Original article

The Value of Presepsin and Mean Platelet Volume in the Diagnosis and Assessment of Severity of Childhood Pneumonia

Amira S. Mohammed[a], Mohamed M. Rashad[a], Dina A. Ali [b], Ahmad A. Sobieh[a]

Abstract

[a] Department of pediatrics, Benha faculty of medicine, Benha University, Egypt. [b] Department of clinical and chemical pathology, Tanta University, Egypt .

Correspondence to: Amira S. Mohammed, Department of pediatrics, Benha faculty of medicine, Benha University, Egypt.

Email:

amiraaa.com@yahoo.com

Background: Community-acquired pneumonia (CAP) is one of the most common causes of death among children all over the world, especially in the developing countries. Late diagnosis is one of the main causes for increasing morbidity and mortality. Non-invasive biomarkers could provide an early and non-invasive technique for both diagnosis and assessment of severity of pneumonia. **Aim and objectives**: The aim of the current study was to evaluate the mean platelet volume (MPV) and presepsin as diagnostic markers in childhood pneumonia and to estimate their reliability in assessing the severity of the disease. **Subjects and methods:** The study included 90 children who were distributed into three groups as follows, 30 healthy children as a control group, 30 cases with pneumonia and 30 cases with severe pneumonia. Full history taking, clinical examination and laboratory investigation (including measurement of serum presepsin and MPV) were conducted for every child. **Results**: The mean MPV in the control group was 7.94 ± 0.84 that was statistically significantly lower as compared with the cases with pneumonia (9.81 ± 0.97). Both groups had statistically significantly lower MPV as compared with the severe pneumonia group (10.7 ± 0.89) ($p< 0.001$). The mean presepsin level in the control group was 141.14 ± 71.4 that was statistically significantly lower as compared with the cases with pneumonia (605.80 ± 176.11). Both groups had statistically significantly lower Presepsin level as compared with the severe pneumonia group (1276.72 ± 1061.64) ($p< 0.001$). AUC of presepsin and MPV in identifying cases with pneumonia was (0.963 and 0.912 respectively) while AUC of presepsin and MPV in identifying cases with severe pneumonia was (0.877 and 0.789 respectively)

Conclusion: This study has shown the diagnostic validity of presepsin and MPV in diagnosis of pneumonia and assessment of the disease severity. The study revealed higher value of presepsin as non-invasive diagnostic tool.

Keywords: Pneumonia, CAP, Biomarker, MPV, Presepsin.

Introduction

Community-acquired pneumonia (CAP) as a lower respiratory infection in children is one of the leading causes of hospitalization in the world [1]. Hospitalization of children with CAP is highly prevalent in developing countries, and CAP is one of the major causes of death of the infected children [2]. However, CAP is often misdiagnosed, leading to a delay in the treatment process [3]. Thus, timely diagnosis and treatment of CAP children play an important role in preventing and reducing the mortality [4].

Thus, a simple, reliable, sensitive, rapid, and cost-effective point-of-care test is an important requirement [5]. During the last decade, several immunologic biomarkers have been evaluated as indicators of various infections [6, 7]

Presepsin, the soluble CD14 subtype (sCD14-ST), has been proposed as a new, emerging, early biomarker for the detection of different infections [8 & 9], is increased in response to bacterial infections and reduced after efficient treatment [6 & 10].

Membrane CD14 (mCD14) is expressed as monocytes and airway macrophages, while sCD14 is found in the tracheal aspirate as well. The mCD14 and sCD14 level in the respiratory tract is positively related to the inflammatory response [11].

Platelet volume may reflect the platelet function better than the platelet count itself. Mean platelet volume is a simple measure of platelet size [12]. Increased MPV suggests an increased platelet production and/or increased platelet destruction [13]. Likewise, MPV is an indicator of increased platelets activity and increased thrombotic potential. This is attributed to more dense granules, and enhanced metabolic and enzymatic activity of large sized platelets [14].

Mean platelet volume (MPV) is done as a routine laboratory test that is measured in complete blood count, and it is considered a marker of platelet function and activation [15 & 16]. A single elevated MPV measurement has been found to be associated with increased morbidity and

mortality in various patient populations **[17 & 18]**.

