HAEMATOLOGICAL AND COAGULATION PROFILE IN PEDIATRIC PATIENTS WITH COVID 19

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ABSTRACT

Background :COVID 19caused by severe acute respiratory syndrome corona virus2(SARS Cov2) involves respiratory and other systems. Patient with Covid 19 presents with wide range of hematological and coagulation abnormalities. Hemostatic abnormalities in Covid 19 are related with disease progression, severity and mortality. The objective of our study is to evaluate the role of hematological and coagulation parameters in determination of Covid 19 severity.**Materials and methods**: Total 70 cases were enrolled in the study, conducted in department of pathology at Bangalore Medical college and research institute, Bangalore. Hematological and coagulation parameters were compared with mild, moderate, severe and critical. Appropriate statistical analysis is applied.**Result:** Parameters like WBC, Neutrophils, HCT,NLR were higher in patients with severe disease when compared to mild and moderate cases.PT, D-Dimer did not show statistically significant association with severity of disease.**Conclusion:** The study concluded that leukocytosis, neutrophilia,elevated NLR are associated with severity of the disease

Key words: Covid 19disease, Hematological, Coagulation, Pediatric, Clinical severity

INTRODUCTION

The novel coronavirus disease 2019 (COVID-19) is a member of Beta corona virus family caused by severe acute respiratory syndrome corona virus two (SARS-CoV 2) and was declared as a global pandemic by WHO on March 11 2020.This novel strain is highly contagious and spreads by contact by droplets causing mild symptoms to severe illness. Globally United states and China has reported a percentage of 1.7% and 2.2% pediatric COVID 19 cases respectively.[1,2]

COVID 19 is associated with increase in Concentrations of pro inflammatory cytokines mainly IL -6 which induces tissue factor expression subsequently initiating activation of coagulation and thrombin generation and also activation of fibrinolytic system.[3] Thrombotic complications emerge as an important issue in patients with COVID 19.Emerging data supports that Increased D-dimer and fibrin degradation products levels, and prolonged Prothrombin time have been associated with poor prognosis in patients affected by the novel coronavirus.[4]

The documentation of the hematological parameter and coagulation profile alterations are very limited in the pediatric COVID-19 cases worldwide and in Indian populationwhere the pandemic is spreading with gradual and greater involvement of the pediatric population, as a whole owing to the relatively lower incidence of the disease, additionally it servesas an indicators to provide guidance for the diagnosis, treatment and prognosis of covid19 patients.[5]

When compared to adult's laboratory profile in asymptomatic to severe COVID 19 patients, Consistent alteration in hematology parameters and coagulation studies on pediatric patients with confirmed COVID 19 cases are yet to be observed.
The present study was undertaken with the aim to assess the characteristic changes in the value of hematology routine parameters and coagulation profile in the pediatric COVID19 cases in the Indian scenario.

Objectives :
1.To document the alterations in hematological profile in pediatric covid patients.
2.To study the alterations in coagulation profile in pediatric covid patients.
3.To compare these parameters in the context of clinical severity.

MATERIALS AND METHODS
It is cross sectional prospective study. Total 70 pediatric cases were included in the study.Study was carried out in department of pathology at Bangalore medical college and research institute for a period of 6 months (May -October 2020).
Inclusion criteria: All CBC samples of covid 19 positive pediatric patients.
Exclusion criteria:
- Patients who have declined to participate in the study
- Patients who lost follow up due to unforeseen causes
All CBC samples received at central laboratory; Department of pathology were included in the study. Blood samples received was checked for the details of the patient and was processed by Beckman LH 780 analyzer to obtain Hematological and coagulation parameters. EDTA and Citrate Blood samples submitted for routine hematologicaland coagulation workup will be utilized to obtain the following parameters :HB, HCT, Total count ,Differential count, Platelet count, PT and D-dimer from automated analyzers. Clinical severity of the patients is graded as mild, moderate and severe based on established criteria.
Clinical severity: categorized Stage A, B,C, D[6]
Stage A (Asymptomatic): Patients with no signs or symptoms of infection

Stage B (Mild infection): Patient presented with upper respiratory tract infection symptoms and other mild symptoms (including fever and gastrointestinal symptoms without evidence of pneumonia.

Stage C (Moderate infection): Patient with hypoxia with oxygen saturation less than 93%at rest or presence of pneumonia not requiring ICU admission.

Stage D (Severe infection): Pneumonia requiring ICU admission

1. Respiratory rate of 30 breaths/min
2. Arterial oxygen partial pressure to fractional inspiratory oxygen ratio(PaO2/FiO2)less than 300
3. More than 50%lung involvement on imaging within 24-48 hours.
4. Critical respiratory failure requiring mechanical ventilation, septic shock or multiorgan dysfunction.
5.

STATISTICAL ANALYSIS

Data will be analysed by descriptive statistics such as mean,standarddeviation,percentage,tables and graphs where ever applicable.Student T test and ANOVA will be used to determine significant difference between two or more groups.

RESULTS:

Total 70 pediatric cases were enrolled in the study. Out of 70 cases, Age ranged from (1-19 years),females were 37 and males were 33. Most of the mild cases presented with mild fever, moderate cases presented with fever, cough and breathlessness. 1 severe case had multiorgan failure with septicemia. 60cases(85.71%) of them showed mild severity(Stage B),9 cases(12.8%) of them showed moderate severity(Stage C), 1case(1.4%) was severe(Stage D). The hematological and coagulation parameters in mild, moderate, severe and critical disease are shown in Table 1.

