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Original Research Article

A STUDY ON SIGNIFICANCE OF VARIATIONS OF PLATELET COUNTS ON OUTCOME IN COMMUNITY ACQUIRED PNEUMONIA AMONG CHILDREN AGED 2 MONTHS TO 5 YEARS IN A TERTIARY CARE HOSPITAL

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Abstract

Background: Platelets have a vital role in hemostasis and wound healing. However, platelets have historically been overlooked for their contributions to antimicrobial host defense. Platelets are essential inflammatory cells that can be recruited to the site of inflammation and platelets secrete various substances, such as cytokines, pro-coagulants, oxidants and antimicrobial peptides, which are involved in immune response. Thrombocytopenia is a well-known marker of adverse outcome in patients diagnosed with pneumonia, as decreased platelet count is linked to severe intravascular coagulation and severe sepsis. On the other hand, thrombocytosis has been recognized as a normal response to infection, but not as a marker of an unfavorable outcome. **Aim:** The present study aims to study the significance of variation of platelet counts with respect to severity,complications and outcome in community acquired pneumonia in children aged between 2 months to 5 years. **Materials and Methods:** The present study is an observational study conducted in the Department of Pediatrics at Niloufer hospital, Hyderabad, Telangana from June 2020 to November 2021.The institutional ethics committee approval was obtained. This prospective observational study included 1200 children hospitalized with CAP.A Complete history was taken and Clinical examination was done followed byComplete hemogram, C-reactive protein, Chest radiograph, Blood cultures were done on the study population, who were followed till discharge. Descriptive and inferential statistical analysis were used in the present study. Results on continuous measurements were presented on Mean±SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5% level of significance.Chi square test and Student t-test were used to compare inter group variation for continuous variables. **Results:** 1031(85.9%) of the children were between the age group 2 to 12 months. Male to female ratio was 1.6:1. Pneumonia and severe pneumonia was seen in 34.5%(n-414) and 65.5% (n-786)children respectively. At admission, leucocytosis was seen in 53.5% and leukopenia was seen in 6% of the children. Leucocytosis was found to be statistically significant with the severity of pneumonia.(pvalue-0.003) At admission, 56.5% children had normal platelet count, 5.5% had thrombocytopenia, 38% had thrombocytosis. Thrombocytopenia at the time of admission was significantly associated with severity and thrombocytosis at the time of admission was significantly associated with complications (p = 0.02) and outcome.17.5% children developed complications with Seizures (8%) being the most common complication. Other complications were pleural effusion (3.5%), shock (5%), and empyema (1%). The overall mortality was 3.5% seen in children with severe pneumonia. **Conclusion:** In the present study, significance of platelet counts variations with severity, complications

389

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and outcome was estimated and the observations showed that thrombocytopenia is associated with severity and thrombocytosis is associated with complications and mortality. The results of the study suggest that the platelet count can be used as a marker to prognosticate the severity and complications of community acquired pneumonia.

INTRODUCTION

Globally Pneumonia is the leading cause of under-5 (U-5) mortality with an estimated 808,920 deaths of children in 2017. As per World Health Organization (WHO) data ,acute respiratory infections (ARIs) are the second common cause of disability-adjusted life years lost around the globe.[1]The introduction of WHO-led ARI control program under the Millennium Development Goal era from 2000 to 2015, resulted in 30% decrease in deaths.[2] and 51% reduction in mortality rate due to pneumonia.[3,4] The ARI control program is implemented for the early recognition and management of children with clinical features suggestive of pneumonia, presumed to be of bacterial etiology.[5]

