The Predictive Role of Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio on Intensive Care Unit Admission and Mortality of COVID-19 Patients in Iran

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Research Article

Keywords: COVID-19, predictive factor, death, intensive care unit, neutrophil-to-lymphocyte ratio (NLR); platelet-to-lymphocyte ratio (PLR)

DOI: https://doi.org/10.21203/rs.3.rs-334097/v1

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Abstract

Since the outbreak of COVID-19 several studies conducted to identify predictive factors which are associated with prognosis of COVID-19. In this study we aimed to determine whether the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) could help the clinicians to predict intensive care unit (ICU) admission and mortality of COVID-19 patients. This retrospective cohort study involved examining the medical records of 311 Iranian COVID-19 patients from 22 July 2020 to 22 August 2020. All characteristic data and laboratory results were recorded. The receiver operating characteristic (ROC) curve was used to identify the predictive value of studied parameters for ICU admission and death. Comparison of data revealed that some factors were jointly higher in non-survivors and ICU admitted patients than survivors and non-ICU admitted patients, such as: age, hemoglobin (HB), NLR, derived neutrophil-to-lymphocyte ratio (dNLR), PLR, systemic inflammatory index (SII), lactate dehydrogenase (LDH), Respiratory diseases, ischemic heart disease (IHD). Multivariate logistic regression analysis showed that only hypertension (OR 3.18, P=0.02) is an independent risk factor of death in COVID-19 patients, and also PLR (OR 1.02, P=0.05), hypertension (OR 4.00, P=0.002) and IHD (OR 5.15, P=0.008) were independent risk factor of ICU admission in COVID-19 patients. This study revealed that the NLR, PLR, platelet-to-white blood Cell ratio (PWR), dNLR and SII are valuable factors for predicting ICU admission and mortality of COVID-19 patients.

Introduction

In late December 2019, several cases of pneumonia with unknown etiology reported in Wuhan city of China. The pneumonia was called new coronavirus disease 2019 (COVID-19) and officially named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the WHO [1, 2]. COVID-19 shortly spread throughout the world and due to the considerable impact of COVID-19 on the world's people's health the WHO declared it as a pandemic on 11 March 2020 [3]. Although all ages are susceptible to infected with COVID-19, older patients with underlying diseases predisposed to a several conditions of comorbidity such as severe acute respiratory distress due to diffuse alveolar damage with cellular fibromyxoid exudates [4]. However most patients are asymptomatic or have a mild upper respiratory tract symptoms, COVID-19 in some cases causes pneumonia that can be severe and characterized by dyspnea, fever, cough, pulmonary edema, bilateral pulmonary infiltration and acute respiratory distress syndrome with high mortality rate requiring comprehensive care [5]. Restriction of hospital facilities as like mechanical ventilators and ICU beds, and presence of new mutations in the novel coronavirus that may increase its pathogenicity cause COVID-19 be considered as a life-treating disease so far, therefore it is critical to determining the risk factors that are attendant with the poor prognosis and predictive indicators of a severe condition. Also is of great importance to identify individuals with intrinsic predisposition to be in a severe or critically ill condition upon infection, for the purposes of conducting a specific prevention and treatment framework.

Since the outbreak several studies conducted to identify predictive factors which are associated with poor
cardiovascular disease, hypertension), gender, C-reactive protein, interleukin (IL)-6 and D-dimer [1, 6–8]. Recent studies have demonstrated that inflammatory response could be associated with disease progression and have a significant predictive and prognostic value, subsequently inflammation due to COVID-19 plays an important role in progression of pneumonia [9]. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as the markers of systemic inflammation were recently investigated as a novel prognostic indicators and it has been discovered the raised levels of them might lead to a poor prognosis in various and different disease such as infectious disease, malignant tumors and inflammatory disorders [10–17]. Recent investigations suggested that NLR and PLR are valuable predictive factors for severity and prognosis of COVID-19 and the mortality of patients [18]. However, it’s needed to conduct investigations with larger population to explore and confirm the values of NLR and PLR in predicting the hospital stay days, need for intensive care unit (ICU) and ICU stay days, complementary interventions (such as mechanical ventilation etc.), severity and mortality in COVID-19. In the current study, we aimed to determine whether the NLR, PLR during the hospitalisation could help health providers to predict of need for ICU admission and mortality of hospitalized patients with COVID-19.

