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RESEARCH ARTICLE

Comparison of haematological parameters and c-reactive protein in children admitted with influenza, adenovirus, and other respiratory illness – A retrospective observational study.

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Abstract: Introduction: Respiratory diseases such as Adenovirus and Influenza are frequently occurred in young children. Children have high susceptibility to respiratory infections, with adenovirus, Influenza A, and Influenza B, as predominant etiological factors. Haematological markers and C-reactive protein (CRP) levels fluctuate in exposure to viral infections. The purpose of this study was to evaluate complete blood count (CBC) parameters as well as CRP levels in children with Adenovirus, Influenza, and other respiratory conditions, with a focus on Platelet-to-Lymphocyte Ratio (PLR), lymphocyte count, white blood cell (WBC) count, neutrophil count, Platelet-to-Neutrophil Ratio (PNR), and Neutrophil-to-Lymphocyte Ratio (NLR). Methods: A cross-sectional retrospective investigation was performed with 268 children (aged 6 months to 5 years) hospitalized to SRM Medical College Hospital from January to December 2024. Data has been obtained via medical records and subjected to statistical analysis. Results: Among 268 children's, 60.1% and 39.9% were male and female respectively. Influenza was the most prevalent at 27.2%, preceded by 16.8% of Adenovirus and 16.0% of RSV. Haematological and CRP markers shown variability among various diseases. Adenovirus exhibited notable alterations in WBC, CRP, NLR, ALC and haemoglobin. NLR was high in Influenza A, but PNR was diminished in Influenza B, highlighting importance for integrated diagnoses. Conclusion: Haematological markers such as CRP, NLR and WBC facilitate the identification of viral infections, particularly adenovirus. Accurate diagnosis necessitates the integration of clinical evaluation, laboratory tests, and PCR.

Keywords: Haematological parameters, Public heath, Children, respiratory viral pathogens

INTRODUCTION

Acute respiratory illness in children was one of the significant cause of morbidity and mortality across the world. India accounts for 20% of acute respiratory illness related deaths in the world. Factors like poverty, overcrowding, poor nutrition, poor air quality and antibiotics misuse were found to associated with acute respiratory infections. Among all the viral causes for infections, influenza A, influenza B and adenovirus were found to be the major causes of illness. Few other viruses that cause infections include parainfluenza, respiratory syncytial, rhinovirus, and enterovirus (1).

Influenza A and B are the common viral infections and these infections affect millions of children globally. The clinical presentation ranges from mild upper respiratory symptoms to severe lower respiratory illness (2). Appropriate diagnosis and treatment of these infections is crucial and these infections is not treated which results in various complications ultimately cause death in children because of a weakened immune system.

Complete blood count and C-reactive protein were the commonly used laboratory tests to diagnose these infections because these infections result in altered haematological parameters and CRP levels (3, 4). Haematological indicators such as haemoglobin, WBC,

neutrophil, lymphocyte, and platelet counts were used to determine the kind of infection. Using these characteristics, inflammatory markers such as the Neutrophil Lymphocyte ratio (NLR), Platelet Lymphocyte ratio (PLR), and Platelet Neutrophil ratio (PNR) were estimated to diagnose the specific infectious disease (5). Studies show that CRP levels were raised in viral infections, and the diagnostic value of various haematological parameters and CRP helps in the identification of various respiratory illnesses among children (6, 7). Paediatric patients with Influenza A and B exhibit distinct haematological profiles compared to those with adenovirus infections, characterized by different levels of NLR, PLR, PNR, and CRP (8, 9). Specifically, it is hypothesized that children with Influenza A and B will show higher NLR and PLR, but lower PNR and elevated CRP levels compared to those with adenovirus infections (10).

Accurate and timely diagnosis of influenza is essential for appropriate treatment and management, which can significantly impact patient outcomes and resource utilization. Influenza and adenovirus shares symptoms with other viral and bacterial respiratory infections, making differential diagnosis challenging. This overlap can complicate clinical decisions and lead to delays in appropriate treatment. While PCR testing is the gold standard for confirming influenza and adenovirus, it is not always immediately available or practical in all settings. Therefore, identifying supplementary diagnostic markers that can aid in distinguishing influenza from other infections is crucial.

