The role of inflammatory indices in the outcome of COVID-19 cancer patients

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Abstract
To assess the prognostic role of different inflammatory indices on the outcome of cancer patients with COVID-19. Sixty-two adults and 22 pediatric cancer patients with COVID-19 infection were assessed for the prognostic value of certain inflammatory indices including the neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), platelet to lymphocyte ratio (PLR), derived NLR (dNLR), systemic inflammation index (SII), mean platelet volume to platelet ratio (MPR), C-reactive protein to lymphocyte ratio (CRP/L), aggregate index of systemic inflammation (AISI), systemic inflammation response index (SIRI), and neutrophil to lymphocyte, platelet ratio (NLPR). Data were correlated to patients’ outcome regarding ICU admission, and incidence of mortality. Increased CRP/L ratio in adult COVID-19 cancer patients was significantly associated with inferior survival [152 (19–2253) in non-survivors, compared to 27.4 (0.8–681) in survivors (P = 0.033)]. It achieved a sensitivity (60%) and a specificity (90.2%) at a cut-off 152, while it achieved a sensitivity of 60% and specificity 95.1% at a cut-off 252 (AUC 0.795, P = 0.033). When combining both CRP/L and NLPR for the prediction of poor outcome in adult cancer patients with COVID19, the sensitivity increased to 80% and the specificity was 70.7% (AUC 0.805, P = 0.027). Increased incidence of ICU admission in pediatric cancer patients associated significantly with the severity of covid19 infection, decreased mean corpuscular hemoglobin (MCH) < 28.3, increased red cell distribution width (RDW) > 16, lymphopenia < 1.04, pseudo Pelger-Huet appearance, and PLR < 196.4 (P = 0.004, P = 0.040, P = 0.029, P = 0.039, P = 0.050, and P = 0.040; respectively). The mean corpuscular volume (MCV), MCH, and RDW could be useful prognostic markers for poor outcome in COVID-19 pediatric cancer patients (P < 0.05 for all). Increased both CRP/L and NLPR associated significantly with poor survival in adult COVID-19 cancer patients, while PLR associated significantly with ICU admission in pediatric COVID-19 cancer patients.

Keywords COVID-19 · Inflammation index · Cancer · Pediatric · PLR · CRP/L and NLPR

Introduction
The pandemic of COVID-19 has become a worldwide healthcare problem, as it is responsible for about 62,773 deaths globally in the period between the end of 2019 and the 5th of April 2020 [1]. In fact, the COVID-19 pandemic is considered a life-threatening disease especially in patients who have comorbidities [2, 3]. Among them were the cancer patients, who are at a higher risk of developing adverse events including intensive care unit (ICU) admission, mechanical ventilation, and/or death more than patients without cancer [4]. Therefore, it is necessary for COVID-19 cancer patients to undergo special medical care, in addition, more research regarding the diagnosis and management is highly recommended to save these vulnerable patients.
It had been reported that most of COVID-19 patients have mild to moderate infection, while about 15–20% of cases develop severe form and require hospitalization, ICU admission, and/or mechanical ventilation [5–7]. A growing body of evidence indicates the important role of the inflammatory response accompanied by the virus infection, which is responsible for the pulmonary complications of COVID-19, that leads to acute respiratory distress syndrome (ARDS), and finally septic shock or multiple organ system failure (MOSF) [8, 9]. This inflammatory response is formed of uncontrolled production of inflammatory cytokines with the recruitment of inflammatory cells as macrophages and granulocytes that leads to cytokine storm [9, 10]. Peripheral white cell count (WBC) count with its subtypes are good predictors for this systematic inflammatory response, and thereby the prognosis of the disease [10]. Many recently published studies demonstrated that many combined ratios of complete blood count (CBC) parameters such as NLR, dNLR, PLR, MLR, and SII could be useful diagnostic and prognostic markers for the severity of COVID-19 patients [11–13]. However, this situation would be different in cancer patients, as they have an incompetent immune system that is caused by either the nature of the cancer itself or the anticancer treatment [14, 15].

Therefore, the aim of the current study was to assess the prognostic role of different inflammatory indices including NLR, MLR, dNLR, PLR, SII, MPR, CRP/L, AISI, SIRI, and NLPR in cancer patients with COVID-19 infection. Data were correlated to the clinical features of both adult and pediatric cancer patients. As this may help to find an accurate, early, and accessible marker that could predict the prognosis and outcome of such COVID-19 cancer patients.

**Patients and methods**

This is a retrospective cohort study conducted on 84 pediatric and adult patients with different types of cancer and got COVID-19 infection. Those patients were admitted and treated at the National Cancer Institute (NCI) between June 2020 and March 2021. All patients were subjected to full history taking, full clinical examination, laboratory assessment in the form of complete hematological (Sysmex XN1000 and Sysmex XT1800) and coagulation profile, kidney function and liver function tests, serum Ferritin and D-dimer. Also, full radiological assessment especially chest X-ray and computed tomography (CT) on chest. Patients were proved to be COVID-19 positive based on the molecular, laboratory, and radiological findings according to the guidance of the world health organization (WHO) [16]. The adult cancer patients were assessed for the severity of SARS-COV-2 infection according to the WHO classification into; mild infection in patients with mild symptoms and normal imaging findings, moderate COVID-19 infection in patients with fever and lung affection by chest X-ray and CT, while severe infection in patients who had severe respiratory symptoms, respiratory rate > 30/min and O₂ saturation was < 93% in the rest state [16]. While pediatric cancer patients were classified according to the severity of SARS-COV-2 infection into asymptomatic infection in patients who had no symptom of COVID-19 at any time point, mild infection in patients who had mild symptoms and did not require hospitalization, moderate severity in patients who required inpatients management without ICU care, while severe infection in patients who required ICU care for COVID-19 symptoms [17].

Most of the patients 65/84 (77.4%) were receiving chemotherapy; 36 (42.9%) were on induction chemotherapy, 11 (13.1%) were on maintenance, and 8 (9.5%) patients were on consolidation chemotherapy. While the remaining 28 (33.3%) patients were post-surgery, and only one was receiving radiotherapy. In addition, there were 40 (47.6%) patients received intensified chemotherapy according to their risk stratification.

We tried to investigate the association between complete blood cell count (CBC)-derived different inflammatory indices and patients’ outcome regarding ICU admission, and incidence of mortality, in both adult and pediatric COVID-19 cancer patients.

