fever. 15% children had fever with bleeding. 23% children had fever with shock. 31% of children admitted with respiratory distress. Among admissions 55% children admitted with platelet count less than 1lakh. 86% children had ascites.

Conclusion: Late visit to hospital with prolonged fever and warning symptoms influence poor outcome in these children. Children presenting with altered sensorium, respiratory distress, abdominal distension, hepatomegaly and dehydration had poor outcome as bleeding and shock. Chest X-ray, Ultrasonagram chest and abdomen revealing pleural effusion and ascites at the time of admission showed more morbidity. Children with Positive C-Reactive protein at the time of admission and serology positive for Dengue had more morbidity as bleeding and shock.

Keywords: Fever, Thrombocytopenia, Children.

Introduction

Thrombocytopenia can be defined as a low number of platelets in the circulating blood. A normal platelet count ranges from 1, 50,000 to 4, 50,000 platelets/μL of blood [1]. Many times they are asymptomatic. Some patients will develop symptoms like bruising, purpura, petechiae, nose bleeding and gum bleeding.

Rarely, there may be life threatening symptoms like CNS bleeding, GIT bleeding when platelet count falls below 5000/mm3. Infections with protozoa, bacteria and viruses can cause thrombocytopenia with or without disseminated intravascular coagulation [2]. Commonly dengue, malaria, scrub typhus and other rickettsial infections, meningococci, leptospira and certain viral infections present as fever with thrombocytopenia [3]. Fever with thrombocytopenia is commonly seen in OPD setup especially during monsoon and perimonsoon period. Occasionally these patients can go on to develop a stormy course with multiorgan dysfunction requiring intensive care unit admission associated with high morbidity and mortality [4]. Some of the infections are self-limiting but some patients should be continuously monitored to prevent lethal complications [5].

With early recognition and prompt initiation of treatment, disease related morbidity and mortality can be limited. With there being an increasing number of cases detected, a study for the prognostic factors considered important [6].

Fever with thrombocytopenia is one of the leading cause of mortality and morbidity in children <12 yrs. There are various infectious causes for fever with thrombocytopenia including deadly dengue fever and bacterial sepsis. The admission rate of fever with thrombocytopenia in tertiary care hospital remains high in previous 5 years. The mortality and morbidity also remains high.

Various studies have showed that there are many prognostic factors which are very useful in predicting the outcome. These factors also alert the treating pediatrician in taking many crucial decisions like whether to treat the case as opd or to admit and treat aggressively. This study includes all the children below 12yrs admitted as fever with thrombocytopenia and aims to identify various clinical, laboratory parameters for predicting the outcome in tertiary care centre hospital. Based on this aim of our study is to evaluate the clinical and laboratory parameters in predicting the outcome of children with fever with thrombocytopenia below 12 years.

Materials and Methods

Our study was conducted at Department of Pediatrics, Tirunelveli Medical College Hospital in All cases of fever with thrombocytopenia age less than 12yrs and more than 1month admitted in Pediatric Department of Tirunelveli Medical College Hospital as a prospective observational study for a period of 18 months

All the patients between 1month to 12 years presenting with the complaints of fever (>99.9degree F) with thrombocytopenia (less than 1,50,000/μL) were included in the study , whereas patient presenting with thrombocytopenia without fever, diagnosed case of immune thrombocytopenic purpura, patient with thrombocytopenia already diagnosed to have hematological disorder/malignancy or on treatment with chemotherapy and other immunosuppressive agent Diagnosed cases of platelet disorder and dysfunction, patients on treatment with antiplatelet drugs and other drugs causing thrombocytopenia, patients with cirrhosis and chronic liver disease were excluded. Children of those parents who did not give consent to undergo study was excluded.

Pre structured proforma was used to obtain information from the parents which includes general characteristics and blood parameters, after getting consent, detailed history, clinical details and investigations were collected and entered in the proforma. It includes age, sex, and locality. History regarding day of fever, warning symptoms including abdominal pain, vomiting, hemetemesis, reduced feeding, reduced urine output, passing black colored stools are recorded at the time of admission. Clinical features includes general condition, respiratory distress (tachypnea,

retractions), abdominal distension, hepatomegaly, dehydration (dry oral cavity, increased thirst) are recorded at the time of admission.