Patients And Methods

Patient selection and Study deign

An initial sample of 311 consecutive patients’ medical records with COVID-19 diagnosis from 22 July 2020 to 22 August 2020 were screened for possible inclusion in the study. All the patients were whom admitted to Imam Reza Hospital in Tabriz (the referral hospital in the northwestern region of the Iran). The patients with hematologic disorders and any active condition which could significantly influence the blood cell count were excluded. The exclusion criteria were: a. patients received preoperative chemotherapy/radiotherapy (n = 8); b. patients with hematological or autoimmune disease (n = 12); c. lack of complete medical records (n = 41). Totally, 61 patients were excluded from this study. The enrollment process was presented in Fig. 1. Only the laboratory-confirmed patients (based on the diagnostic criteria of WHO guidance) were enrolled in the analysis.

The demographic, clinical, laboratory data, radiological findings and outcome were extracted from medical records and electronic case records. All laboratory results of the patients upon admission were recorded. The baseline parameters were selected to predict if patients die during hospitalization or not and if need ICU stay or not. All patients had definite outcome: death, discharge with ICU stay and discharge without ICU. The current study was approved by the Regional Medical Ethics Committee of the Tabriz University of Medical Sciences (IR.TBZMED.REC.1399.180) and all methods were performed in accordance with the relevant guidelines and regulations.

Statistical analysis

For statistical analysis, SPSS V 25 was used. The normality of the data distribution was analyzed by the
reported as mean (SD) and median (IQR) respectively. The categorical and nominal variables were reported as frequency (%). Between-group comparisons were performed using the independent test and Mann-Whitney U test for continuous variables and by the chi-square test for categorical variables. Logistic regression was used to analyze the risk factors for ICU admission and death in patients with COVID-19 in univariate and multivariate models. The covariate candidates for inclusion were those statistically significant in univariate analyses. Receiver operating characteristic (ROC) curve was used to identify the diagnostic value of studied parameters for ICU admission and death and also the sensitivity, specificity, and best cut-off value. A p-value of less than 0.05 was considered significant.

Results

Demographic characteristics and initial laboratory indices

A total of 250 patients with COVID-19 were included in the present study from which 58 (23.2%) patients died during hospitalization that was considered as non-survivors group and the remained 192 (76.8%) patients as survivors group. Among the 250 consecutive patients with COVID-19 confirmed diagnosis, 127 (50.8%) cases were admitted in ICU at least for one day as ICU admission group and 123 were not admitted in ICU that considered as non-ICU admission group. The mean age of participants was 61.44 ± 16.47 years. The mean age of non-survivors was significantly higher than that of survivors (P = 0.001). Also the mean age of case in ICU admission group were significantly higher than non-ICU admission group (P = 0.002). In terms of underlying diseases, ischemic heart disease (IHD) (P < 0.001), respiratory disease (P = .001) and hypertension (P = 0.05) were more frequently observed in non-survivors and ICU admission group. Moreover frequency of hypertension was significantly higher in ICU admitted patient compare with non-ICU admission cases (P = 0.03). The leucocytes, neutrophil and lactate dehydrogenase (LDH) were significantly higher in non-survivors and ICU admission group. Whereas the level of hemoglobin and lymphocytes were significantly lower in non-survivors and ICU admission group. The median level of NLR was 9.83 and 5.62 in non-survivors and survivors groups, respectively (P < 0.001). Also there were significant differences in derived neutrophil to lymphocyte ratio (dNLR), PLR and systemic inflammatory index (SII) for non-survivors, when compared to survivors. Data analysis showed significant difference in NLR, dNLR, PLR, and SII that were higher in ICU admission group compared to non-ICU admission group. However platelet to white blood cell ratio (PWR) was significantly lower in ICU admitted patients. The demographic data and clinical laboratory data of hospitalized patients with COVID-19 stratified by death and ICU admission status showed in Table 1.
Table 1
Demographic characteristics and clinical laboratory data of hospitalized patients with COVID-19 stratified by death and ICU admission status