Previous clinical studies have confirmed that Presepsin levels increased in sepsis and with severity of disease **[19-21]**.

However, the correlation between presepsin and MPV with pneumonia and its relation with disease severity has not extensively studied especially in children.

The aim of the current study was to evaluate the MPV and presepsin as diagnostic markers in childhood pneumonia and to estimate their reliability in assessing the severity of the disease.

Patients and methods

This is **a case control study that was** conducted at Pediatric Department of Benha University Hospital, Benha, Egypt within the period between January 2021 and June 2021.

The study included 60 patients aged 2 months up to 5 years who were diagnosed to have pneumonia (according to WHO, 2019) **in addition to** 30 apparently healthy subjects as a control group. The patients with pneumonia were subdivided according to WHO (2014) into; pneumonia group and severe pneumonia group (Each of 30 patients)

The cases with the following criteria were excluded; age younger than 2 months or older than 5 years, infants with any disease other than pneumonia including cardiovascular diseases, perinatal abnormality, other pulmonary disease or immunodeficiency, infants on immunosuppressants and infants without written consent from their parents.

The study is conducted in accordance with Helsinki Standards as revised in 2013 **[22]**. The study was conducted after obtaining the approval from the local ethics committee, Faculty of Medicine, Benha University. The cases were included after obtaining a written informed consent form their guardians.

The cases were subjected to the

following; All the infants will be subjected to the following; full medical and demographic history taking, thorough clinical examination [General examination, vital signs and systemic examination with especial emphasis on cardiac (gallop rhythm, tachycardia, murmurs) and abdominal examination (distention, tenderness, organomegaly), local chest examination by Inspection for (retractions either generalized or localized , chest movements, or localized bulge and signs of respiratory distress), palpation for (tracheal

shift, palpable bronchi), percussion and auscultation for (breath sounds and adventious sounds)]

All cases with pneumonia were evaluated by chest X ray and CT (when needed). Laboratory assessment included complete blood count (hemoglobin level, hematocrit value, WBC count (total and differential), platelet count and MPV with quantitative measurement of the serum level of C-reactive protein. Complete blood counts were performed for all patients on presentation using a commercially available analyzer (Sysmex XT 2000i, Roche Diagnostics GmnH, Mannheim, Germany).

Venous blood samples were obtained at ED admission and collected in tubes containing heparin or ethylenediamine tetraacetate and stored at –80°C after collection for analysis within 24 hours. Plasma presepsin concentrations were determined with ELISA (Sandwich technique).

Statistical analysis of data

The data collected were coded, processed and analyzed with SPSS version 27 for Windows® (Statistical Package for Social Sciences) (IBM, SPSS Inc, Chicago, IL, USA). Qualitative data as number (frequency) and percent was presented. The Chi-Square test (Fischer's exact test/ Monte-

Carlo test) made the comparison between groups.

The Kolmogorov-Smirnov test tested quantitative data for normality. Parametric data were expressed as median ± SD while the non-parametric data were expressed as median (Range). To compare three groups with normally distributed quantitative variables, One-way analysis of the variance (One-way ANOVA) was used and Kruskal Wallis test was used if the data were abnormally distributed.

Correlation of numeric data was done by Pearson's or Spearman correlation (r). The optimal cutoff value of presepsin and MPV to differentiate between different groups was determined using **Youden index J** that is the farthest point on receiver operator characteristic (ROC) curve and expressed in terms of sensitivity and specificity. For all tests, P values <0.05 are considered significant.

Results

As shown in table (1), there was no statistically significant difference in the age between the cases in the three study groups. The age range was from 6 months to five years, 7 months to 5 years and 4 months to 5 years in the control, pneumonia and severe

pneumonia groups respectively. Moreover, there was no statistically significant difference between the three groups regarding the sex (p=0.875).

The median disease duration in the cases with pneumonia was 1 day (range 1-3) that was statistically significantly shorter as compared with the cases with severe pneumonia [7 days(range 5 to 8 days)] (p< 0.001).

Previous hospital admission was reported in 70% and 53.3% in the cases with pneumonia and severe pneumonia respectively with no statistically significant difference between the two groups. Positive family history of similar conditions was reported in 73.3% in

the cases with severe pneumonia that was statistically significantly higher as compared with the cases with pneumonia (46.7%) (p=0.035). Danger signs of pneumonia were reported in all the cases with severe pneumonia while no cases in the pneumonia group showed danger signs.