Blood investigations including total count (age specific values taken as normal), platelet count, PCV, RFT (normal Urea <40, creatinine 0.5-0.8), Liver enzymes (normal AST <40, ALT <40, ALP <150), serum proteins (normal Total protein 6, serum albumin 4, serum globulin 2), coagulation profile (normal PT 16, APTT 36, INR <1.5), C-Reactive protein (Positive: >0.6mg/dl), Serology & Culture sensitivity are recorded at the time of admission. Chest x-ray, Ultrasonogram abdomen and chest findings including ascites, pleural effusion is also recorded. Outcome was assessed as morbidity in the form of only fever, fever with bleeding and fever with shock.

Data collected and recorded in the proforma during the whole study period were entered in Microsoft Excel Sheet and analyzed by Kruskal Wallis test using SPSS software version 23.0 to identify whether various risk factors for morbidity and mortality for fever with thrombocytopenia are statistically significant or not.

Results:

Among 100 cases taken in our study, 62% children had only fever. 15% children had fever with bleeding. 23% children had fever with shock.

In our study 42% children were less than 5yrs and 58% were more than 5yrs. Among which 6 had bleeding in less than 5 yr age group 9 had bleeding in more than 5 year age group. There is no significance in age factor regarding the morbidity in these children admitted for fever with thrombocytopenia. Among total admissions 49% were male children and 51% were female children. There is no significant influence of sex of children in the morbidity of these children admitted for fever with thrombocytopenia.

In our study population, 89% were from rural areas and 11% were from urban areas. There is no significant influence of locality in predicting the morbidity of children admitted for fever with thrombocytopenia.

Among our admissions 35% of children presented with fever less than 4 days and 65% of children presented with fever more than 4 days. There is a significant influence of day of fever at presentation in the outcome. Among 15% children developed fever with bleeding, 12% of them admitted with fever for more than 4 days. Among 23% children developed fever with shock, 20% of them admitted with fever for more than 4 days. Among admissions 54% of children admitted with warning symptoms including abdominal pain, vomiting, reduced urine output and black colored stools. There is a significant influence of warning symptoms in

predicting the outcome of fever with thrombocytopenia. Among 15% children developed fever with bleeding, 12% children admitted with warning symptoms. Among 23% children developed fever with shock, 20% children admitted with warning symptoms

Among admissions 73% children admitted with normal general condition and 27% children admitted with altered general condition. There is a significant influence of general condition at presentation in the outcome. Among 73% children presented with normal general condition, 62% children developed only fever .21% of children developed fever with shock among 27% children admitted with altered general condition.

Among admissions 31% of children admitted with respiratory distress. There is a significant influence of respiratory distress at presentation in the outcome. Among 31% of children admitted with respiratory distress, 21% of them developed fever with shock and 8% of them developed fever with

bleeding. Among admissions, 30% children admitted with abdominal distension. There is a significant influence of abdominal distension at presentation in the outcome. Among 30% of children admitted with abdominal distension, 21% of them developed fever with shock and 7% of them developed fever with bleeding.

Among admissions, 68% children admitted with hepatomegaly. There is a significant influence of hepatomegaly at presentation in the outcome. Among 68% of children admitted with hepatomegaly, 22% of them developed fever with shock and 14% of them developed fever with bleeding.

Among admissions, 40% children admitted with features of dehydration. There is a significant influence of dehydration at presentation in the outcome. Among 40% of children admitted with dehydration, 21% of them developed fever with shock and 12% of them developed fever with bleeding.