| Variables                  | ICU admission status | Death status | P value* | Survivors | Non-survivors | P value* |
|----------------------------|----------------------|--------------|----------|-----------|---------------|----------|
|                            | Total (250)          | ICU admission (127) | Non-ICU admission (123) |          | Survivors (192) | Non-survivors (58) |  
| Age (years) mean ± SD      | 61.44 ± 16.47        | 64.64 ± 16.85 | 58.14 ± 15.46 | 0.002     | 59.30 ± 16.44   | 68.53 ± 14.68  | 0.001     |
| Gender n (%)               |                      |              |          | 0.96      | 113 (58.9)     | 31 (53.4)     | 0.46      |
| Male                       | 144 (57.6)           | 73 (57.5)    | 71 (57.7) |          |               |           |           |
| Female                     | 106 (42.4)           | 54 (42.5)    | 52 (42.3) |          |               |           |           |
| Comorbidities n (%)        |                      |              |          |           |               |           |           |
| Hypertension               | 92 (36.8)            | 55 (43.3)    | 37 (30.1) | 0.03      | 65 (33.9)      | 27 (46.6)    | 0.07      |
| Diabetes                   | 53 (21.2)            | 29 (22.8)    | 24 (19.5) | 0.52      | 42 (21.9)      | 11 (19.0)    | 0.63      |
| IHD                        | 47 (18.8)            | 39 (30.7)    | 8 (6.5)   | < 0.001   | 26 (13.5)      | 31 (36.2)    | < 0.001   |
| CKD                        | 25 (10)              | 16 (12.6)    | 9 (7.3)   | 0.16      | 18 (9.4)       | 7 (12.1)     | 0.54      |
| Respiratory diseases       | 26 (10.4)            | 19 (15.0)    | 7 (5.7)   | 0.01      | 13 (6.8)       | 13 (22.4)    | 0.001     |
| WBC median (IQR)           | 8300 (5700, 11400)   | 9400 (6700, 12600) | 7000 (5200, 10500) | < 0.001 | 9600 (6775, 13450) | 8000 (5325, 11200) | 0.02     |
| HB mean(SD)                | 13.10 (2.24)         | 12.89 (2.39) | 13.46 (1.99) | 0.04**    | 12.68 (2.20)   | 13.28 (2.24) | 0.03**    |
| PLT median (IQR) \(\times 10^3\) | 196 (155, 246)      | 205 (164, 248) | 188 (153, 245) | 0.12      | 207 (166, 271)   | 193 (155, 243) | 0.14      |
| PMN median (IQR)           | 6691 (4429, 9591)    | 7953 (5650, 10720) | 5380 (3860, 8307) | < 0.001   | 8014 (5847, 11813) | 6391 (4117, 9211) | 0.002    |
|                | ICU admission status | Death status |
|----------------|----------------------|--------------|
|                | median (IQR)         |              |
| LYMPH         | 995 (845, 1341)      | 791 (628, 934) |
| LDH           | 607 (430, 598)       | 685 (482, 1103) |
| NLR           | 6.62 (4.45, 9.48)    | 9.83 (8.14, 14.16) |
| dNLR          | 4.48 (3.34, 6.37)    | 5.97 (4.91, 8.11) |
| PLR           | 194.17 (148.41, 238.31) | 292.98 (224.58, 35.61) |
| PWR           | 24.28 (17.90, 32.56) | 26.86 (20.73, 35.34) |
| SII           | 1270 (799, 2032)     | 2262 (1480, 3049) |

Univariate and multivariate logistic regression analysis to predict death and ICU admission of COVID-19 in hospitalized patients