The inflammatory indices were calculated as follows: NLR (neutrophils/lymphocytes), MLR (monocyte/lymphocyte ratio), PLR (platelet/lymphocyte ratio), dNLR (neutrophils/(white blood cells – neutrophils)), MPR (mean platelet volume/platelet ratio), CRP/L (CRP/lymphocyte ratio), NLPR (neutrophil/(lymphocyte × platelet ratio)), SII ((neutrophils × platelets)/lymphocytes), AISI ((neutrophils × monocytes × platelets)/lymphocytes), and SIRI ((neutrophils × monocytes)/lymphocytes).

**Statistical analysis**

Data were analyzed using the SPSS package (version 22; SPSS Inc., Chicago, IL, USA). It was tested for normalization using Shapiro test. Continuous variables were expressed as median and interquartile range (IQR), while categorical variables were expressed as frequencies and percentages. Comparisons between groups were performed using Mann–Whitney test and Chi-square test for numerical and categorical variables, respectively. A receiver operating characteristic (ROC) curve analysis was performed to determine the ability of the inflammatory indices for association with mortality in adult and pediatric COVID-19 cancer patients. Univariate and multivariate regression analyses were performed to detect the prognostic value of the inflammatory indices regarding association with ICU admission in COVID-19 adult and pediatric cancer patients. All tests were
two-tailed and P value < 0.05 was considered a statistically significant.

**Results**

The current study included 84 cancer patients with COVID-19, 22 (26.1%) of them were pediatrics [50% (11/22) were male & 50% (11/22) were female], and 62 (73.8%) were adult patients [62.9% (39/62) were males and 37.1% (23/62) were females, P = 0.320]. Hematological malignancies were more common than solid tumors in pediatric patients [16 (72.7%) vs. 6 (27.3%); respectively], while solid tumors were more commonly observed in adults than hematological malignancies [35 (56.5%) vs. 27 (43.5%); respectively, P = 0.025]. The disease course was progressive in 72.6% (45/62) in adults compared to 68.2% (15/22) in pediatric cancer patients (P = 0.785).

The degree of COVID-19 infection in pediatric cancer patients was asymptomatic to mild in 7 (31.8%) patients, moderate in 5 (22.7%), and severe in 10 (45.5%) patients. While in adults, the degree of COVID-19 infection was mild in 26 (41.9%), moderate in 25 (40.3%), and severe in 11 (17.7%) patients, (P = 0.033). The ICU admission was encountered in 50% (11/22) of the pediatric patients, compared to 22.6% (14/62) of the adult patients (P = 0.028).

There were 50% (11/22) of the pediatric cancer patients mechanically ventilated, compared to only 8.1% (5/62) of the adult patients (P < 0.001). Neutropenic sepsis was found in 9 (10.7%) patients [4/62 (6.5%) of adults, and 5/22 (22.7%) in pediatric patients, (P = 0.049)].

Of the adult patients, 14.5% (9/62) had one or more pre-existing diseases, including hypertension, cardiovascular disease, and diabetes, compared to only 9.1% (2/22) of pediatric COVID-19 cancer patients who had hypertension (P = 0.575). Finally, 40.9% (9/22) of pediatric patients, and 9.7% (6/62) of the adult patients died (P = 0.002). The other clinical features of the assessed patients were illustrated in Table 1.

**Laboratory findings of the adult and pediatrics COVID-19 cancer patients**

The morphological changes of the monocytes regarding being vacuolated, aggressive, and granular with cytoplasmic tail were significantly detected in pediatric patients (P = 0.035), where the monocytes’ changes were positive in 19/22 (86.4%) and negative in 3/22 (13.6%). Meanwhile, in adult COVID-19 cancer patients, the monocytes’ changes were positive in 38/62 (61.3%) and negative in 24/62 (38.7%). The acute phase reactants, e.g., Ferritin was increased in pediatrics than adults, but it did not reach a significant level [4337 (3610–6180) vs. 72 (10–135)];

| Clinical variable | Patients | P value |
|-------------------|---------|---------|
| Age Median (IQR)  | Pediatric (22) | Adult (62) | <0.001 |
| Gender Male       | 11 (50%) | 39 (62.9%) | 0.320 |
|                   Female | 11 (50%) | 23 (37.1%) |
| Type of cancer    | Hematological malignancies 16 (72.7%) | 27 (43.5%) | 0.025 |
|                   Solid tumors 6 (27.3%) | 35 (56.5%) |
| Disease status    | Remission 7 (31.8%) | 17 (27.4%) | 0.785 |
|                   Stationary or progressed 15 (68.2%) | 45 (72.6%) |
| Degree of COVID infection | Mild 7 (31.8%) | 26 (41.9%) | 0.033 |
|                   Moderate 5 (22.7%) | 25 (40.3%) |
|                   Severe 10 (45.5%) | 11 (17.7%) |
| ICU admission Yes | 11 (50%) | 14 (22.6%) | 0.028 |
|                   No | 11 (50%) | 48 (77.4%) |
| Mechanical ventilator Yes | 11 (50%) | 5 (8.1%) | <0.001 |
|                   No | 11 (50%) | 57 (91.9%) |
| Death No | 13 (59.1%) | 56 (90.3%) | 0.002 |
|                   Yes | 9 (40.9%) | 6 (9.7%) |
| Comorbidities No | 20 (90.9%) | 53 (85.5%) | 0.575 |
|                   HTN 2 (9.1%) | 4 (6.5%) |
|                   Cardiac disease 0 (0.0%) | 4 (6.5%) |
|                   DM 0 (0.0%) | 1 (1.6%) |
| Blood stream infection –ve | 17 (77.3%) | 57 (91.9%) | 0.118 |
|                   +ve 5 (22.7%) | 5 (8.1%) |
| Neutropenic sepsis No | 17 (77.3%) | 58 (93.5%) | 0.049 |
|                   Yes | 5 (22.7%) | 4 (6.5%) |
| DCL No | 18 (81.8%) | 57 (91.9%) | 0.232 |
|                   Yes | 4 (18.2%) | 5 (8.1%) |
| Liver disease No | 19 (86.4%) | 55 (88.7%) | 0.717 |
|                   Yes | 3 (13.6%) | 7 (11.3%) |
| Renal disease No | 19 (86.4%) | 56 (90.3%) | 0.691 |
|                   Yes | 3 (13.6%) | 6 (9.7%) |
| Duration of hospital stay Median (IQR) | 11 (0–42) | 10 (0–30) | 0.656 |
|                   < 10 days 11 (50%) | 33 (55.0%) | 0.804 |
|                   > 10 days 11 (50%) | 27 (45.0%) |

Bold values indicate statistically significant
respectively, \( (P = 0.064) \). Also, there was a significant difference between the pediatric and adult patients regarding the kidney functions laboratory tests including Urea \([24 (12–54) \text{ vs. } 31 (13–86); \text{ respectively, } (P = 0.022)]\) and Creatinine \([0.55 (0.3–1.2) \text{ vs. } 0.8 (0.3–3.6); \text{ respectively, } (P < 0.001)]\). The other different laboratory parameters including Total Leukocyte Count (TLC), Hemoglobin concentration (Hb), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH), Red Cell Distribution Width (RDW), Neutrophil, lymphocytes, and monocytes absolute and relative values did not show any statistical difference between the assessed adult and pediatric patients’ groups (Table 2).