According to the revised World Health Organization(WHO),pneumonia is defined as the presence of cough with fast breathing (≥60 breaths/min in <2 months of age, ≥50 breaths/ min in 2–12 months of age, and ≥40 breaths/min in 1–5 years of age) and/or lower chest in drawing, which requires home therapy with oral amoxicillin; and severe pneumonia is defined as pneumonia with any danger sign(presence of refusal to feed, persistent vomiting, convulsions, lethargy or unconsciousness, cyanosis, and stridor in a calm child with chest indrawing), which requires a referral and intravenous therapy.[6] In 2013, the WHO and United Nations Children's Fund (UNICEF), published the integrated Global Action Plan for Pneumonia and Diarrhea (GAPPD), which proposed a framework to curtail the preventable child deaths due to diarrhea and pneumonia by 2025.[2]The GAPPD emphasizes a "protect, prevent and treat" approach and includes proven effective interventions.[2]It is estimated that unless the childhood deaths due to pneumonia are significantly reduced, it is difficult to achieve the sustainable development goal to eliminate preventable child deaths by 2030.[7]

Platelet plays an important role in thrombosis and hemostasis. Many studies have shown that platelets have a vital role in the immune response to infections.[8-10]During the process of infection and inflammation, platelets secrete various mediators, such as cytokines, pro-coagulants, oxidants and antimicrobial peptides, which have beneficial or harmful effects.[11-13]Hence, an abnormal platelet count may be a biomarker for predicting the disease severity. Previous studies have confirmed that thrombocytopenia and/or thrombocytosis were associated with mortality in adult CAP, but the effect of thrombocytopenia or thrombocytosis on the outcomes of pediatric patients with community-acquired pneumonia (CAP) has been rarely studied.[14-17]In children thrombocytosis is more common.[18] Two studies on pediatric CAP showed that thrombocytosis is observed more frequently in severe bacterial infections, and is associated with severity.[19,20]However, the drawbacks of these studies were inadequate study sample thrombocytosis and normal platelet count have not been explained. So far, only a few large-scale studies have investigated the effect of abnormal plate count on the outcomes of children with CAP. The present study evaluates the significance of variation of platelet count (high/low) with the severity, complications and outcome in children admitted with community acquired pneumonia, with the hypothesis that abnormal platelet count (high/low) is a prognostic marker of severity and outcome in children with CAP.

MATERIALS AND METHODS

The present study is a cross sectional study conducted in the Department of Pediatrics at Niloufer hospital, Hyderabad, Telangana from June 2020 to November 2021. The sample size was calculated based on the prevalence of Community acquired Pneumonia and relative precision by using formula 4pq/l2, and the maximum allowable error as 20 was taken. The institutional ethics committee approval was obtained letter -19101001017D, October, 2019. A written informed consent was obtained from parents of children included in the study.

Inclusion Criteria
- All infants and children aged 2 months to 5 years admitted in pediatric department fulfilling the criteria for pneumonia according to ARI control programme and were classified into pneumonia and severe pneumonia.[6]
- A total of 1200 children were included in the study.

Exclusion Criteria
The following infants and children were excluded from the study:
- Children <2 months and >5 years and
- Children with anemia (Hb<11g/dl), neuroinfections, known cases of connective tissue disorders, or congenital heart diseases, malignancy and associated viral hemorrhagic fever, COVID, other co-morbidities.

Methodology
Infants and children aged 2 month to 5 years admitted with symptoms and signs of pneumonia in pediatric department, Niloufer hospital, Telangana, satisfying the inclusion criteria were enrolled into

390

the study after getting informed consent from the parents/guardians.

A complete history and clinical examination was done for study population and in all these children Complete hemogram, C-reactive protein, chest radiograph, blood cultures were done.The study population was followed till they were discharged. The details of history, clinical examination, treatment, complications and investigations were documented in a predesigned proforma.

Based on clinical examination the children were classified in to Pneumonia and Severe Pneumonia as per ARI classification.[6]

The normal range of respiratory rate in children as per age are in newborn 30-50 per minute, 1to 5 months 25-40 per minute, 6months to 12 months-20-30 per minute, 1 yr to 5 yrs- 20-30 per minute.[21] The normal level of CRP in a newborn is between 0 and 5 mg / l, and in children standard ranges from 0 to 10 mg / l.[21] Total WBC count in neonates -9000 to 20,000/mm^3,in children 1month to 2 years- 6200 to 11,000/mm^3, above 2 years-5000 to 10,000/mm^3.[21]normal platelet count for all ages 1.5 lakh to 4 lakh cells per mm^3.[21]

Statistical Analysis

The data was entered in Microsoft Excel 2010 version. Data was analyzed using Microsoft Excel 2010 and Epi Info 7.2.0. Descriptive and inferential statistical analysis were used in the present study. Results on continuous measurements were presented on Mean±SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5% level of significance.Chi square test and Student t-test were used to compare inter group variation for continuous variables.