Univariate logistic regression analysis showed that all variables significant in initial comparison to predict death of COVID-19 in hospitalized patients except for hemoglobin (OR 0.89, P = 0.08) were statistically significant in univariate logistic regression analysis. Multivariate logistic regression analysis revealed that only hypertension (OR 3.18, P = 0.02) as independent risk factor of death in COVID-19 hospitalized patients (Table 2). Logistic regression analysis were also conducted for characteristics with statistically different in initial comparison to predict ICU admission of COVID-19 in hospitalized patients and showed in Table 3. Univariate logistic regression analysis showed that all variables significant in initial comparison were still significant. Multivariate logistic regression analysis revealed that PLR (OR 1.02, P = 0.05), hypertension (OR 4.00, P = 0.002) and IHD (OR 5.15, P = 0.008) were independent risk factor of ICU admission in COVID-19 hospitalized patients.
Table 2
Univariate and multivariate logistic regression analysis of risk factors for death of COVID-19 in hospitalized patients

| Variables                  | Univariate model | Multivariate model |
|----------------------------|------------------|-------------------|
|                            | OR   | 95% CI | P-value | OR   | 95% CI | P-value |
| Age                        | 1.03 | 1.01–1.05 | 0.001   | 1.004 | 0.99–1.03 | 0.79 |
| Hypertension               | 1.70 | 0.93–3.08 | 0.08    | 3.18  | 1.17, 8.64 | 0.02 |
| IHD                        | 3.62 | 1.14–7.12 | < 0.001 | 2.60  | 0.84–7.99 | 0.09 |
| Respiratory diseases       | 3.97 | 1.72–9.17 | 0.001   | 2.31  | 0.57–9.24 | 0.23 |
| WBC                        | 1.00 | 1.001–1.003 | 0.007  | 1.00  | 0.99–1.003 | 0.92 |
| HB                         | 0.89 | 0.77–1.01 | 0.08    | 0.96  | 0.77–1.18 | 0.71 |
| PLT                        | 1.00 | 1.00–1.00 | 0.006   | 1.00  | 1.00–1.00 | 0.71 |
| LYMPH                      | 0.99 | 0.99–0.99 | < 0.001 | 0.99  | 0.98–1.005 | 0.40 |
| PMN                        | 1.00 | 1.00–1.00 | < 0.001 | 1.00  | 0.99–1.003 | 0.86 |
| LDH                        | 1.00 | 1.00–1.00 | 0.05    | 1.00  | 1.00–1.00 | 0.64 |
| NLR                        | 1.50 | 1.33–1.70 | < 0.001 | 1.44  | 0.61–3.36 | 0.39 |
| dNLR                       | 1.44 | 1.26–1.64 | < 0.001 | 0.82  | 0.41–1.64 | 0.58 |
| PLR                        | 1.01 | 1.01–1.02 | < 0.001 | 0.99  | 0.98–1.01 | 0.84 |
| PWR                        | 0.98 | 0.95–1.01 | 0.33    |       |        |        |
| SII                        | 1.00 | 1.00–1.00 | < 0.001 | 1.00  | 1.00–1.00 | 0.64 |
Table 3
Univariate and multivariate logistic regression analysis of risk factors for ICU admission of COVID-19 in hospitalized patients

| Variables                  | Univariate model | Multivariate model |
|----------------------------|------------------|--------------------|
|                            | OR               | 95% CI             | P-value | OR               | 95% CI             | P-value |
| Age                        | 1.02             | 1.00-1.04          | 0.002   | 0.99             | 0.96–1.02          | 0.58    |
| Hypertension               | 1.77             | 1.06–2.99         | 0.03    | 4.00             | 1.69–9.48         | 0.002   |
| IHD                        | 6.39             | 2.83–14.31        | < 0.001 | 5.15             | 1.53–17.32        | 0.008   |
| Respiratory diseases       | 2.91             | 1.17–7.20         | 0.02    | 2.08             | 0.50–8.68         | 0.31    |
| WBC                        | 1.77             | 1.06–2.99         | 0.03    | 1.00             | 0.99–1.002        | 0.58    |
| HB                         | 6.39             | 2.83–14.31        | < 0.001 | 0.88             | 0.73–1.05         | 0.16    |
| PLT                        | 2.91             | 1.17–7.20         | 0.02    | 1.00             | 1.00–1.00         | 0.96    |
| LYMPH                      | 1.77             | 1.06–2.99         | 0.03    | 1.00             | 0.99–1.003        | 0.94    |
| PMN                        | 6.39             | 2.83–14.31        | < 0.001 | 0.99             | 0.99–1.001        | 0.57    |
| LDH                        | 2.91             | 1.17–7.20         | 0.02    | 1.00             | 1.00–1.00         | 0.19    |
| NLR                        | 1.63             | 1.43–1.86         | < 0.001 | 1.06             | 0.53–2.14         | 0.85    |
| dNLR                       | 1.64             | 1.40–1.93         | < 0.001 | 1.08             | 0.58–2.02         | 0.78    |
| PLR                        | 1.02             | 1.01–1.03         | < 0.001 | 1.02             | 1.00–1.01         | 0.05    |
| PWR                        | 0.97             | 0.94–0.99         | 0.01    | 0.91             | 0.79–1.04         | 0.18    |
| SII                        | 1.00             | 1.00–1.00         | < 0.001 | 1.00             | 1.00–1.00         | 0.91    |