### Inflammatory indices in adult and pediatric COVID-19 cancer patients

The median NLR in pediatric patients was 1.889 (IQR 0.1–16.6), while in adults it was 2.838 (IQR 0–30.3, \( P = 0.345 \)). The median LMR in pediatric patients was 2.072 (IQR 0.1–18.5), and in adults was 2.550 (IQR 0.4–120, \( P = 0.274 \)). The median PLR in pediatric patients was 196.428 (IQR 4.4–2054.5), and in adults, it was 156

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**Table 2** Laboratory findings of the adult and pediatric COVID-19 cancer patients

| Clinical variable | Patients | \( P \) value | Clinical variable | Patients | \( P \) value |
|-------------------|----------|--------------|-------------------|----------|--------------|
|                  | Pediatric (22) | Adult (62) |                  | Pediatric (22) | Adult (62) |
| TLC 5.3 (49–12.7) | 7.9 (27–31) | 0.068 MCV 83.9 (70–96.5) | 84.9 (51–807) | 0.749 |
| Hb 10.3 (7.7–16) | 10.9 (4.9–16.3) | 0.791 MCH 28.3 (21.5–34.3) | 28.2 (19.2–85.4) | 0.891 |
| RDW 16.2 (13.3–43.8) | 15 (11.6–21.2) | 0.338 Normoblast 0 (0–1.3) | 0 (0–1.3) | 0.126 |
| Platelet count 225 (31–724) | 284 (5–666) | 0.583 MPV 10 (7.6–11) | 10.3 (6.6–13.1) | 0.284 |
| Neutrophil 1.9 (0.4–10.9) | 4.9 (0.3–28.6) | 0.54 Neutrophil% 47.9 (7–86) | 65 (11–92.4) | 0.241 |
| IG 0.02 (0.02–0.53) | 0.04 (0.01–1.4) | 0.650 IG% 0.6 (0–2.87) | 0.5 (0.1–22.1) | 0.107 |
| Lymphocytes 1.04 (12–2.86) | 1.7 (0.9–4.4) | 0.109 Lymphocytes% 21.1 (6.9–53.7) | 20.5 (3–85.3) | 0.734 |
| Monocytes 0.58 (0.4–1.79) | 0.73 (0.2–4.2) | 0.263 Monocytes% 7.9 (0.8–71.9) | 8.6 (1.7–34.5) | 0.089 |
| Eosinophil 0.03 (0–1.4) | 0.09 (0–0.56) | 0.192 Basophil 0 (0–2) | 0 (0–0.06) | 0.247 |
| Giant | | | | |
| Negative | 10 (45.5%) | 21 (33.9%) | 0.441 Negative | 20 (90.9%) | 52 (83.9%) | 0.724 |
| Positive | 12 (54.5%) | 41 (66.1%) | 0.617 Positive | 2 (9.1%) | 10 (16.1%) |
| Toxic granulation | | | Pelger-huet Negative | 15 (68.2%) | 38 (61.3%) | 0.617 Negative | 8 (36.4%) | 20 (32.3%) | 0.795 |
| Positive | 7 (31.8%) | 24 (38.7%) | Positive | 14 (63.6%) | 42 (67.7%) |
| Hypogranulation | | | Shift to left Negative | 20 (90.9%) | 55 (88.7%) | 0.774 Negative | 18 (81.8%) | 45 (72.6%) | 0.568 |
| Positive | 2 (9.1%) | 7 (11.3%) | Positive | 4 (18.2%) | 17 (27.4%) |
| Mature | | | Plasmoid Negative | 3 (13.6%) | 10 (16.1%) | 0.781 Negative | 3 (13.6%) | 13 (21.0%) | 0.543 |
| Positive | 19 (86.4%) | 52 (83.9%) | Positive | 19 (86.4%) | 49 (79.0%) |
| Monocytoid & Ballerina | | | Vacculated, aggressive, monocovicyte Negative | 8 (36.4%) | 27 (43.5%) | 0.621 Negative | 3 (13.6%) | 24 (38.7%) | <0.001 |
| Positive | 14 (63.6%) | 35 (56.5%) | Positive | 19 (86.4%) | 38 (61.3%) |
| LDH 221 (127–762) | 237 (129–1890) | 0.990 Albumin 3.4 (1.9–4.2) | 3.2 (1.8–4.6) | 0.534 |
| D-Dimer 0.5 (0–123) | 4 (1–95) | 0.414 Ferritin 4337 (3610–6180) | 72 (10–135) | 0.064 |
| CRP 22.9 (0–248) | 42 (1.8–406) | 0.212 Total bilirubin 0.45 (0.2–2.5) | 0.45 (0.1–4.7) | 0.842 |
| AST 20.5 (9–42) | 19 (9–275) | 0.142 ALT 20 (8–52) | 21 (6–280) | 0.051 |
| Urea 24 (12–54) | 31 (13–86) | 0.022 Creatinine 0.55 (3–1.2) | 0.8 (0.3–3.6) | 0.035 |
| PT 1.12 (1–4.1) | 1.14 (0.96–1.9) | 0.849 |