RESULTS

The majority of the children 85.9%(1031) were of age group 2 months to 12 months. Male to female ratio was 1.6:1. 52%(624) of the children were from urban areas and 48%(576) were from rural areas. Pneumonia and severe pneumonia were present in 35% (420)and 65% (780) of the children respectively.

Among these 1200 children with CAP, 22%(264) had weight less than 3rd centile, 56.5%(678) had weight between 3-50th centile, 16%(192) had weight between 50-97th centile, 5.5%(66) had weight between >97th centile. Severe pneumonia was seen in 65%(780) and of these about 52.9%(413) of the children had weight 3rd – 50th percentile and 22.9%(179) had weight <3rd percentile. The correlation between the weight percentiles and severity of pneumonia was found to be statistically not significant. [Table 1]

All the children had fever, cough, and fast breathing at the time of admission.

Chest indrawing and retractions were present in 94.5% of cases. Streptococcus pneumonia was the most common (45.3%) isolate from the throat. The mean platelet count was 4.38 +_1.89/mm3 (ranging from 249000 to 627,000/mm3), mean TLC was 12864+_6936/mm3 (range – 5928 to 19800/mm3). CRP was increased in 92.6% cases and the mean CRP was 11.6 mg/L. 38% (456) of the children had thrombocytosis and 5.5%(66) had thrombocytopenia. Leucocytosis was seen in 53.5% (642) and leucopenia was seen in 6%.(72)

Elevated Total WBC count and thrombocytopenia detected at the time of admission were found to be statistically significant with the severity of pneumonia. (Table 2 & 3).

About 48% of the children with severe pneumonia had leucocytosis at admission suggestive of that higher the wbc count at admission more severe is the pneumonia.

90.9% of the children with severe pneumonia had thrombocytopenia at admission which was statistically significant.

43.8% of the children had thrombocytosis at admission had severe pneumonia and 27.2 % of children with pneumonia had thrombocytosis at admission. The association between thrombocytosis at the time of admission and severity was not statistically significant. [Table 4]

Most common Chest Xray findings were bronchopulmonary infiltrates seen in 81%(972) followed by lobar pneumonia seen in 8%(96),lobar pneumonia with pleural effusion seen in 1%(12), cavitations were seen in 0.5%(6) children. [Table 5]

Complications were seen in 17.5% children and seizures were most common (8%) complication seen in 8%(96),followed by congestive cardiac failure (secondary to myocarditis) shock seen in 5%(60), Empyema seen in 3.5%(42)),lobar pneumonia with pleural effusion seen in 1%(12).(Table 6) .

Among the study population,156 children with complications had high platelet count at admission and thrombocytosis at the time of admission was significantly associated with the complications with P value of 0.02. [Table 7]

About 1158 children (96.5%) were recovered and mortality was seen in 42 children (3.5%). [Table 8]

Among the study population, the mean platelet counts in children who died was

1.38±0.23 /mm3 and in children who recovered was 3.88±1.44 /mm3.This observation shows that children who died had high mean platelet values than who recovered. The difference between the mean platelet values between the ones survived and died was statistically significant. [Table 9]

Table 1: Association between Severity of pneumonia and Weight percentile

Grade	Weight Percentile				Total	p value
	<3rd	3rd – 50th	50th – 97th	>97th		
Pneumonia	85	265	168	54	420	0.109

Severe Pneumonia	179	413	24	12	780	
Total	264	678	192	66	1200	

Table 2: Association between the Severity of pneumonia and WBC count at the time of admission

Type of pneumonia	Leucocyte count			Total	P value
	High	Low	Normal		
Pneumonia	276	18	126	420	Chi square:11.32 P=0.003
Severe Pneumonia	372	54	354	780	
Total	648	72	480	1200	