Calculated cut-off values of laboratory results to predict death and ICU admission of COVID-19 in hospitalized patients

We used ROC curve analysis to calculate optimal cut-off values of laboratory results. Figure 2 depicted the result of ROC curve analysis of NLR, PLR, PWR, dNLR, and SII in predicting death in hospitalized patients with COVID-19. Table 4 shows the performance of studied indices for predicting death in patients with COVID-19. Areas under the curve (AUC) of NLR (0.847, 95% CI 0.79–0.89, P < 0.001), PLR (0.866, 95% CI 0.81–0.91, P < 0.001), d-NLR (0.790, 95% CI 0.73–0.84, P < 0.001) and SII (0.807, 95% CI 0.74–0.87, P < 0.001), significant values for predicting the death of patients with COVID-19. NLR level of 7.61, PLR level of 202.7, dNLR level of 4.54, and SII level of 1409248.02 could significantly predict the death in patients with COVID-19 as optimal cut-off values. The highest sensitivity was related for PLR (91%) and the highest specificity was related for NLR (72%).
Table 4
Performance of studied indices for predicting death in patients with COVID-19

| Variables | Cut-off | AUC   | 95% CI     | P value | Sensitivity (%) | Specificity (%) |
|----------|---------|-------|------------|---------|----------------|-----------------|
| NLR      | 7.61    | 0.847 | 0.79, 0.89 | < 0.001 | 84             | 72              |
| dNLR     | 4.54    | 0.790 | 0.73, 0.84 | < 0.001 | 86             | 63              |
| PLR      | 202.7   | 0.866 | 0.81, 0.91 | < 0.001 | 91             | 69.8            |
| PWR      | 45.6    | 0.419 | 0.33, 0.50 | 0.06    | 8              | 96              |
| SII      | 1409248.02 | 0.807 | 0.74, 0.87 | < 0.001 | 84             | 66              |

Based on ROC curve analysis (Fig. 3 and Table 5), AUC of NLR (0.808, 95% CI 0.75–0.86, P < 0.001), PLR (0.771, 95% CI 0.71–0.83, P < 0.001), d-NLR (0.773, 95% CI 0.71–0.83, P < 0.001) and SII (0.774, 95% CI 0.71–0.83, P < 0.001) significant values for predicting the ICU admission of patients with COVID-19. Also ROC curve analysis of PWR (0.373, 95% CI 0.30–0.44, P = 0.001), showed that the level of PWR could be used as a predicting factor for ICU admission of patients with COVID-19 in which the lower level of PWR related with higher probability of ICU admission. The optimal cut-off values for NLR, PLR, dNLR and SII were 6.22, 202.7, 43.98 and 1219463, respectively; that could significantly predict the ICU admission in patients with COVID-19. The highest sensitivity was related for NLR (81%) and the highest specificity was related for PLR (79%).