Bold values indicate statistically significant

The \( P \) value is significant if < 0.05

**ALT** alanine transaminase, **AST** aspartate transaminase, **CRP** C- reactive protein, **Hb** hemoglobin concentration, **IG** immature granulocyte, **LDH** lactate dehydrogenase, **MCH** mean corpuscular hemoglobin, **MCV** mean corpuscular volume, **MPV** mean platelet volume, **PT** prothrombin time, **RDW** red cell distribution width, **TLC** total leukocyte count.
The median d(NLR) in pediatric patients was 0.8878 (IQR 0.08–9.50), and in adults it was 1.5874 (IQR 0–12.07, \( P = 0.203 \)). The median SII index in pediatric patients was 291.64 (IQR 1–8154), and in adults it was 615.98 (IQR 0–9752, \( P = 0.303 \)). The median CRP/L in pediatric patients was 55.84 (IQR 0–998.33), and it was 30.92 (IQR 0.79–2253.3, \( P = 0.985 \)) in adults. The median MPR in pediatric patients was 0.0437 (IQR 0.01–0.35), and it was 0.0342 (IQR 0.01–0.45, \( P = 0.384 \)) in adults. The median NLPR in pediatric patients was 0.0107 (IQR 0–0.07), while in adults it was 0.0114 (IQR 0–0.35, \( P = 0.726 \)). The median SIRI in pediatric patients was 0.61 (IQR 0–20.16), while in adults it was 1.516 (IQR 0–23.56, \( P = 0.146 \)). The median AISI in pediatric patients was 98.58 (IQR 0–1459.9), while it was 289.51 (IQR 0–8821.9, \( P = 0.091 \)) in adult COVID-19 cancer patients (Fig. 1).

### Association between inflammatory indices and the outcome of the assessed COVID-19 cancer patients

Patients were categorized according to their outcome regarding ICU admission and mortality.

Increased CRP/L ratio in adult COVID-19 cancer patients was significantly associated with inferior survival, as it was 152 (19–2253) in non-surivors, compared to 27.4 (0.8–681) in survivors (\( P = 0.033 \)). Other inflammatory indices showed no statistical difference between ICU admitted/non admitted patients nor survivors/non-survivors COVID-19 cancer patients (Table 3).

Regarding COVID-19 pediatric cancer patients, the association between inflammatory indices and patients’ outcome showed no statistically significant difference between ICU admitted pediatric patients and non-ICU patients. Also, there were no significant differences between survivors and non-survivors in pediatric COVID-19 cancer patients (Table 4).

The ROC curve analysis of inflammatory indices showed that CRP/L associated significantly with increased mortality in adult COVID-19 cancer patients with a sensitivity of 60% and a specificity of 90.2% at a cut-off 152, while it achieved a sensitivity of 60% and specificity 95.1% at a cut-off 252 (AUC 0.795, \( P = 0.033 \), Fig. 2). While, when combining both CRP/L and NLPR for the prediction of the poor outcome in adult COVID19 cancer patients, the sensitivity increased to 80% and the specificity was 70.7% (AUC 0.805, \( P = 0.027 \), Table 5). However, ROC analysis did not reveal any statistical significance of the assessed other inflammatory indices for predicting mortality in either adult or pediatric COVID-19 cancer patients (Figs. 2 and 3).

### Univariate analysis of risk factors for COVID-19 associated ICU admission in cancer patients

Increased incidence of ICU admission in pediatric cancer patients associated significantly with increased severity of covid19 infection (OR 72, \( P = 0.004 \)), as out of the 11 patients who admitted to the ICU, 10 patients had severe COVID-19 infection. Also, increased incidence of ICU admission in pediatric cancer patients associated significantly with decreased MCH below 28.3 (O.R 7.1, \( P = 0.040 \)), increased RDW > 16 (OR 12, \( P = 0.029 \)). In addition, the degree of lymphopenia (lymphocytes < 1.04) associated significantly with poor prognosis (OR 1.77, \( P = 0.039 \)). Similarly, abnormality in neutrophils morphology with pseudo Pelger-Huet appearance associated with dismal outcome (OR 8, \( P = 0.050 \)). The PLR as an inflammatory index (<196.4 vs >196.4) significantly predicts poor patients’ prognosis (OR 7.11, \( P = 0.040 \), Table 6).

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**Fig. 1** Expression levels of different inflammatory indices (NLR, MLR, PLR, dNLR, SII, MPR, CRP/L, AISI, SIRI, and NLPR) in adult and pediatric COVID-19 cancer patients
However, univariate analysis for COVID-19 associated ICU admission in adult cancer patients revealed that disturbed conscious level (DCL) associated significantly with inferior outcome of the patients (OR 11.1, \( P = 0.046 \)). The other clinico-pathological features assessed did not show any significant difference (Table 7).

### Table 3  
Association between inflammatory indices and patients’ outcome in adult cancer patients with COVID-19

| Index     | ICU admission |  
|-----------|---------------|
|           | Yes \((n = 14)\) | No \((n = 48)\) | \( P \) value | Death |  
|           | Yes \((n = 6)\) | No \((n = 56)\) | \( P \) value |        |
| NLR       | 4.8 (1.7–24.5) | 3.3 (0–25.1) | 0.957 | 2.99 (0.2–24.5) | 3.2 (0–30.3) | 0.437 |
| LMR       | 2.6 (0.9–10) | 2.5 (0.4–20) | 0.204 | 1.7 (0.8–18) | 2.5 (0.4–25) | 0.910 |
| PLR       | 241 (81–2322) | 161 (5–519) | 0.722 | 128 (3.4–386.7) | 167 (5–2322) | 0.821 |
| dNLR      | 2.8 (1.2–11.3) | 2.1 (0.12–11.8) | 0.762 | 1.1 (0.16–11.3) | 2.1 (0.12–12.1) | 0.192 |
| SII       | 1301 (446–7878) | 704 (0–6946) | 0.423 | 570 (1–7878) | 754 (0–9752) | 0.281 |
| CRP/L     | 27.8 (2–289) | 23.9 (0.8–250) | 0.278 | 152 (19–2253) | 27.4 (0.8–681) | 0.033 |
| MPR       | 0.03 (0.01–0.05) | 0.04 (.02–1.96) | 0.072 | 0.0 (0.03–0.03) | 0.04 (.01–1.96) | 0.595 |
| NLPR      | 0.01 (0–0.08) | 0.01 (0–1.7) | 0.915 | 0.04 (0–0.08) | 0.01 (0–1.7) | 0.408 |
| SIRI      | 2.9 (0.2–23.6) | 2 (0–21.1) | 0.845 | 12 (0.5–23.6) | 2 (0–20.1) | 0.802 |
| AISI      | 1211 (39–7960) | 501 (.01–8822) | 0.557 | 3866 (169–7963) | 501 (.01–8822) | 0.341 |