There is limited research specifically comparing CBC and CRP values between influenza, adenovirus and other respiratory illness Identifying distinct CBC and CRP patterns could enhance diagnostic accuracy and help clinicians make more informed decisions regarding treatment and management.

MATERIALS AND METHODS

Sample Size Calculation

The sample size was calculated using the previous study's proportion of 82%. Precision was taken as 10% of the proportion. Zα was taken as 2.58. The formula applied was:

$N = Z2 \times P (1-P)d2$

The total sample size was calculated as 268.

Study design

This retrospective cross-sectional study was performed among 268 children aged between (6 to 60 months), admitted in Department of Paediatrics, SRM Medical College Hospital and Research Centre, during the period of January 2024 to December 2024.

Inclusion Criteria

Children aged (6 to 60 months), children those admitted to tertiary care centre with symptoms of respiratory illness, confirmed diagnosis of influenza A or B or adenovirus through PCR or reliable testing methods were included. Those with other respiratory illnesses or conditions confirmed through clinical and diagnostic testing were included.

Exclusion Criteria

Children with incomplete laboratory data, those with significant comorbidities or conditions affecting CRP levels, those receiving antiviral therapy or systemic corticosteroids, those with immunodeficiency or other chronic respiratory conditions were excluded.

Ethics statement and informed consent

The research was performed in compliance with the ethical standards. Ethical Approval was secured from the Institutional Human Ethics Committee of SRM Medical College Hospital and Research Centre (SRM IEC-ST1124-1887) before the initiation of the project.

This retrospective study, which includes the examination of unidentified medical information, did not need informed consent from every participant. Although, Data was acquired in compliance with ethical principles, preserving confidentiality and identity.

Statistical analysis

Statistical analysis was performed using SPSS software. Statistical analysis such as t test, chi square test and fisher exact test were used. Diagnostic value was estimated using ROC curve. p value of <0.05 was considered as statistically significant.

RESULTS

Sociodemographic Features of the Study Cohort

The study involved 268 children aged around 6 and 60 months. The interquartile range (IQR) those who participated in the study was 20 months. Within the study cohort, 60.1% (161 individuals) and 39.9% (107 individuals) were male and female, respectively, also demonstrating a male predominance (Fig 1).

Etiology about virus positivity

The virus positivity analysis across 268 tested cases revealed that Influenza A was the most frequently detected virus, accounting for 27.2% of all positive cases, followed by Adenovirus (16.8%) and RSV (16.0%). Influenza B contributed 10.1%, while other respiratory viruses such as Parainfluenza, Enterovirus, and Rhinovirus were present in smaller proportions, collectively forming part of the 45.9% classified under other respiratory illness. Notably, 13.1% of samples showed no viral presence (Fig 2). A statistically significant association ($\chi^2 = 0.000$) was found for Adenovirus cases.

The investigation of haematological parameters in the 268 participants provided the following results. The table 1 shows that mean haemoglobin is 10.4 ± 1.4. Then mean platelet count is 344412.6 ±143581.5, while the average WBC count is 11039.8 ± 5328.7. The mean neutrophil count is 52.6±17.3 and the mean lymphocytes, leucocytosis and leukopenia are 41.2±16.7, 115±42.9 and 13 ± 4.9 correspondingly. The average children with thrombocytopenia was 23±8.6, whereas without thrombocytopenia was 245±91.4. The average children with neutrophilia was 13 ± 4.9, whereas without neutrophilia was 255 ± 95.1. In participants with positive and negative status were 149 ± 44.4, 119 ± 32.8 and 61 ± 22.8 respectively. The mean NLR, ANC, ALC, PNR and PLR is 1.79±1.53, 6029.5 ±4344, 4325.6±2412.5, 80.9±56.2, and 101.4±67.4 respectively.