Table 5
Performance of studied indices for predicting ICU admission in patients with COVID-19

| Variables | Cut-off | AUC   | 95% CI     | P value | Sensitivity (%) | Specificity (%) |
|----------|---------|-------|------------|---------|----------------|-----------------|
| NLR      | 6.22    | 0.808 | 0.75, 0.86 | < 0.001 | 84             | 72              |
| dNLR     | 3.98    | 0.773 | 0.71, 0.83 | < 0.001 | 85             | 61              |
| PLR      | 202.78  | 0.771 | 0.71, 0.83 | < 0.001 | 70             | 79              |
| PWR      | 43.92   | 0.373 | 0.30, 0.44 | 0.001   | 5              | 95              |
| SII      | 1219463 | 0.774 | 0.71, 0.83 | < 0.001 | 84             | 66              |

Discussion

COVID-19 has elicits a rapid spread of outbreak with the human-to-human transmission [19, 20]. COVID-19 pneumonia patients on early stage were not very severe. In initial of sever stage, patients show severe pneumonia and passed away on 7–14 days, considering that there are several controversial declarations about predictive indices for COVID-19 severe illness has been published so far, a necessary need for prediction of progression chance of COVID-19 is felt and more investigations is pivotal in this regards. Recently, it has been documented that the NLR level, as a novel inflammatory index, is as an early risk factor for prediction of ICU admission rate and severity of COVID-19 disease [21, 22]. As hypothesized in
bedridden in intensive care units [23]. Also in other study it revealed that the decrease of lymphocyte count pointed to the disease progress [24]. A large body of scientific literature has been declared that blood lymphocyte and neutrophil-related indices may be a potential predictors of this disease. For more validation of this declaration, in present study, we evaluate these indices in Iranian population of COVID-19. In recent decay, the NLR index was considered as a marker of the severity of bacterial infections [25].

In this study, the data of 250 patients with COVID-19 were analyzed and the laboratory indices were presented. Our results indicated that NLR factor could be one of the most significant factor affecting the severe illness. In support of our finding, Jingyuan Liu compared NLR with MuLBSTA and CURB-65 scoring models. They documented that NLR factor have higher AUC, c-index, sensitivity and specificity than the other two models [23]. Recently, Ai-Ping Yang et al reported that elevated NLR is an independent prognostic biomarker that affected pneumonia progression in COVID-19 patients [21]. Our results were consistent with previously published studies in respect of the relationship between NLR and prognosis of COVID-19. The following reasons may account for the findings. Regarding this findings, it could be hypothesized that immune response initiated by viral infection mostly depends on lymphocyte [26], whereas systematic inflammation drastically suppress cellular immunity, significantly decreasing CD4+ T lymphocytes and increasing CD8+ T lymphocyte [27]. Another the possible mechanism for reduction of lymphocytes in COVID-19 infection is that lymphocytes are the target of virus because the angiotensin converting enzyme 2 receptor of the virus is expressed on lymphocytes, too [28, 29]. In other hand, Neutrophilia may stem from the cytokine storm initiated by virus infection [30, 31]. Thus, virus-related inflammation escalated NLR factor.

In present study, the optimal cut-off value for NLR, dNLR, SII, PWR, and PLR were observed via the ROC curve. The optimal threshold at 7.61 for NLR showed a prognostic possibility of clinical symptoms to mortality rate of disease. The highest level of AUC for predicting death in patients with COVID-19 related to PLR (0.866) with a sensitivity and specificity of 91% and 69.8% respectively. Moreover, our analysis publicized that, along with NLR, dNLR, SII, and PLR may be used as a predictive diagnostic value for determining subjects needing ICU support. Previous studies have stated that the authentication of PLR factor is required [32]. In our study, the optimal threshold value of PLR was identified with highest sensitivity (91 %) with an acceptable specificity (69.8%). The AUC of NLR arrived the highest value (0.808) at the optimal cut-off value to predict the ICU admission (sensitivity, and specificity of NLR is 84% and 72%, respectively). Our outcomes are consistent with previous reports signifying higher NLR value as a predictive factor for severity of COVID-19 infection. Along with NLR factor, we saw the optimum AUC, sensitivity, and specificity of threshold value of dNLR (0.773, 85% and 61%, respectively), PLR (0.771, 70% and 79%, respectively) and SII (0.774, 84% and 66%, respectively). According to our results, not also NLR, but also dNLR, PLR, and SII could have prognostic value for predicting ICU admission in patients with COVID-19. The useful application of NLR, PLR, SII has been documented in many disease including tumor-related diseases [33, 34], autoimmune diseases [35], bacterial infectious pneumonia [36], and tuberculosis [37], secondary pulmonary infectious diseases [38]. It has been well-documented that these indices could be able to predict survival rate and severity of above mentioned disease. However, the pneumonia was poorly reported. Based on our study and
recently published documents, in could be said that NLR, PLR, dNLR, PWR and SII indicate the progression trend of COVID-19 and could be used as a prognostic value for COVID-19 condition.