Table 3: Association between the Severity of pneumonia and Thrombocytopenia at the time of admission

Type of pneumonia	Platelet count		P value
	Low	Normal	
Pneumonia	6	300	Chi square:3.54 P=0.02 (Significant)
Severe Pneumonia	60	378	
Total	66	678	

Table 4: The Association between the Severity of pneumonia and Thrombocytosis at the time of admission

Severity	Thrombocytosis	Normal	P value
Pneumonia	114	246	0.09 (Not significant)
Severe pneumonia	342	438	

Table 5: Patterns of Chest X ray findings

Chest X ray	Frequency	Percentage
Broncho Pulmonary infiltrates	972	81
Cavitations	6	0.5
Hyperinflation	30	2.5
Lobar Pneumonia	96	8
Lobar Pneumonia + Pleural effusion	12	1
Normal	84	7
Grand Total	1200	100

Table 6: Complications in community acquired pneumonia

Complications	Frequency	Percentage
CCF, shock	60	5.0
LP+PE	12	1.0
Empyema	42	3.5
seizures	96	8.0
None	990	82.5
Grand Total	1200	100

Ccf- congestive cardiac failure, LP-lobar pneumonia, PE –pleural effusion

Table 7: Association of Complications and platelet count at the time of admission

Platelet count	Complications		Total	P value
	Present	Absent		
High	156	470	626	Chi square:7.16 P=0.02 (Significant)
Low	9	49	58	
Normal	45	471	516	
Total	210	990	1200	

Table 8: Outcome in children with community Acquired Pneumonia

Outcome	Frequency	Percentage
Death	42	3.5
Recovered	1158	96.5
Grand Total	1200	100

Table 9: The correlation of mean platelet values with outcome

Outcome	Mean platelet values	P value
Discharged	1.38±0.23	0.03
Death	3.88±1.44	(Significant)

DISCUSSION

In India, around 1.7 million children died before reaching the age of 5 years in 2010 and more than half of them (52%) died in the 1st month of life. The major cause of death was pneumonia(24%),prematurity(20%),and diarrhea(13%). [1] The reduction of mortality and morbidity depends on prevention,timely diagnosis and appropriate treatment. There is a need for prognostic markers that aid in evaluating and treating the children with pneumonia in addition to

clinical findings and laboratory parameters like WBC count and CRP.[22]

In the present study, 85.9% were of age less than a year, which is comparable with Kasundriya et al,[23]the study showed 55% of children withcommunity acquired pneumonia were in the age group between 2 months to 12 months . Baruah and Paul et al,[24] conducted an observational study on children aged 2 months–5 years admitted with pneumonia and this study showed 85.9% of children were in the age between 2 months to 12 months with Male to female ratio 1.6:1, similar to the study by Baruah et al(1.6:1);and Kasundriya et al(1.5:1).

94.5% of children in the present study had retractions, similar to Baruah et al.[24]

In the present study,17.5% children developed complications and 82.5% of children had no complications during the course of the hospital stay, which was similar to the study by Baruah et al, where in 76.84 % of children had complications. In the present study, seizures (8%) were found to be the most common complication. Other complications were pleural effusion (3.5%), shock(5%), empyema(1%).

In the present study, 42 children died and 1158 children had recovered and discharged.

The mortality rate in the present study was3.5% which was comparable to study by Choudhury et al,[25]which showed a mortality rate of 2.2%.

In the present study mortality wasseen in children with severe pneumonia who presented with congestive cardiac failure and shock. Baruah and Paul et al,[24] mortality rate was 11.4%.

In present study, 56.5% of the children had normal platelet counts, 5.5% had thrombocytopenia, and 38% had thrombocytosis similar to study by Huiming Sun et al,[26] Thrombocytosis and thrombocytopenia were found in 36.0% and 0.5% patients, respectively. Normal platelet count was observed in 63.5% patients where as in a study by Baruah et al,[24] 23% children had thrombocytopenia, 68% had normal platelet counts and 8% had thrombocytosis.