Bold value indicates statistically significant

The \( P \) value is significant if < 0.05

AISI aggregate index of systemic inflammation, CRP/L C-reactive protein to lymphocyte ratio, dNLR derived neutrophil to lymphocyte ratio, MLR monocyte to lymphocyte ratio, MPR mean platelet volume to platelet ratio, NLPR neutrophil to lymphocyte, platelet ratio, NLR the neutrophil to lymphocyte ratio, PLR platelet to lymphocyte ratio, SII systemic inflammation response index, and SIRI systemic inflammation response index

### Table 4  
Association between inflammatory indices and patients’ outcome in pediatric cancer patients with COVID-19

| Index     | ICU admission |  
|-----------|---------------|
|           | Yes \((n = 11)\) | No \((n = 11)\) | \( P \) value | Death |  
|           | Yes \((n = 9)\) | No \((n = 13)\) | \( P \) value |        |
| NLR       | 2.9 (0.2–11.3) | 2 (0.3–10.6) | 0.718 | 2.9 (0.2–11.3) | 2 (0.3–10.6) | 0.973 |
| LMR       | 1.9 (0.5–3.1) | 1.4 (0.3–3.4) | 0.768 | 1.9 (0.5–3.1) | 1.4 (3–3.4) | 0.713 |
| PLR       | 176 (9.5–862) | 604 (119–970) | 0.250 | 176 (9.5–862) | 604 (119–970) | 0.713 |
| dNLR      | 2 (0.1–3.6) | 0.5 (0.2–6.2) | 0.974 | 2 (0.1–3.6) | 0.5 (0.2–6.2) | 0.973 |
| SII       | 863 (7–8154) | 302 (119–2344) | 0.718 | 863 (7–8154) | 302 (119–2344) | 0.920 |
| CRP/L     | 2.9 (0.8–203) | 54.8 (0–332) | 0.600 | 2.9 (0.79–203) | 54.8 (0–332) | 0.223 |
| MPR       | 0.03 (0.01–0.35) | 0.05 (0.03–0.06) | 0.560 | 0.03 (0.01–0.35) | 0.05 (0.03–0.06) | 0.674 |
| NLPR      | 0.01 (0–0.02) | 0.01 (0–0.05) | 0.250 | 0.01 (0–0.02) | 0.01 (0–0.05) | 0.243 |
| SIRI      | 1.5 (0.12–20) | 0.72 (0.07–7.6) | 0.870 | 1.5 (0.12–20) | 0.72 (0.07–7.6) | 0.764 |
| AISI      | 492 (9–14,594) | 139 (24–1687) | 0.718 | 492 (9–14,595) | 140 (24–1688) | 0.973 |

The \( P \) value is significant if < 0.05

AISI aggregate index of systemic inflammation, CRP/L C-reactive protein to lymphocyte ratio, dNLR derived neutrophil to lymphocyte ratio, MLR monocyte to lymphocyte ratio, MPR mean platelet volume to platelet ratio, NLPR neutrophil to lymphocyte, platelet ratio, NLR the neutrophil to lymphocyte ratio, PLR platelet to lymphocyte ratio, SII systemic inflammation response index, and SIRI systemic inflammation response index

The prognostic role of RBCs indices in COVID-19 cancer patients

The ROC analysis was performed to evaluate the role MCV, MCH, and RDW in predicting the outcome in COVID-19 cancer patients. It showed that the sensitivity, specificity,
and AUC of MCV were 90%, 100%, and 0.926; respectively, \((P = 0.001)\), at a cut-off (83.6 fL), MCH were 81.8%, 72.7%, and 0.802; respectively, \((P = 0.017)\), at a cut-off (27.7 Pg), and the RDW were 72.7%, 90%, and 0.841; respectively, \((P = 0.008)\) at a cut-off (16.3 fL), for association with increased incidence of ICU admission in pediatric COVID-19 cancer patients (Fig. 4A–C). Where the mean Hb concentration for these children was 9.9 ± 2.5 gm/dl. While for increased mortality rates, the sensitivity, specificity, and AUC of MCV were 88.9%, 92.3%, and 0.889; respectively, \((P = 0.002)\), at a cut-off (84.4 fL), MCH were 77.8%, 61.5%, and 0.752; respectively, \((P = 0.049)\) at a cut-off (27.7 Pg), and for RDW, they were 77.8%, 83.3%, and 0.778; respectively, \((P = 0.033)\) at a cut-off (16.3 fL, Fig. 4E–G). Regarding the combination of MCV, MCH, and RDW together in pediatric COVID-19 cancer patients, it showed a sensitivity (81.8%), specificity (100%), AUC (0.927) for association with ICU admission \((P = 0.001, \text{Fig. 4D})\), and the mean Hb concentration for these children was 10.4 ± 2.5 gm/dl. While it achieved a sensitivity (77.8%), specificity (83.3%), AUC (0.843) for association with increased incidence of mortality \((P = 0.009, \text{Fig. 4H})\). However, these parameters did not show any significant association with the outcome of adult COVID-19 cancer patients (data not shown).

### Discussion

Many studies have reported the useful diagnostic and prognostic roles of different inflammatory indices in COVID-19 infection in noncancer population [11–13]; however, their role in COVID-19 cancer patients is not well assessed. In the current study, we could not find any significant impact of NLR, MLR, dNLR, SII, AISI, SIRI, MPR, CRP/L, and NLPR on the outcome of both adult and pediatric cancer patients with COVID-19 infection, which was in contrast to that observed in COVID-19 non-cancer patients [18–20]. Meanwhile, other studies demonstrated that increased levels of NLR, PLR, and SII associated significantly with death in patients with lung, bladder, and cervical cancer [21–23]. This discrepancy in the results could be explained by that cancer patients with COVID-19 viral infection have underlying risk factors regarding the type of cancer, as well as the type of treatment, e.g., chemotherapy, radiotherapy, or cytotoxic drugs with their known myelosuppressive and immunosuppressive consequences [24]. As this myelosuppressive and/or immunosuppressive effect causes reduction in the neutrophil, monocyte, platelets, RBCs, T-cell, and B-cell populations [25], which affects their derived inflammatory indices. Therefore, it will eventually elucidate a different response to...
the COVID-19 infection or its treatment, unlike in COVID-19 non-cancer patients.