Clinical Attributes and Supplementary Interventions Across Research Participants

Table 2 showed that study involving 268 patients, the average hospital stay was 2.5 to 5 days. Concerning oxygen support, almost fifty percent of the patients (54.5%) did not necessitate any oxygen support during their hospitalization. Approximately 35.4% needed

standard oxygen assistance, but a lesser fraction (10.1%) necessitated High-Flow Nasal Cannula (HFNC) therapy. Significantly, no instances of organ dysfunction were documented in the study cohort (268 patients) throughout their hospitalization.

Comparison of CRP and Haematological parameters with the infections

There was no statistically significant correlation between CRP and Influenza A infections (Table 3). Haematological parameters such as haemoglobin, WBC, ANC, platelet count, ALC, PNR, and PLR showed no statistically significant differences between influenza A non-infected and infected individuals. Influenza A-positive individuals had significantly higher NLR levels than uninfected individuals.

No notable variations were detected in CRP levels or haematological variables among participants with and without Influenza B illness (Table 4). The infected group exhibited a lower PNR than the non-infected group, with this variation being statistically significant.

Adenovirus infection showed a strong correlation with CRP positivity. Individuals with adenovirus infection had reduced levels of haemoglobin and elevated white blood cell counts.

The NLR was markedly increased in adenovirus-positive individuals relative to participants with no infection. Furthermore, ALC was substantially reduced in the infected group.

No notable variations were seen in PNR, platelet count, ANC, and PLR for infections caused by adenoviruses.

ROC curve analysis of Haematological parameters with the infections

Haematological indicators exhibited diverse relationships with infections caused by these viruses. NLR, NLR, ANC, and the combined levels of CRP, PLR, and PNR had greater associations with Adenovirus than Influenza A and B. The WBC count had a moderate correlation with Adenovirus. The results presented here emphasize the utility of inflammatory indicators in the identification and monitoring of respiratory infections caused by viruses.

The ROC assessment evaluates the predictive capabilities of NLR and PNR regarding viral positivity (Fig 3). The NLR exhibited moderate to low diagnostic accuracy, reflecting restricted sensitivity and specificity. Conversely, PNR exhibited better results, characterized by a steeper curve and enhanced discriminative capability. ns. Among all the parameters, none showed better discrimination for influenza A infection (AUC <0.6) and ANC showed better discrimination for influenza B infection (AUC >0.6). Among all the parameters, WBC, NLR and ANC showed better discrimination for adenovirus infection (AUC >0.6). A composite score was created for parameters to find the combined diagnostic analysis after doing the logistic regression analysis and arriving the logit equation. The ROC curve analysis using combined parameters showed that the combined parameters showed better discrimination with adenovirus infection alone not with influenza A or B infection (AUC >0.6).

DISCUSSION

This study exhibits a gender distribution characterized by a predominance of male child participants relative to female child participants, aligning with results from many paediatric studies. Another study identified that the early childhood health well-being ratio, the male children ratio is higher than the female children ratio (11, 12).

This study identified Influenza A, Adenovirus, and RSV are 27.2%, 16.8% and 16.0% respectively, were the three most prevalent viruses of the respiratory tract among patients. These results align with prior research, which typically identifies the influenza A virus as the primary respiratory viral pathogen. A study indicated that children's respiratory infections are predominantly caused by the Influenza A virus, Adenovirus, and RSV virus (13, 14). Viruses such as Parainfluenza, Enterovirus, Rhinovirus, and Metapneumovirus were identified in lesser quantities, aligning with worldwide epidemiological patterns where these types of viruses show periodically or during particular outbreaks (15, 16). Notably, 13.1% of patients exhibited not unidentified viral pathogen; similar to this, other investigations also indicated that a modest respiratory-related cases remained etiologically unclassified despite thorough viral screening (17). This may indicate non-viral causes or constraints in detection techniques.