In the present study though a higher proportion (43.8%) of children with severe pneumonia had thrombocytosis, the association of thrombocytosis with the severity of pneumonia was not statistically significant which was not comparable with Usha et al study,[27] showed that there was a Significant association between thrombocytosis and severity of pneumonia.

In the present study, thrombocytopenia at the time of admission was associated with the severity of pneumonia and the correlation was statistically significant similar to a study Huiming Sun et al,[26] which showed that thrombocytopenia was an independent risk factor of severe CAP. Thrombocytopenia is also a recognized marker of poor outcomes in patients with pneumonia, due to the association of low platelet counts with disseminated intravascular coagulation and severe sepsis.[28]

In the present study, the mean platelet counts at admission were raised in the children who died than in those who recovered. There was a statistically significant difference between the mean platelet values among the ones survived and in those who died.

Limitation

The present study has some limitations.First, Platelet counts only at admission were done, Serial measurements of the platelet count were not done. Second,Sample size is small in the present study and multicentric studies would give better insight about the prognostic value of platelet count in CAP. Third, biomarkers were not analyzed in the study population

CONCLUSION

The present study concludes that abnormal platelet count can be used as a prognostic marker in children with community acquired pneumonia. Thrombocytopenia is associated with severity and thrombocytosis is associated with complications and mortality.

While interpreting a complete blood count report in children with CAP, platelet count is more informative for predicting the outcomes than the most commonly used leukocyte count Abnormal platelet count is a better predictor for severity and mortality and can be used as a marker to predict the severity of community acquired pneumonia and its complications. A better understanding of the role of platelets in the outcomes of patients with pneumonia may generate new therapeutic modalities for patients with severe disease.

REFERENCES

1. UNICEF. One Is Too Many Ending Child Death from Pneumonia and Diarrhoea; UNICEF: New York, NY, USA, 2016; Available online: https://data.unicef.org/wp-content/uploads/2016/11/UNICEF-Pneumonia-Diarrhoeareport2016-web-version_final.pdf (accessed on 20 May 2020).
2. UNICEF. End Preventable Deaths: Global Action Plan for Prevention and Control of Pneumonia and Diarrhoea; World Health Organization: Geneva, Switzerland, 2013; Available online: http://apps.who.int/iris/bitstream/handle/10665/79200/9789241505239_eng.pdf;jsessionid=837AEC1288C76D2368F1E8F8DAB86B55?sequence=1 (accessed on 20May 2020).
3. WHO. Global Burden of Disease Estimates 2000–2015; WHO: Geneva, Switzerland, 2016; Available online:http://www.who.int/healthinfo/global_burden_disease/estimates/en/index2.html (accessed on 20 May 2020).
4. McAllister, D.A.; Liu, L.; Shi, T.; Chu, Y.; Reed, C.; Burrows, J.; Adeloye, D.; Rudan, I.; Black, R.E.;Campbell, H.; et al. Global, regional, and national estimates of pneumonia morbidity and mortality in children younger than 5 years between 2000 and 2015: A systematic analysis. Lancet Glob. Health 2019, 7, e47–e57. [CrossRef]
5. https://www.who.int/news-room/fact-sheets/detail/pneumonia,11
6. Park K. Acute respiratory infections. In: Park's Text Book of Preventive and SocialMedicine.20thed.Jabalpur:M/sBan 13.

393

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7. Lancet, T. The case for action on childhood pneumonia. Lancet 2017, 390, 2122. [CrossRef]

8. Yeaman MR: The role of platelets in antimicrobial host defense. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America 1997, 25(5):951-968; quiz 969-970.

9. Fitzgerald JR, Foster TJ, Cox D: The interaction of bacterial pathogens with platelets. Nat Rev Microbiol 2006, 4(6):445-457.

10. Elzey BD, Sprague DL, Ratliff TL: The emerging role of platelets in adaptive immunity. Cell Immunol 2005, 238(1):1-9.