Moreover, many recent series reported that cancer patients infected with COVID-19 had more severe outcomes compared to those noncancer COVID-19 patients, especially in those with hematological or lung malignancies [24, 26]. Mehta et al. demonstrated increased case fatality rate (CFR) in cancer patients with COVID-19 infection, it was 37% for hematologic malignancies and 25% for solid tumors. They proposed this high CFR in cancer patients with COVID-19 might be due to the presence of co-morbidities associated with cancer patients, or due to the myelosuppressive effect of the anticancer treatment received. Moreover, they also concluded that COVID-19 infection could increase the risk of mortality regardless of the cancer type [24].

The present study demonstrated that increased CRP/L ratio was the only index associated significantly with lower survival in adult COVID-19 cancer patients. Furthermore, these data were confirmed by the ROC curve analysis which showed that CRP/L associated significantly with increased mortality in adult COVID-19 cancer patients with a sensitivity of 60% and a specificity of 90.2% at a cut-off 152, and the specificity increased to 95.1% at a cut-off 252. While, when combining both CRP/L and NLPR for the prediction of the poor outcome in adult COVID19 cancer patients, the sensitivity increased to 80% and the specificity was 70.7% (AUC 0.805). Therefore, increased both CRP/L and NLPR could be useful prognostic markers for the prediction of poor outcome in adult COVID-19 cancer patients. These data are in agreement with many recent reports concluded that decreased lymphocyte to C-reactive protein ratio is considered a predictor factor for poor outcome and mortality in COVID-19 patients [19, 27, 28].

Fig. 3  ROC curve analysis of inflammatory indices (NLR, MLR, PLR, dNLR, SII, AISI, SIRI, MPR, CRP/L, and NLPR) for association with mortality in pediatric cancer patients
Table 6  Bivariable regression models of potential prognostic variables associated with ICU admission in COVID-19 pediatric cancer patients

| Variable                                      | Odds ratio | 95% CI Lower | 95% CI Upper | P value |
|-----------------------------------------------|------------|--------------|--------------|---------|
| Gender male vs female                         | 2.917      | 0.442        | 19.234       | 0.266   |
| Disease (progression vs remission)            | 1.500      | 0.189        | 11.927       | 0.702   |
| Degree of COVID-19 (sever vs moderate or mild)| 72.000     | 3.841        | 1349.547     | 0.004   |
| DCL (+ve vs −ve)                              | 3.429      | 0.287        | 40.946       | 0.330   |
| Blood stream infection (+ve vs −ve)           | 1.500      | 0.189        | 11.927       | 0.702   |
| Comorbidities (+ve vs −ve)                    | 2.000      | 0.150        | 26.734       | 0.600   |
| Liver disease (+ve vs −ve)                    | 2.000      | 0.150        | 26.734       | 0.600   |
| Type of cancer                                | 2.000      | 0.250        | 15.991       | 0.513   |
| Hematological vs solid                        |            |              |              |         |
| TLC (< 10 vs > 10)                            | 2.000      | 0.150        | 26.734       | 0.600   |
| Hb (< 10 vs > 10)                             | 1.867      | 0.283        | 12.310       | 0.517   |
| MCV (< 90 vs > 90)                            | .000       | .000         |              | 0.999   |
| MCH (< 28.3 vs >28.3)                         | 7.111      | 1.089        | 46.441       | 0.040   |
| RDW (>16 vs <16)                              | 12.000     | 1.294        | 111.323      | 0.029   |
| NRBC (< 1 vs > 1)                             | .000       | .000         |              | 0.999   |
| PLTs (>150 vs < 150)                          | 2.000      | 0.312        | 12.840       | 0.465   |
| MPV (< 10 vs > 10)                            | 2.667      | 0.347        | 20.508       | 0.346   |
| Giant (+ve vs −ve)                            | 1.250      | 0.205        | 7.615        | 0.809   |
| Neutrophil > 7.5 vs < 7.5                     | 2.000      | 0.150        | 26.734       | 0.600   |
| Neutrophil < 70 vs > 70                       | 1.143      | 0.126        | 10.386       | 0.906   |
| Toxicgran (+ve vs −ve)                        | 1.333      | 0.204        | 8.708        | 0.764   |
| Pelger-huet (+ve vs −ve)                      | 8.000      | 1.001        | 63.963       | 0.050   |
| Hypogranulation (+ve vs −ve)                  | .000       | .000         |              | 0.999   |
| Shift to left (−ve vs +ve)                     | 2.571      | 0.192        | 34.473       | 0.476   |
| IGRc(1)                                       | 2.000      | 0.134        | 29.808       | 0.615   |
| Lymphocyte (< 1.04 vs > 1.04)                 | 1.77       | 56.123       | 1.105        |         |
| Lymphocyte % (>21.1 vs <21.1)                 | 5.4        | 0.088        | 0.778        | 37.505  |
| Mature (+ve vs −ve)                           | 0.500      | 0.037        | 6.683        | 0.600   |
| Plasmoid (+ve vs −ve)                         | 0.500      | 0.037        | 6.683        | 0.600   |
| Monocytoid (+ve vs −ve)                       | 1.333      | 0.204        | 8.708        | 0.764   |
| Monocyte (< 1 vs > 1)                         | 3.429      | 0.287        | 40.946       | 0.330   |
| Monocyte % (< 10 vs > 10)                     | 1.200      | 0.194        | 7.441        | 0.845   |
| Vacuolated (+ve vs −ve)                       | 2.571      | 0.192        | 34.473       | 0.476   |
| PT (> 1 vs < 1)                               | 3.333      | 0.384        | 28.959       | 0.275   |
| CRP (> 6 vs < 6)                              | 1.905      | 0.340        | 10.667       | 0.464   |
| LDH (> 220 vs < 220)                          | 2.519      | 0.460        | 13.801       | 0.287   |
| Albumin (< 3.5 vs > 3.5)                      | 3.000      | 0.562        | 16.013       | 0.199   |
| ALT (< 55 vs > 55)                            | 6.545      | 0.541        | 79.232       | 0.140   |
| AST (< 34 vs > 34)                            | 1.937      | 0.396        | 9.491        | 0.415   |
| Total bilirubin (< 1.2 vs > 1.2)              | 2.000      | 0.146        | 27.447       | 0.604   |
| Creatinin (< 1.25 vs > 1.25)                  | 1.500      | 0.241        | 9.345        | 0.664   |
| Urea (< 45 vs > 45)                           | 1.212      | 0.212        | 6.935        | 0.829   |
| NLR (< 1.89 vs > 1.89)                        | 1.440      | 0.269        | 7.721        | 0.675   |
| LMR (> 2.07 vs < 2.07)                        | 1.400      | 0.256        | 7.714        | 0.670   |
| PLR (> 196.4 vs > 196.4)                      | 7.111      | 1.089        | 46.441       | 0.040   |
| dNLR (> 0.89 vs < 0.89)                       | 3.062      | 0.539        | 17.401       | 0.207   |
| SII (> 291.6 vs < 291.6)                      | 1.440      | 0.269        | 7.714        | 0.670   |
| CRP/L (<55.8 vs >55.8)                        | 2.778      | 0.367        | 21.029       | 0.323   |
infection in non-cancer patients. However, the explanation could be that cancer patients already had lymphopenia prior to infection with COVID-19, which is responsible for lack of significant association with the COVID-19 severity. Also, it made cancer patients liable for more severe COVID-19 infection and poorer outcome rather than non-cancer patients [34]. In addition to the presence of neutropenic sepsis which contributed to the neutropenia encountered in our cohort of cancer patients. On the other hand, regarding the recruited pediatric cancer patients, children with lymphopenia (< 1.04 × 10⁹/l) were significantly at a higher risk for ICU admission rather than those who had PLR > 196.4. As PLR is considered as an indicator of inflammation and cytokine storm, hence associated with the severity of COVID-19 infection, and consequently poor outcome [41].