Table 1 : Hematological and coagulation parameters according to disease tseverity

		N	Mean	Std. Deviation	F	P
AGE	Mild	60	13.833	4.5554	.399	.673
	Moderate	9	13.778	11.1555		
	Severity	1	19.000	.		
HB	Mild	60	12.718	1.8241	2.541	.086
	Moderate	9	11.789	2.7597		
	Severity	1	9.000	.		
HCT	Mild	60	39.9635	4.35809	5.094	.009
	Moderate	9	36.6000	8.75114		
	Severity	1	26.2000	.		
TC	Mild	60	8.080	2.4670	68.486	.000
	Moderate	9	10.111	5.6193		
	Severity	1	43.500	.		
Neutrophils	Mild	60	58.150	14.7715	6.338	.003

	Moderate	9	73.667	18.3712		
	Severity	1	93.000	.		
Lymphocytes	Mild	60	31.900	12.6407	5.658	.005
	Moderate	9	19.111	12.7519		
	Severity	1	7.000	.		
Monocytes	Mild	60	7.617	2.1870	9.721	.000
	Moderate	9	4.778	3.7676		
	Severity	1	.000	.		
Eosinophils	Mild	60	2.100	2.8505	.271	.763
	Moderate	9	1.889	3.2956		
	Severity	1	.000	.		
Basophils	Mild	60	.183	.3902	.149	.862
	Moderate	9	.222	.4410		
	Severity	1	.000	.		
PLT	Mild	60	3.0708	1.04471	4.260	.018
	Moderate	9	4.4167	3.18460		
	Severity	1	1.1500	.		
PT	Mild	60	11.168	1.6534	.541	.585
	Moderate	9	10.678	.7276		
	Severity	1	12.000	.		
NLR	Mild	60	2.5900	2.36797	12.085	.000
	Moderate	9	7.2067	7.02125		
	Severity	1	13.0000	.		
DDIMER	Mild Moderate Severity	60 9 1	.65 1.70 1.97	1.331 1.501 1.407	,.315	.524

Mean values of WBC (P value – 0.0001), HCT (P value- 0.001),Neutrophils(P value- 0.0003),Lymphocytes(P value – 0.005),Monocytes(P value- 0.0001), NLR – (P value - 0.0001) were increased in patients with critical disease as compared to the patients with mild, moderate and severe disease, other parameters like Hb, Eosinophils, Basophils, Prothrombin time and D-Dimer did not show any significant association with severity of disease(Table 1). Out of 70 patients, 1(1.4%) was diagnosed as Multiorgan disease with septicaemia**.**

DISCUSSION
COVID-19 related pediatric disease has an array of symptomatic presentations and outcomes. The study reported that females were affected more than males.
In a study on pediatric COVID 19 cases done by Xia et al noted that WBC was normal (5.5-12.2) in 14 cases (14/20, 70%), decreased (12.2) in two cases (2/20, 10%).[7]

Huan Hana et al in his study on 94 adult patients noted that Prothrombin time was found to be lower in patients than that in controls (81% vs. 97%; $p < 0.001$).D-dimer (10.36 vs. 0.26 ng/L) and FDP (33.83 vs. 1.55 mg/L; $p < 0.001$)were higher in patients than those in controls. Fibrinogen values in SARS-CoV-2 patients were also higher than those in the control group (5.02 vs. 2.90 g/L; $p < 0.001$).[8]

Jiehao et al in his study of a case series of 10 children noted that median white blood cell count (WBC) 7.35×109/L and D – dimer was 0.45 μg/mL.[9]

Wang et al in his study said that only 3.0% (n = 2) infants experienced lymphopenia.[10]

In a study done by Henry et al summary of 80 laboratory-confirmed cases of SARS in children, leucopenia was observed in 47%, neutropenia in 52%, and lymphopenia in 46%.[11]

In a study conducted by Li et al the lymphocyte percentage (Lym%) was found to be inversely related to the severity and prognosis of patients, which in turn could be used to predict the severity and prognosis of patients with COVID-19.[12]

IN a study done by Devajit Nath et al showed that PLR was slightly higher in the Pediatric patients (mean=109.31) and 27.3% (3/11) of the pediatric cases had lymphopenia. Neutrophilia is observed in 36.3% cases in children younger than 10 years.[13]

Our study demonstrated that leucocytosis, neutrophilia, platelet count and increased neutrophil to lymphocyte ratio, which might be due to inflammatory response, have significant association with disease severity. Neutrophil to lymphocyte ratio was highest in patients with critical disease.

Our study did not show significant association of HB,PT and D-Dimer with the severity of the disease.

CONCLUSION

The study concluded that leukocytosis, neutrophilia,elevated NLR are significantly increased in patients with severe and critical disease. Platelet count reduced as the severity increased. PT, D Dimer did not show significant association with severity. Hematological manifestations are directly related to Covid 19 disease and these markers may be utilized as useful prognosticator for early prediction of disease severity. Thus appropriate management can be planned for such patients before they develop organ failure.

Limitation of the study was it was done in First wave where disease severity was mild and also because of small size sample and is a single center study. Furthermore, larger sample size is needed to verify the current findings.

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