Finally, the findings of this study indicated that elevated NLR was an independent prognostic biomarker for COVID-19 patients. Therefore, the applicable NLR is suggested as practical tools to evaluate the severity of COVID-19 individuals. Also, as can be seen in our findings, according to obtained values of AUC, sensitivity, and specificity for dNLR and SII parameters, it could be concluded that dNLR and SII, also could be applicable for predicting death and ICU bed management in patients with COVID-19. Another finding of this study is related to PWR index. In conjugation with other scientific reports, our obtained data showed that PWR has a reverse relation with ICU care and mortality rate of COVID-19. Because of huge medical and economic burden of COVID-19, compared with other factors, such as IL-6, NLR and other novel parameters are simple, fast and economical to achieve directly from the blood samples, and this can help clinicians identify the severe ill patients and progress rate of COVID-19 [39]. Although prognostic value of NLR and PLR, and dNLR factors was shown recently in COVID-19 patients, in present study, we further authorized these prognostic factors in Iranian COVID-19 population. Along with, SII factor was introduced, for a first time, for prognostic aims in COVID-19 patients.

Conclusion

In conclusion, this retrospective cohort study completed in the Iranian population declare that the NLR, PLR, PWR, dNLR and SII are valuable factors for predicting ICU admission and mortality rate of patients with COVID-19. Due to restriction of hospital facilities it is important to early identification of patients with higher risk for progression and further need to ICU admission. Monitoring of COVID-19 severity predictors could assist clinicians to identify and follow-up these patients. Further researches are required to authorize our findings in other cohort studies and to associate the predictive potential of NLR and other novel parameters.

List Of Abbreviations

COVID-19: Coronavirus disease 2019

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

IL: Interleukin

NLR: Neutrophil-to-lymphocyte ratio

PLR: Platelet-to-lymphocyte ratio

ICU: Intensive care unit

PWR: Platelet to white blood cell ratio
dNLR: Derived neutrophil to lymphocyte ratio

SII: Systemic inflammatory index

AUC: Areas under the curve

ROC: Receiver operating characteristic

LDH: Lactate dehydrogenase

IHD: Ischemic heart disease

**Declarations**

**Acknowledgment**

The research protocol was approved and supported by Student Research Committee Tabriz University of Medical Sciences (Grant number: 65263) and We wish to thank all staffs of archive office for their kind full cooperation and all nurses and staffs of ward at Imam Reza hospital for their kind full cares of all patients.

**Authors' contributions:**

PF and MV and HA designed the study and carried out coordination and contributed in manuscript writing, MH, MA, BA contribution in literature search, data collection and manuscript writing, HA, ZN and contribution in data analysis and manuscript writing and editing.

**Competing interests:**

The authors declare no competing interests.

**Data availability:**

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Ethics declarations:**

Written informed consent was obtained from each patient during questionnaire administration for the collection and analysis of applicable clinical data. Protocol was approved by the Regional Ethics Committee headed by the Vice-Chancellor of Research and Development at Tabriz University of Medical Sciences (Ethical approval code: IR.TBZMED.REC.1399.180).

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Figure 1

Flow diagram for the identification of eligible studies
Figure 2

The ROC curve analysis of NLR, PLR, PWR, dNLR, and SII in predicting dearth in hospitalized patients with COVID-19 (AUC: area under curve; CI: confidence interval; NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio)
Figure 3

The ROC curve analysis of A: NLR; B: PLR in predicting ICU admission in hospitalized patients with COVID-19 (AUC: area under curve; CI: confidence interval; NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio)