ORIGINAL ARTICLE

COMPARISON OF SOME HEMATOLOGICAL VALUES BETWEEN COVID-19 POSITIVE AND NEGATIVE CHILDREN

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ABSTRACT

Background: Severe acute respiratory syndrome corona virus 2 is the causative agent of the current pandemic of corona virus disease 2019 (COVID-19). A complete blood count, obtainable within a short time, is the most commonly performed hematological laboratory test worldwide. Though many papers have been published describing hemocytometric changes in COVID-19 patients in abroad, but data in this regard is lacking in our patients. **Objective:** To compare hemocytometric changes in pediatric patients with COVID-19 with age and gender matched non-COVID-19 normal children. **Materials and methods:** This was a cross-sectional comparative study conducted in the department of clinical pathology, Bangladesh Shishu Hospital and Institute, Dhaka from August 2020 to April 2021. Among 30 children with COVID-19 positive and 33 children with COVID-19 negative children. The measurements of hemoglobin (Hb), haematocrit (Hct), the RBC count, total and differential count of WBC and platelet count of both group of children were done from an accredited laboratory. The study was approved by Institutional Ethics review Board. A questionnaire was used to obtain the data including age and sex of the children. Statistical analysis was performed by using software 'Statistical Package for Social Science (SPSS)' for windows version 22(SPSS Inc., Chicago, IL). The variables compared between two groups by using independent sample Student *t* test for continuous values and the chi-square or Fisher exact test for categorical values.Statistical significance was set at *p* value less than 0.05. **Result:** The mean ±SD age of the group 1 was 50.82±47.73 months and of the group 2 was 35.86±35.13 months with no significant (p=0.159) difference. There were 36.7% females in group I and 27.27% females in group II, but their difference was not statistically significant (p=0.424). No significant difference between groups was observed in Hb (p=0.453), Hct (p=0.382), RBC count (p=0.453), MCV (p=0.872), MCH (p=0.890), MCHC (p=0.974), and RDW (p=0.178) and WBC count (p>0.05). However, Monocyte was significantly higher in group I than group II (5.03±1.77 vs 3.79±1.82%, p=0.008). Five (16.7%) children in group I and no children in group II had Thrombocytopenia and 10 (33.3%) children in group I and 15(45.5%) children in group II had Thrombocytosis, and the difference was statistically significant (p=0.046). **Conclusion:** Children with COVID-19 positive have more monocyte count and develop more thrombocytopenia than COVID-19 negative children.

Key words: *COVID positive and negative children, haematological values.*

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) corresponds to a new coronavirus subtype, which was first identified in December 2019 inWuhan City, Hubei Province, China. This virus is the causative agent of the current pandemic of coronavirus disease 2019 (COVID-19). SARS-CoV-2 has spread quickly across the world. It has been causing various economic and social impacts, affecting globally the health systems and the routine of the population[1]. In Bangladesh the first three known cases were reported on March 8, 2020 and first death on March 21, 2020. On 6 May 202, cases were confirmed in all districts of Bangladesh.[2] The COVID-19 clinical features can include various symptoms, such as fever, myalgia, dry cough, dyspnea, fatigue, radiological evidence of ground glass lung opacities compatible with atypical pneumonia, diarrhea, and neurological manifestations. Furthermore, its severity is extremely variable, and for this reason, this disease can be classified as asymptomatic, mild, moderate, or severe.[1,3] With the emergence of SARS-CoV-2 mutants, the number of children infected with SARS-CoV-2 has gradually increased worldwide.[4,5]. According to a report issued by the American Academy of Pediatrics (APP) and Children's Hospital Association (CHA) on April 29, 2021, in the United States alone, there are 3,782,724 children were diagnosed with COVID-19, accounting for 13.8% of the total number of COVID-19.[5] The positive rate of SARS-CoV-2 in children in the United States is 5.3–33.4%, 1.2–3.1% of COVID-19 hospitalized patients are children, and 0.00–0.21% of COVID-19 deaths are children.[6]Bolanos analyzed the 54,971 confirmed cases of novel coronavirus pneumonia (NCP) registered by the Colombian National Institute of Health (CNIH) and found that the number of confirmed cases of COVID-19 in children accounted for 9.2% of all cases (5062 cases), and the number of confirmed cases of COVID-19 in Omani children accounted for 6.6% of all cases[7].

Knowledge of widely available diagnostic tools indicating a COVID-19 infection would help to control the pandemic. Molecular techniques to detect the virus have been developed, but a few healthcare settings have limited access to these tests as they require specialized equipment and expertise. Serology tests, which are even more limited, are still being

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evaluated and their use is more appropriate for epidemiological purpose[8]. In daily practice, indirect indicators of COVID-19, such as increases in C-reactive protein (CRP),D-dimer, albumin, ferritin and LDH levels, are also used and have proven to be of value, especially to estimate the severity of infection. Also, hemocytometric changes have been identified as supporting evidence of a COVID-19 infection and as possible indicators of severe disease.[8] A complete blood count, which results can be obtained within a short time, is the most commonly performed hematological laboratory test worldwide. Though many papers have been published describing hemocytometric our changes in COVID-19 patients in abroad, but researches are lacking in hemocytometric changes in our COVID-19 positive pediatric patients. The primary objective of the present study is to compare hemocytometric changes in pediatric patients with COVID-19 with age and gender matched non-COVID-19 normal children.

2. MATERIALS AND METHODS

2.1 Study design

This cross-sectional comparative study was conducted in the department of clinical pathology, Dhaka Shishu (Children) Hospital, Dhaka from August 2020 to April 2021 among 30 children with COVID-19 positive and 33 children with COVID-19 negative normal children. Patients who were referred to the department of clinical pathology of Bangladesh Shishu (Children) Hospital, Dhaka for hematological parameters during the study period were recruited for the study. The study was approved by Institutional Ethics review Board. A questionnaire was used to obtain the data including age and sex of the children. COVID-19 children were suspected by observing symptoms and signs and confirmed by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR).

2.2 Grouping of samples

COVID-19 positive children were classified as group I (n=30) and COVID-19 Negative children as group II(n=33).

2.3 Laboratory analysis

Peripheral venous blood samples were collected under sterile conditions into EDTA (2 ml) tubes. The measurements of hemoglobin (Hb), haematocrit (Hct), the RBCcount, total and differential count of WBC and platelet count were obtained by haematology analyser: Mythic -22 using reagent kits (Diluent, cleaner, lytic) from an accredited laboratory.

2.4 Working definition

Normal reference values: white blood cells, $(3.5–9.5)\times10^9$ /L; lymphocytes, $(2.1–5.7)\times10^9$ /L (<3 years) $(1.4–4.2)\times10^9$/L (4–6 years), $(1.1–3.2)\times10^9$ /L (≥6 years); haemoglobin, 130–175 g/L; platelet count, $(125–350)\times10^9$ /L.[9]

2.5 Statistical analysis

Statistical analysis was performed by using software 'Statistical Package for Social Science (SPSS)' for windows version 22 (SPSS Inc., Chicago, IL). The concentration of Hb, HCT, the RBC count, total and differential count of WBC and platelet count were expressed as mean±SDcompared between two groups by using independent sample Student *t* test. Categorical variables were expressed as frequencies and percentages and were analyzed by using the chi-square or Fisher exact test. Statistical significance was set at *p* value less than 0.05.

3. RESULT

Table I: Comparison of age between COVID-19 positive and negative children.

Group	Age (month)	p	95% Confidence Interval	
			Lower	Upper
Group I (n=30)	50.82 ± 47.73 (0.55-168)	0.159	-6.031	35.938
Group II (n=33)	35.86 ± 35.13 (1-120)			

The mean ±SD age of the group I was 50.82±47.73 months with a range of 0.55-168 months and the mean ±SD age of the group II was 35.86±35.13 months with a range of 1-120 months. The mean difference of age between two groups was not statistically significant (p=0.159, 95% CI: -6.031, 35.938) (Table-I).