The mean duration of hospitalization in this study was 2.5 ± 5 days, suggesting mild progression of disease. About 35.4% had normal O2, 10.1% had HFNC O2 support, and 54.5% had no oxygen support. None of thaem had organ dysfunction. These results align with research conducted by Jerath (2021) (18), indicating that the majority of infants with respiratory viral infections healed with minimal treatment.

The present investigation evaluated haematological and inflammatory indicators of individuals with Influenza A, B, and Adenovirus infections. A notable correlation was identified between Influenza A and an increased NLR, suggesting an enhanced inflammation reaction. This corresponds with the findings, which indicated that an increased NLR is frequently linked to infections caused by viruses, such as Influenza, and may function as a predictive marker of disease severity (19, 20).

In Influenza B, the PNR was substantially reduced, indicating modified platelet activity. Also Kim et al. (2016) (21) and Assinger (2024) (22) identified analogous patterns, observing diminished platelet indices in individuals with viral respiratory ailments. Furthermore, several studies observed that Patients with a wide age group infected with adenovirus exhibited increased CRP positivity, WBC counts, and NLR levels, whereas haemoglobin levels were decreased (23, 24). A reduced ALC in adenovirus-positive people indicates lymphocyte reduction, a typical reaction in severe viral infections (25). In the current investigation, platelet counts, ANC, and PLR exhibited no significant changes throughout the groups. The other findings also indicating that these types of indicators could minimize the discriminatory capacity among various viral etiologies (26, 5).

Our work emphasizes the efficacy of fundamental haematological measures such as NLR, WBC count, and CRP in distinguishing viral infections and evaluating inflammatory load. The results indicate that Adenovirus could cause a more severe inflammatory response than Influenza A and B, necessitating enhanced surveillance

(27).

This study demonstrated that NLR and ANC exhibited modest accuracy in diagnosing for adenovirus (AUC 0.62 and 0.65). Nonetheless, PNR exhibited a low predictive value (AUC 0.34. The research conducted by Biserni et al. (28), revealed an excessive number of neutrophils in viral infections, aligning with our observations. Conversely, Hong et al. (29), recognized the PLR as an essential indicator for Influenza A infection, whereas our work emphasized other characteristics. Likewise, Fu et al. (30), identified NLR as a strong marker of Influenza A infection. Qi et al. (31), detected multiple important indicators of Influenza B infection, including NLR, PLR, WBC count, and CRP. These investigations highlight the potential efficacy of numerous indicators in detecting viral infections.

CONCLUSION

This study is one of the few investigations that illustrate changes in haematological markers and CRP levels in the paediatric population with viral infections. Among the parameters, adenovirus infection can be diagnosed using parameters like CRP, haemoglobin, WBC, NLR and ALC. Influenza A virus can be diagnosed with NLR, and influenza B with PNR. ROC curve analysis showed that parameters like WBC, NLR, and ANC show better discrimination for adenovirus infection. Despite these findings, none of the single parameters showed high accuracy, indicating the need for a combination of clinical evaluation, laboratory results, and PCR testing for accurate diagnosis and effective management of these viral respiratory infections in paediatric patients.

Based on the findings from our study, it's found the laboratory parameters play a major role in identifying these viruses implicated in the study. Hence in research limited settings, we can use the laboratory parameters to identify these infections

TABLES

Table 1: Hematological parameters (N=268)

S.No	Variable	Mean	SD
	Haemoglobin	10.4	1.4
	Platelet count	344412.6	143581.5
	Thrombocytopenia (Yes)	23	8.6
	Thrombocytopenia (No)	23	91.4
	WBC	11039.8	5328.7
	Neutrophil	52.6	17.3
	Lymphocytes	41.2	16.7
	Leucocytosis	115	42.9
	Leukopenia	13	4.9
	No abnormality (Leucocytosis or Leukopenia)	140	52.2
	Lymphocytosis (yes)	34	12.7
	Lymphocytosis (No)	234	87.3
	Neutrophilia (Yes)	13	4.9
	Neutrophilia (No)	255	95.1
	CRP (Positive)	119	44.4
	CRP (Negative)	88	32.8
	CRP (Not done)	61	22.8
	NLR	1.79	1.53
	ANC	6029.5	4344.0
	ALC	4325.6	2412.5
	PNR	80.9	56.2
	PLR	101.4	67.4

Table 2: Clinical Characteristics of Study Participants

S.No	Variable	Category	Mean	SD	P Value
1	Days of stay	-	5.2	2.5	0.41
2	Oxygen support	Normal O2	95	35.4	0.18
		HFNC	27	10.1	0.51
		No	146	54.5	0.32
3	Organ dysfunction	No	268	-	

Table 3: Comparison of CRP and Haematological parameters with the infections (N=268)

Influenza A					
S.No	Variable	Category	Yes	No	p value
1	CRP	Positive	33 (27.7%)	86 (72.3%)	0.59
		Negative	37 (24.8%)	112 (75.2%)	
2	Hemoglobin	Mean (SD)	10.4 (1.3)	10.5 (1.5)	0.63

3	Platelet count	Mean (SD)	344735.7 (143989)	344298.4 (143802)	0.98
4	WBC	Mean (SD)	10755.8 (4747)	11140.3 (5527)	0.60
5	NLR	Mean (SD)	2.17 (2)	1.66 (1.3)	0.01*
6	ANC	Mean (SD)	6164.1 (3641)	5981.9 (4574)	0.76
7	ALC	Mean (SD)	4073.1 (2609)	4414.9 (2339)	0.30
8	PNR	Mean (SD)	70.4 (37.8)	83.9 (61.1)	0.08
9	PLR	Mean (SD)	112.6 (73.3)	87.4 (64.9)	0.10
Influenza B					
1	CRP	Positive	12 (10.1%)	107 (89.9%)	0.40
		Negative	20 (13.4%)	129 (86.6%)	
2	Haemoglobin	Mean (SD)	10.5 (1.6)	10.4 (1.4)	0.85
3	Platelet count	Mean (SD)	342631.2 (132917)	344654.2 (145230)	0.94
4	WBC	Mean (SD)	12137.1 (5204)	10891.1 (5338)	0.21
5	NLR	Mean (SD)	2.19 (1.5)	1.74 (1.5)	0.12
6	ANC	Mean (SD)	7122.7 (3830)	5881.3 (4395)	0.13
7	ALC	Mean (SD)	4120.6 (2109)	4353.4 (2453)	0.60
8	PNR	Mean (SD)	57.9 (28)	83.4 (58.4)	0.01
9	PLR	Mean (SD)	120.2 (102)	98.8 (61)	0.09
Adenovirus					
1	CRP	Positive	28 (23.5%)	91 (76.5%)	0.02
		Negative	19 (12.8%)	130 (87.2%)	
2	Haemoglobin	Mean (SD)	10 (1.4)	10.5 (1.4)	0.02
3	Platelet count	Mean (SD)	344163.8 (149214)	344465.6 (142704)	0.99
4	WBC	Mean (SD)	13177 (6965)	10585.3 (4809)	0.002
5	NLR	Mean (SD)	2.18 (1.6)	1.71 (1.5)	0.001
6	ANC	Mean (SD)	8136.7 (6161)	5881.4 (3716)	0.77
7	ALC	Mean (SD)	4235.2 (2058)	4344.9 (2485)	0.002
8	PNR	Mean (SD)	57.2 (33.4)	85.3 (58.8)	0.49
9	PLR	Mean (SD)	95.2 (46.8)	102.7 (71)	0.09

Table 4: Haematological parameters with the infections (N=268)

S. No	Variable	Influenza A	Influenza B	Adenovirus
1	Haemoglobin	0.50	0.53	0.42
2	Platelet count	0.49	0.48	0.50
3	WBC	0.49	0.57	0.61
4	NLR	0.55	0.59	0.62

5	ANC	0.54	0.63	0.65
6	ALC	0.43	0.49	0.50
7	PNR	0.48	0.38	0.34
8	PLR	0.55	0.53	0.51
9	CRP, NLR, PLR, PNR	0.51	0.57	0.68

FIGURES

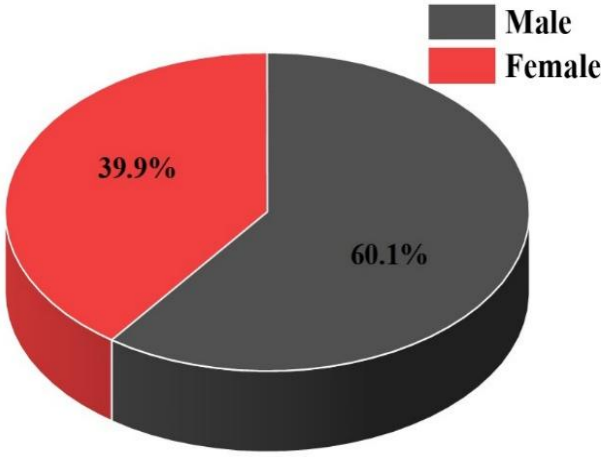

Figure 1: Gender distribution of study population

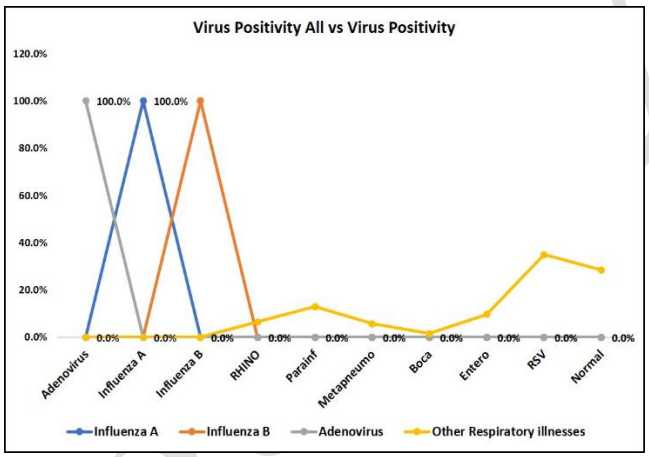

Figure 2: Etiology about virus positivity

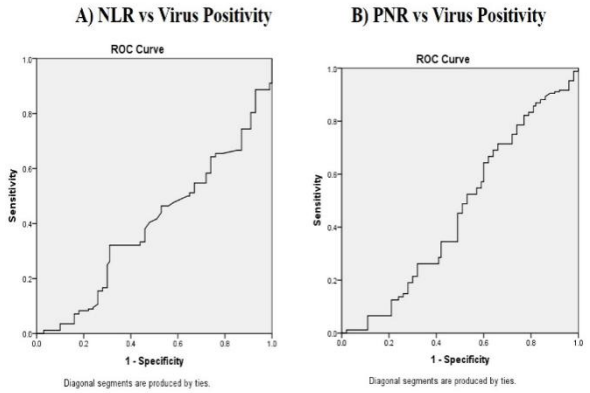

Figure 3: ROC curve for NLR and PNR vs virus positivity

DECLARATION

CONFLICT OF INTEREST

No conflict of interest.

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AUTHOR'S CONTRIBUTION

Name: Conceptualization, data collection, statistical analysis, manuscript writing, and revision. Name: Study design, manuscript drafting, and methodology development, Name: Supervision, validation of results, analysis of findings. Name: Data collection, writing/review and editing. Name: Validation and formal analysis, overall study supervision, and final manuscript review.

FUNDING

The study did not receive any funding

ETHICS STATEMENT

The research was performed in compliance with the ethical standards. Ethical Approval was secured from the Institutional Human Ethics Committee of SRM Medical College Hospital and Research Centre before the initiation of the project.

INFORMED CONSENT

This retrospective study, which includes the examination of unidentified medical information, did not need informed consent from every participant. Although, Data was acquired in compliance with ethical principles, preserving confidentiality and identity.

DATA AVAILABILITY

All datasets collected or examined in the current study are incorporated in the publication

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