Moreover, increased incidence of ICU admission in pediatric cancer patients associated significantly with the severity of covid19 infection (OR 7), decreased MCH below 28.3, increased RDW > 16, lymphopenia (lymphocytes < 1.04), and presence of abnormality in neutrophils’ morphology could predict computed tomography (CT) results in pediatric COVID-19 patients. Similarly, other recently published studies reported the association of peripheral pseudo Pelger-Huet appearance associated with dismal outcome. These data are consistent with Ma et al. [42] who concluded that lymphopenia and neutrophil abnormality could predict computed tomography (CT) results in pediatric COVID-19 patients. Interestingly, the present study demonstrated the important prognostic role of MCV, MCH, and RDW in predicting the outcome of pediatric COVID-19 cancer patients. As these markers (MCV < 83.6 fL, MCH < 27.7 Pg, and RDW > 16.3 fL) could possibly predict the incidence of ICU admission and/or death in these patients. Regarding the combination of MCV, MCH, and RDW together in pediatric COVID-19 cancer patients, it showed a sensitivity (81.8%), specificity (100%), and AUC (0.927) for association with ICU admission. While it achieved 77.8% sensitivity, 83.3% specificity, and AUC of 0.843 for association with increased incidence of mortality. However, these parameters did not show any significant association with the outcome of adult COVID-19 cancer patients. These data are partially comparable to that found by Wang et al. [46], who performed their study on adult non-cancer patients with COVID-19 infection, and reported that MCV and MCH were significantly lower in COVID-19 patients with poor outcome than in the good outcome group. Also, they reported that RDW was

### Table 6 (continued)

|                      | Odds ratio | 95% CI     | P value |
|----------------------|------------|------------|---------|
| MPR (> 0.044 vs < 0.044) | 1.667      | 0.227      | 12.221  | 0.615    |
| SIRI (> 0.61 vs < 0.61) | 1.440      | 0.269      | 7.714   | 0.670    |
| AISI (> 98.5 vs < 98.5) | 1.440      | 0.269      | 7.714   | 0.670    |
| NLPR (< 0.012 vs > 0.012) | 3.062      | 0.539      | 17.401  | 0.207    |

Bold values indicate statistically significant

The P value is significant if < 0.05

ALAT alanine transaminase, AST aspartate transaminase, CRP C- reactive protein, dNLR derived neutrophil to lymphocyte ratio, Hb hemoglobin concentration, IG immature granulocyte, LDH lactate dehydrogenase, MCH mean corpuscular hemoglobin, MCV mean corpuscular volume, MLR monocyte to lymphocyte ratio, MPV mean platelet volume to platelet ratio, MPR mean platelet to lymphocyte ratio, NLR the neutrophil to lymphocyte ratio, PLR platelet to lymphocyte ratio, PT prothrombin time, RDW red cell distribution width, SII systemic inflammation response index, and SIRI systemic inflammation response index, TLC total leukocyte count.
Table 7  Bivariable regression models of potential prognostic variables associated with ICU admission in COVID-19 adult cancer patients