Table II: Comparison age between COVID-19 positive and negative children.

Sex	Group I (n=30)	Group II (n=33)	P
Female	11(36.7%)	9(27.27%)	0.424
Male	19(63.3%)	24(72.73%)	
Total	30(100%0	33(100%)	

There were 11(36.7%) females in group I and 9(27.27%) females in group II, but their difference was statistically significant (p=0.424) (Table II)

Table 4: Comparison WBC variables between COVID-19 positive and negative children.

WBC variables	Group I (n=30)	Group II (n=33)	p	95% Confidence Interval of the Difference	
				Lower	Upper
WBC (total)(10^9/L)	9.55 ± 4.93 (2.80-19.70)	10.95 ± 3.96 (3.20-19.40)	0.216	-3.64902	.83993
Neutrophil(%)	48.67 ± 17.64 (2.0-73.0)	46.42 ± 15.00 (17.00-74.00)	0.588	-5.98578	10.47063
Lymphocyte (%)	44.00 ± 18.72 (14.00-94.00)	47.24 ± 14.69 (20.00-77.00)	0.445	-11.67971	5.19486
Monocyte (%)	5.03 ± 1.77 (2-10)	3.79 ± 1.82 (2-11)	0.008	.340	2.151
Eosinophil (%)	2.00 ± 2.14 (.00-9.00)	2.39 ± 1.43 (1.00-6.00)	0.392	-1.30704	.51916
Platelet (10^9/L)	305.2 ± 177.99 (8.00-728)	371.00 ± 164.58 (162-848)	0.133	-152.10046	20.50046

The mean ± SD WBC count was 9.55±4.93 x10^9/L in group I and 10.95 ± 3.96x10^9/L in group II with no significant difference between two groups (p=0.216). Similarly, no difference was between group I and group II in Neutrophil (48.67 ± 17.64 vs 46.42 ± 15.00%, p=0.588), Lymphocyte, (44.00 ± 18.72 vs 47.24 ± 14.69%. p=0.445), Eosinophil (2.00 ± 2.14 vs 2.39 ± 1.43%, p=0.392), and Platelet (305.2 ± 177.99 vs 371.00±164.58 x 10^9/L, p=0.133) count. However, Monocyte was significantly higher in group I than group II (5.03 ± 1.77 vs 3.79 ± 1.82%, p=0.008). (Table 4)

Table 5: Comparison Haemoglobin level between COVID-19 positive and negative children.

Haemoglobin level	Group I (n=30)	Group II (n=33)	P
Below	26(86.7%)	31(93.9%)	0.412
Normal	4(13.3%)	2(6.1%)	
Total	30	33	

Twenty-six (86.7%) children in group I and 31(93.9%) children in group II had Haemoglobin level lower than normal, but the difference was not statistically significant (p=0.412) (Table 5)

Table 6: Comparison Platelet level between COVID-19 positive and negative children.

Platelet level	Group I (n=30)	Group II (n=33)	P
Thrombocytopenia	5(16.7%)	0(0%)	0.046
Normal	15(50.0%)	18(54.5%)	
Thrombocytosis	10(33.3%)	15(45.5%)	
Total	30	33	

Five (16.7%) children in group I and no children in group II had Thrombocytopenia and 10(33.3%) children in group I and 15(45.5%) children in group II had Thrombocytosis, and the difference was statistically significant (p=0.046) (Table 6)

Table 7: Comparison of absolute count of Lymphocyte between COVID-19 positive and negative children

Lymphocyte absolute count	Group I (n=30)	Group II (n=33)	P
Lymphopenia	2(6.7%)	1(3.0%)	0.626
Normal	19(63.3%)	19(57.6%)	
Lymphocytosiss	9(30.0%)	13(39.4%)	
Total	30	33	

Two (6.7%) children in group I and 1(3.0%) children in group II had lymphopenia and 9(30.0%) children in group I and 13(39.4%) children in group II had lymphocytosis, but the difference was not statistically significant (p=0.626) (Table 7)

Table 8: Comparison WBC level between COVID-19 positive and negative children.