Table 1: Relation between different parameters and outcome

Parameters		Only Fever (N=62)	Fever With Bleeding (N=15)	Fever With Shock (N=23)	Total	P Value
Age	< 5yr	24	6	12	42	0.671
	> 5yr	38	9	11	58	
Sex	Male	29	8	12	49	0.851
	Female	33	7	11	51	
Days Of Fever	< 4 Days	29	3	3	35	0.017
	> 4 Days	33	12	20	65	
Warning Signs	Yes	22	12	20	54	0.001
	No	40	3	3	46	
General Condition	Alert	62	9	2	73	0.001
	Not Alert	0	6	21	27	
Respiratory Distress	Present	2	8	21	31	0.001
	Absent	60	7	2	69	
Abdominal Distension	Present	2	7	21	30	0.001
	Absent	60	8	2	70	
Hepatomegaly	Present	32	14	22	68	0.001
	Absent	30	1	1	32	
Dehydration	Present	7	12	21	40	0.001
	Absent	55	3	2	60	
Ascites	Present	53	13	20	86	0.001
	Absent	9	2	3	14	
Pleural Effusion	Present	58	14	19	91	0.001
	Absent	4	1	4	9	

Among admissions, 55% children had leucopenia, 33% children had normal count and 12% children had leukocytosis. There is no significant influence of total count in predicting the outcome.

Among admissions 55% children admitted with platelet count less than 1lakh. There is a significant influence of initial platelet count at presentation in the outcome. Among 45%of children admitted with platelet count less than 1lakh, 21% of them

developed fever with shock and 10% of them developed fever with bleeding.

Among admissions 29% children admitted with PCV more than 40. There is a significant influence of packed cell volume at presentation in the outcome. Among 29% of children admitted with packed cell volume more than 40, 14% of them developed fever with shock and 7% of them developed fever with bleeding. Among admissions 6% children had renal function test abnormality.

There is a significant influence of abnormal Renal function test at presentation in the outcome. Among 6% of children admitted with abnormal renal function test, 5% of them developed fever with shock and 1% of them developed fever with bleeding.

Among admissions, 16% children had elevated liver enzymes. There is a significant influence of elevated liver enzymes at presentation in the outcome. Among 16% of children admitted with respiratory distress, 3%of them developed fever with shock and 6% of them developed fever with bleeding. Among admissions, no children had reduced serum proteins. Among admissions no children presented with low serum proteins. So no significance of reduced proteins in outcome.

Among admissions 15% children admitted with abnormal coagulation profile. There is a significant influence of abnormal coagulation profile at presentation in the outcome. Among 15% of children admitted with abnormal coagulation profile, 2% of them developed fever with shock and 11% of them developed fever with bleeding.

Among admissions 86% children had ascites demonstrated by utrasonagram abdomen. There is a significant influence of ascites at presentation in the outcome. Among 86% of children admitted with ascites, 20% of them developed fever with shock and 13% of them developed fever with bleeding. Among admissions 91% children had pleural effusion demonstrated by chest X-ray and ultrasonagram chest.   There is a significant influence of pleural effusion at presentation in the outcome. Among 91% of children admitted with pleural effusion, 19% of them developed fever with shock and 14% of them developed fever with bleeding.

Among admissions 47% children had positive C - reactive protein. There is a significant influence of C - reactive protein at presentation in the outcome. Among 47% of children admitted with positive C - reactive protein, 21% of them developed fever with shock and 11% of them developed fever with bleeding.

Table 2: Relation between blood parameters and outcome

Parameters		Only Fever (N=62)	Fever With Bleeding (N=15)	Fever With Shock (N=23)	Total	P Value
Total Count	Leukopenia	32	9	14	55	0.864
	Normal	29	3	1	33	
	Leucocytosis	1	3	8	12	
Platelet Count	< 1 Lakh	14	10	21	45	0.001
	> 1 Lakh	48	5	2	55	
Pcv	< 40	54	8	9	71	0.001
	> 40	8	7	14	29	
Deranged Rft	Present	0	1	5	6	0.001
	Absent	62	14	18	94	
Elevated Lft	Present	7	6	3	16	0.001
	Absent	55	9	20	84	
Serum Protein	Normal	62	15	22	100	1
	Reduced	0	0	0	0	
Coagulation Profile	Normal	60	4	21	85	0.001
	Abnormal	2	11	2	15	
C Reactive Protein	Positive	15	11	21	47	0.001
	Negative	47	4	2	53	

Among admissions, 66% had dengue serology positive, 11% had positive widal test, 8% children had positive urine culture and sensitivity. There is a significant influence of etiology in predicting the morbidity as 18% of children having positive serology for dengue developed fever with shock among 23%. 13% of children having positive serology for dengue developed fever with bleeding among 15%.

Table 3: Etiology Vs Clinical Outcome

Etiology	OnlyFever (N=62)	Fever With Bleeding (N=15)	FeverWith Shock (N=23)	Total
Dengue	35	13	18	66
Widal	11	0	0	11
Urine Culture	8	0	0	8
Blood Culture	0	1	4	5
Lepto-Igm	0	1	1	2
Scrub-IGM	4	0	0	4
Malaria	4	0	0	4
Kruskal Wallis Test				
P Value - 0.001				
Significant				

Discussion

Fever with thrombocytopenia is one among the common causes for hospital admissions in India in recent times. In some children it can lead to deadly bleeding and shock and leads to death. Dengue and bacterial sepsis are the common causes for these deaths.

Various studies showed some of the predicting factors in the outcome of fever with thrombocytopenia. As the fever cases are increasing in admissions, there is a need of some prognostic factors at admission time to delineate these children to whom the monitoring and treatment is very essential.

The aim of my study is to identify those factors at the time of admission in predicting the outcome of fever with thrombocytopenia in terms of morbidity. It was conducted in pediatrics department of Tirunelveli Medical College during the period of 18 months in children between 1 month to 12 years admitting with fever with thrombocytopenia in this period are studied prospectively.

Totally 100 cases were studied. Among them, 62% developed only fever, 15% developed fever with bleeding and 23% developed fever with shock. In our study, age, sex and locality of the patient didn't show much significance with p values of about 0.671, 0.851 and 0.174.

Among 100 children in our study, 65% children presented with fever more than 4 days. Among these 65% children, 20% children developed fever with shock and 12% children developed fever with bleeding with p value of about 0.017. So day of fever shows significant correlation with outcome. This was comparable with other study done by Akshatha Rao Aroor, Rama Prakasha Saya et al [7].

There is a significant influence of warning symptoms in predicting the outcome of fever with thrombocytopenia with p value of 0.001. Among 15% children developed fever with bleeding, 12% children admitted with warning symptoms. Among 23% children developed fever with shock, 20% children admitted with warning symptoms. This was comparable with the study done by N S Shewale [8] which also showed there was more morbidity if the child presenting with warning signs.

There is a significant influence of general condition at presentation in the outcome with p value of 0.001. Among 73% children presented with normal general condition, 62% children developed only fever .21% of children developed fever with shock among 27% children admitted with altered general condition. This was comparable with the study done by Bhave S, Rajput CS et al [9] which also showed increased morbidity in children presenting with poor general condition.

There is a significant influence of respiratory distress at presentation in the outcome with p value of 0.001. Among 31% of children admitted with respiratory distress, 21% of them developed fever with shock and 8% of them developed fever with bleeding. This was comparable with other study done by Akshatha Rao Aroor, Rama Prakasha Saya et al [7] which also showed that children presenting with respiratory distress had poor prognosis.

There is a significant influence of abdominal distension at presentation in the outcome with p value of 0.001.Among 30% of children admitted with abdominal distension, 21% of them developed fever with shock and 7% of them developed fever with bleeding. This was comparable with the study done by N S Shewale [8] which also showed there was more morbidity if the child presenting with clinical abdominal fluid collection.

There is a significant influence of hepatomegaly at presentation in the outcome with p value of 0.001.Among 68% of children admitted with hepatomegaly, 22% of them developed fever with shock and 14% of them developed fever with bleeding. This was comparable with the study done by Jain H. [10] which also showed increased morbidity with children presenting with hepatomegaly.

There is a significant influence of dehydration at presentation in the outcome with p value of 0.001. Among 40% of children admitted with dehydration, 21% of them developed fever with shock and 12% of them developed fever with bleeding. This was comparable with the study done by Dhooria G, Bhat D et al [11] which also showed increased morbidity if the children presenting with features of dehydration.

There is no significant influence of total count in predicting the outcome with p value of 0.864. There is a significant influence of initial platelet count at presentation in the outcome with p value of 0.001. Among 45%of children admitted with platelet count less than 1lakh, 21% of them developed fever with shock and 10% of them developed fever with bleeding. This was comparable with the study done by Gomber S. Ramachandran VG, Kumar S, et al. [12] which also showed that increased morbidity in children presenting with low platelet count.

There is a significant influence of packed cell volume at presentation in the outcome with p value of 0.001. Among 29% of children admitted with packed cell volume more than 40, 14% of them developed fever with shock and 7% of them developed fever with bleeding. This was comparable with the study done by Balasubramanian S, Anandathan K, Shivabalam S et al. [13] which also showed children with increased hematocrit at presentation had more morbidity.

There is a significant influence of abnormal Renal function test at presentation in the outcome with p value of 0.001. Among 6% of children admitted with abnormal renal function test, 5% of them developed fever with shock and 1% of them developed fever with bleeding. This was comparable with the study done by Christian S. Haas, Walter Lehne et al. [14] which also showed increased morbidity in children presenting with altered renal functions.

There is a significant influence of elevated liver enzymes at presentation in the outcome with p value of 0.001. Among 16% of children admitted with elevated liver enzymes, 3% of them developed fever with shock and 6% of them developed fever with bleeding. This was comparable with the study done by Wahid SF, Sanusi S, Zawawi MM et al [15] which also showed that the morbidity was high if the children presenting with elevated liver enzymes.

There is a significant influence of abnormal coagulation profile at presentation in the outcome with p value of 0.001. Among 15% of children admitted with abnormal coagulation profile, 2% of them developed fever with shock and 11% of them developed fever with bleeding. This was

comparable with the study done by Fariz-Safhan MN, Tee HP, Abu Dzarr GA et al [16] which also showed increased morbidity in children presenting with abnormal coagulation profile.

There is a significant influence of ascites at presentation in the outcome with p value of 0.001. Among 86% of children admitted with ascites, 20% of them developed fever with shock and 13% of them developed fever with bleeding. This was comparable with the study done by N S Shewale [8] which also showed there was more morbidity if the child presenting with clinical abdominal fluid collection.

There is a significant influence of pleural effusion at presentation in the outcome with p value of 0.001. Among 91% of children admitted with pleural effusion, 19% of them developed fever with shock and 14% of them developed fever with bleeding. This was comparable with the study done by N S Shewale [8] which also showed there was more morbidity if the child presenting with pleural fluid collection.

There is a significant influence of C - reactive protein at presentation in the outcome with p value of 0.001. Among 47% of children admitted with positive C - reactive protein, 21% of them developed fever with shock and 11% of them developed fever with bleeding. This was comparable with the study done by Chien-Chih Chen et al [17] which also showed increased morbidity in children presenting with positive C - reactive protein.

There is a significant influence of etiology in predicting the morbidity as 18% of children having positive serology for dengue developed fever with shock among 23%. 13% of children having positive serology for dengue developed fever with bleeding among 15%. This was comparable with the study done by Akshatha Rao et al [7] which also showed that children having serology positive for dengue among the causes for fever with thrombocytopenia had more morbidity.

Conclusion

In our study, 23% developed fever with shock and 15% developed fever with bleeding. Age, Sex and Locality of the children didn't show much influence in outcome. Late visit to hospital with prolonged fever and warning symptoms influence poor outcome in these children. Children presenting with altered sensorium, respiratory distress, abdominal distension, hepatomegaly and dehydration had poor outcome as bleeding and shock. Total count of the children at the time of admission didn't show any influence in outcome. Children with platelet count less than 1 lakh, elevated hematocrit, abnormal renal function test, elevated liver enzymes and abnormal coagulation

profile at the time of admission had poor outcome as bleeding and shock. Chest X-ray, Ultrasonagram chest and abdomen revealing pleural effusion and ascites at the time of admission showed more morbidity. Children with Positive C-Reactive protein at the time of admission and serology positive for Dengue had more morbidity as bleeding and shock.

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