11. Yeaman MR, Bayer AS: Antimicrobial peptides versus invasive infections. Curr Top Microbiol Immunol 2006, 306:111-152.

12. Ware J, Corken A, Khetpal R: Platelet function beyond hemostasis and thrombosis. Curr Opin Hematol 2013, 20(5):451-456.

13. Kamath S, Blann AD, Lip GY: Platelet activation: assessment and quantification. Eur Heart J 2001, 22(17):1561-1571.

14. Mirsaeidi M, Peyrani P, Aliberti S, Filardo G, Bordon J, Blasi F, Ramirez JA: Thrombocytopenia and thrombocytosis at time of hospitalization predict mortality in patients with community-acquired pneumonia. Chest 2010, 137(2):416-420.

15. Prina E, Ferrer M, Ranzani OT, Polverino E, Cilloniz C, Moreno E, Mensa J, Montull B, Menendez R, Cosentini R et al: Thrombocytosis is a marker of poor outcome in community-acquired pneumonia. Chest 2013, 143(3):767-775.

16. Brogly N, Devos P, Boussekey N, Georges H, Chiche A, Leroy O: Impact of thrombocytopenia on outcome of patients admitted to ICU for severe community-acquired pneumonia. J Infect 2007,Page 9/1555(2):136-140.

17. Gorelik O, Izhakian S, Barchel D, Almoznino-Sarafian D, Tzur I, Swarka M, Beberashvili I, Feldman L,Cohen N, Shteinshnaider M: Prognostic significance of platelet count changes during hospitalization for community-acquired pneumonia. Platelets 2017, 28(4):380-386.

18. Matsubara K, Fukaya T, Nigami H, Harigaya H, Hirata T, Nozaki H, Baba K: Age-dependent changes in the incidence and etiology of childhood thrombocytosis. Acta Haematol 2004, 111(3):132-137.

19. Wolach B, Morag H, Drucker M, Sadan N: Thrombocytosis after pneumonia with empyema and other bacterial infections in children. The Pediatric infectious disease journal 1990, 9(10):718-721.

20. Dodig S, Raos M, Kovac K, Nogalo B, Benko B, Glojnaric I, Dodig M, Cepelak I: Thrombopoietin and interleukin-6 in children with pneumonia-associated thrombocytosis. Arch Med Res 2005, 36(2):124-128.

21. American College of Emergency Physicians. ER 101: Vital Signs. American College of Emergency Physicians. Available

22. Singhi S, Deepa A, Kaur H. Prevalence and predictors of hypoxemia in acuterespiratoryinfectionspresentinginpediatricemergencydepartment.IndianJCritCareMed2003; 7:118-23. DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20181981

23. Kasundriya SK, Dhaneria M, Mathur A, Pathak A. Incidence and Risk Factors for Severe Pneumonia in Children Hospitalized with Pneumonia in Ujjain, India. Int J Environ Res Public Health. 2020 Jun 27;17(13):4637. Doi: 10.3390/ijerph17134637. PMID: 32605136; PMCID: PMC7369688.

24. Baruah A, Paul N. Abnormal platelet count as a prognostic indicator in community-acquired pneumonia in children. Indian J Child Health. 2021; 8(2):84-88.

25. Jasashree Choudhury. Thrombocytosis in UnderFive Children with Lower Respiratory Tract Infection. Ann Med Health Sci Res. 2017; 7: 47-51.

26. Sun, H., Li, S., Zhu, C., Yan, Y., Wang, Y., Hao, C., Chen, Z., & Ji, W. (2019). Thrombocytosis and thrombocytopenia are markers of poor outcome in pediatric patients with community-acquired pneumonia. https://doi.org/10.21203/rs.2.9536/v1

27. Usha D, Sudha Rudrappa. Significance of thrombocytosis in lower respiratory tract infections.MedPulse international Medical JournalSeptember 2014; 1(9): 470-475.

28. Yeaman MR, Bayer AS. Antimicrobial peptides versus invasive infections. Curr Top Microbiol Immunol 2006; 306:111-52arasidasBhanotPublisher's; 2009. p. 151-9.

394

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