| Variable                                      | Odds ratio | 95% CI Lower  | 95% CI Upper | P value |
|-----------------------------------------------|------------|---------------|--------------|---------|
| Gender (male vs female)                       | 1.071      | 0.293         | 3.921        | 0.917   |
| Disease (progression vs remission)            | 1.091      | 0.277         | 4.296        | 0.901   |
| Degree of COVID-19 (sever vs moderate or mild)| 3.254      | 0.808         | 13.753       | 0.088   |
| DCL (+ve vs −ve)                              | 11.100     | 1.039         | 118.566      | 0.046   |
| Blood stream infection (+ve vs −ve)           | 3.273      | 0.412         | 26.014       | 0.262   |
| Comorbidities (+ve vs −ve)                    | 1.600      | 0.337         | 7.593        | 0.554   |
| Liver disease (+ve vs −ve)                    | 3.500      | 0.610         | 20.097       | 0.160   |
| Renal disease (+ve vs −ve)                    | 1.029      | 0.097         | 10.853       | 0.981   |
| Type of cancer                                | 1.821      | 0.477         | 6.957        | 0.381   |
| Solid vs Hematological                        |            |               |              |         |
| TLC (< 10 vs > 10)                             | 1.648      | 0.458         | 5.928        | 0.444   |
| Hb (< 10 vs > 10)                              | 1.296      | 0.367         | 4.583        | 0.687   |
| MCV (< 90 vs > 90)                             | 6.094      | 0.758         | 55.732       | 0.095   |
| MCH (< 28.2 vs > 28.2)                        | 1.944      | 0.534         | 7.097        | 0.313   |
| RDW (> 16 vs < 16)                             | 1.179      | 0.317         | 4.384        | 0.806   |
| NRBC (< 1 vs > 1)                              | 1.091      | 0.103         | 11.527       | 0.942   |
| PLTs (> 150 vs < 150)                          | 1.358      | 0.313         | 5.897        | 0.683   |
| MPV (< 10 vs > 10)                             | 1.909      | 0.453         | 8.044        | 0.378   |
| Giant (+ve vs −ve)                             | 1.244      | 0.313         | 4.954        | 0.756   |
| Blast (+ve vs −ve)                             | 2.550      | 0.487         | 13.340       | 0.268   |
| Neutrophil (< 7.5 vs > 7.5)                   | 1.156      | 0.289         | 4.618        | 0.838   |
| Neutrophil % (> 70 vs < 70)                   | 1.432      | 0.369         | 5.551        | 0.604   |
| Toxic granulation (+ve vs −ve)                 | 2.242      | 0.573         | 10.252       | 0.229   |
| Pelger-huet (+ve vs −ve)                      | 3.214      | 0.841         | 12.283       | 0.088   |
| Hypo-granulation (+ve vs −ve)                 | .471       | 0.070         | 3.194        | 0.441   |
| Shift to left (−ve vs +ve)                     | 2.538      | 0.485         | 13.279       | 0.270   |
| Lymphocyte (> 3.5 vs < 3.5)                   | 6.364      | 0.525         | 77.079       | 0.146   |
| Lymphocyte % (> 35% vs < 35%)                 | 1.051      | 0.266         | 4.145        | 0.944   |
| Mature (+ve vs −ve)                            | 2.550      | 0.487         | 13.340       | 0.268   |
| Plasmoid (+ve vs −ve)                         | .805       | 0.145         | 4.476        | 0.804   |
| Monocytes (+ve vs −ve)                        | 2.000      | 0.559         | 7.151        | 0.286   |
| Monocyte (< 1 vs > 1)                         | 1.571      | 0.287         | 8.595        | 0.602   |
| Monocyte % (< 10 vs > 10)                     | 1.600      | 0.371         | 6.906        | 0.529   |
| Vacuolated (+ve vs −ve)                       | 1.071      | 0.293         | 3.921        | 0.917   |
| PT (> 1 vs < 1)                               | 3.333      | 0.384         | 28.959       | 0.275   |
| CRP (> 6 vs < 6)                              | 1.905      | 0.340         | 10.667       | 0.464   |
| LDH (> 220 vs < 220)                          | 2.519      | 0.460         | 13.801       | 0.287   |
| Albumin (< 3.5 vs > 3.5)                      | 3.000      | 0.562         | 16.013       | 0.199   |
| ALT (< 55 vs > 55)                            | 6.545      | 0.541         | 79.232       | 0.140   |
| AST (< 34 vs > 34)                            | 1.937      | 0.396         | 9.491        | 0.415   |
| Total bilirubin (< 1.2 vs > 1.2)              | 2.160      | 0.228         | 20.492       | 0.502   |
| Ceartnin (< 1.25 vs > 1.25)                   | 1.500      | 0.241         | 9.345        | 0.664   |
| Urea (< 45 vs > 45)                           | .825       | 0.144         | 4.725        | 0.829   |
| NLR (< 2.8 vs > 2.8)                          | 1.524      | 0.455         | 5.109        | 0.495   |
| LMR (> 2.55 vs < 2.55)                        | 2.274      | 0.653         | 7.920        | 0.197   |
| PLR (> 156 vs < 156)                          | 1.524      | 0.455         | 5.109        | 0.495   |
| dNLR (< 1.59 vs > 1.59)                       | 1.045      | 0.315         | 3.470        | 0.942   |
| SII (> 615.9 vs < 615.9)                      | 1.524      | 0.455         | 5.109        | 0.495   |
| CRP/L (> 30.9 vs < 30.9)                      | 1.240      | 0.342         | 4.487        | 0.744   |
a prognostic predictor for patients with severe COVID-19 viral infection.

Taken together, we can conclude that cancer patients with COVID-19 have hematological and inflammatory indices different from that in COVID-19 non-cancer patients. Similarly, these inflammation indices are varied between pediatric and adult COVID-19 cancer patients. The increased level of both CRP/L and NLPR associated significantly with poor survival in adult COVID-19 cancer patients, while PLR associated significantly with ICU admission in pediatric COVID-19 cancer patients. Moreover, lymphopenia < 1.04×10^9/l will significantly predict ICU admission. The possibility of the integration of those inflammatory indices in peripheral blood picture could be a very useful method for early prediction and prognosis of COVID-19 cancer patients. As these indices are very easy and rapid

Table 7 (continued)

|                | Odds ratio | 95% CI        | P value |
|----------------|------------|---------------|---------|
| MPR (<0.034 vs >0.034) | 3.000      | 0.655 - 13.747 | 0.157   |
| NLPR (<0.0114 vs >0.0114) | 1.524      | 0.455 - 5.109  | 0.495   |
| SIRI (>1.52 vs <1.52)  | 1.045      | 0.315 - 3.470  | 0.942   |
| AISI (>289.5 vs <289.5) | 1.045      | 0.315 - 3.470  | 0.942   |

Bold value indicates statistically significant

The P value is significant if < 0.05

AISI aggregate index of systemic inflammation, ALT alanine transaminase, AST aspartate transaminase, CRP C-reactive protein, CRP/L CRP to lymphocyte ratio, dNLR derived neutrophil to lymphocyte ratio, Hb Hemoglobin concentration, IG immature granulocyte, LDH lactate dehydrogenase, MCH mean corpuscular hemoglobin, MCV mean corpuscular volume, MLR monocyte to lymphocyte ratio, MPR mean platelet volume to platelet ratio, MPV mean platelet volume, NLPR neutrophil to lymphocyte, platelet ratio, NLR the neutrophil to lymphocyte ratio, PLR platelet to lymphocyte ratio, PT prothrombin time, RDW red cell distribution width, SII systemic inflammation response index, and SIRI systemic inflammation response index, TLC total leukocyte count

Fig. 4 ROC curve analysis of MCV, MCH, RDW and their combination for association with ICU admission (A, B, C, D) and increased incidence of mortality (E, F, G, H) in pediatric COVID-19 cancer patients
for calculations, as well as low-cost wise in low-income countries.

The MCV, MCH, RDW, and lymphopenia could be useful prognostic markers for poor outcome in COVID-19 pediatric cancer patients. However, these data should be verified on a larger number of patients including adult, pediatric, cancer, and non-cancer patients with COVID-19 infection for further confirmation.

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Declarations

Conflict of interest All authors declare that there is no possible conflict of interest.

Ethical approval The manuscript protocol had been approved by the institutional review board (IRB) committee of the National Cancer institute, which is in concordance with 2011 Declaration of Helsinki.

Informed consent A written informed consent had been obtained from all participant patients before inclusion in the study.

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