	Lymphocyte absolute count	Lymphocyte absolute count	P
Lymphopenia	1(3.3%)	1(3.0%)	0.359
Normal	18(60.0%)	14(42.4%)	
Lymphocytosiss	11(36.7%)	18(54.5%)	
Total	30	33	

One (3.3%) children in group I and 1(3.0%) children in group II had absolute lymphopenia and 11(36.7%) children in group I and 18(54.5%) children in group II had absolute lymphocytosis, but the difference was not statistically significant (p=0.359) (Table –8)

4. DISCUSSION

Children with COVID-19 suffer from fever, cough, dyspnoea, tachypnea and runny nose [10]. In our study, we found the age of the patients ranges from 16 days to 14 years and female children was 36.7%. Out findings are consisted with the findings of Soltani et al., (2020) [10] who found the age range of children with COVID-19 positive was 1 day to 15 years. But in their series, females were more (53.3%) than our setting (27.27%). However, the overall world wide data suggest that females suffer less than males.

We found no significant difference in Hb concentration, Hct, red cell count and red cell indices between two groups (p>0.05). This finding was supported by Kosmeri et al., (2020), Lu et al., (2020) and Parri and Lenge (2020) [11, 12,13] [13].In their study **they** found no significant abnormalities in haemoglobin concentration, red cell count in children with COVID-19 positive [10,11,12]. They stated that haemoglobin level was normal in asymptomatic children with COVID-19 positive. They also found no difference in haemoglobin concentration between children admitted to ICU and medical unit [11].

Five (16.7%) children in group I and no children in group II had Thrombocytopenia and 10(33.3%) children in group I and 15(45.5%) children in group II had Thrombocytosis, and the difference was statistically significant (p=0.046) (Table –VI)

We found that thrombocytopenia was more in children with COVID-19 positive than children with COVID-19 negative (16.7% vs 0%) and thrombocytosis was significantly less in children with COVID-19 positive than children with COVID-19 negative (33.3% vs 45.5%) and the difference was significant (p = 0.046). These findings was partially supported by Soltani et al (2020)[10]. They found thrombocytopenia in 13.3% cases in their series but they found thrombocytosis in only 13.3% cases. Whatever may be the difference between two studies, both the studies suggest that abnormality in platelet count occurs in 50% of children suffering from COVID-19.

We observed no significant difference in total WBC count or in differential count like neutrophil, eosinophil and lymphocyte (p>0.05). However monocyte count was significantly higher in COVID-19 positive group than negative group (5.03 ± 1.7% vs 3.79 ± 1.8%, p=0.008). Our findings are supported the finding of study conducted by by Kosmeri et al., (2020) and Henry et al., (2020) studied 66 COVID 19 positive children and found a normal leukocyte count in the majority of children [11, 14]. They found lymphopenia in 2 (3%) patients. We also found lymphopenia in 2(6.7%) patients with COVID -19.

They found that the majority of children with COVID-19 positive had normal white blood cell count.. Most common the most common white blood cell abnormality was leucopenia. Our findings somewhat differ from their findings.[11,14] We found higher monocyte count in COVID-19 positive children than COVID-19 negative children. So far we have reviewed literature; no data supported this higher monocyte count in COVID-19 positive children. It may be the fact that relative decrease of lymphocyte (44.00% in COVID 19 positive and 47.24% in COVID–negative children) may increase the percentage of monocyte in COVID 19 positive children. Yet, further study should be undertaken to confirm these findings with a large number of children and any role of monocyte to be played in COVID-19 positive patients should be sought.

5. CONCLUSION

Children with COVID-19 positive have more monocyte count and develop more thrombocytopenia than COVID-19 negative children.

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