Cough and fast breathing was reported in all the cases with the two groups. Other signs reported in the pneumonia cases were chest indrawing (56.1% in both groups), difficulty of breathing (43.3% and 56.1% in the cases with pneumonia and severe pneumonia respectively) and fever (66.7% and 73.3% in the cases with pneumonia and severe pneumonia respectively).

Table (1): Analysis of the demographic and clinical data in the two studied groups

Variable		Control group (N=30)	Pneumonia (N=30)	Severe pneumonia (N= 30)	Test of sig.
Age (Years)		2.95 (0.5 - 5)	2.8 (0.58 - 5)	2.7 (0.33 - 5)	0.280
sex	Boys	15 (50%)	16 (53.3%)	17 (56.7%)	0.875
	Girls	15 (50%)	14 (46.7%)	13 (43.3%)	
Disease duration (days)		_____	1 (1-3)	7 (5-8)	< 0.001*
Previous hospital admission		_____	21 (70%)	16 (53.3%)	0.184
Family history of similar conditions		_____	14 (46.7%)	22 (73.3%)	0.035*
Danger signs		_____	0 (0%)	30 (100%)	< 0.001*
Cough		_____	30 (100%)	30 (100%)	1
Chest indrawing			17 (56.1%)	17 (56.1%)	1
Difficulty of breathing		_____	13 (43.3%)	17 (56.1%)	0.302
Fever		_____	20 (66.7%)	22 (73.3%)	0.573
Fast breathing		_____	30 (100%)	30 (100%)	1

As shown in table (2), the mean hemoglobin level of the control group was statistically significantly higher as compared with the cases with pneumonia and severe pneumonia (p< 0.001).

The mean WBCs and neutrophil count in the control group was statistically significantly lower as compared with the cases with pneumonia. Both groups had statistically significantly lower WBCs count and neutrophil count as compared with the severe pneumonia group (p< 0.001). The median lymphocytes count in the pneumonia group was 43.05 that was statistically significantly higher as compared with the control group (32.85) and severe pneumonia (29.25) (p= 0.013). There was no statistically significant difference in the platelets count between the three study groups.

CRP was positive in all the cases with pneumonia and severe pneumonia while it was negative in all subjects within the control group with high statistically significant difference between the study groups (P < 0.001).

The mean MPV in the control group was 7.94 ± 0.84 that was statistically significantly lower as compared with the cases with pneumonia (9.81 ± 0.97). Both groups had statistically significantly lower MPV as compared with the severe pneumonia group (10.7 ± 0.89) (p< 0.001).

The mean presepsin level in the control group was 141.14 ± 71.4 that was statistically significantly lower as compared with the cases with pneumonia (605.80 ± 176.11). Both groups had statistically significantly lower MPV as compared with the severe pneumonia group (1276.72 ± 1061.64) (p< 0.001).

As shown in table (3), there was a statistically significant positive correlation between MPV with presepsin level (r= 0.643, P < 0.001), disease duration (r= 0.421, P < 0.001), WBCs count (r= 0.541, P < 0.001) and CRP level (r= 0.478, P < 0.001). Other correlation didn't show a statistically significant value.

There was a statistically significant positive correlation between presepsin level with MPV (r= 0.643, P < 0.001), disease duration (r= 0.619, P < 0.001), WBCs count (r= 0.465, P < 0.001) and CRP level (r= 0.391, P= 0.001). Other correlation didn't show a statistically significant value.

Table (2): Comparison between the two studied groups according to laboratory data

Variable	Control group (N=30)	Pneumonia (N=30)	Severe pneumonia (N= 30)	P value
Hemoglobin (gm/dl)	11.14 ± 1.16 A	10.27 ± 1.07 B	9.96 ± 1.16 B	< 0.001*
WBCs (10^3/ml)	8.78 ± 2.50 A	14 ± 4.45 B	18.29 ± 5.53 C	< 0.001*
Neutrophils (%)	57.97 ± 11.26 A	50.87 ± 13.93 B	64.28 ± 18.62 C	0.003*
Lymphocytes (%)	32.85 (11.5 – 60) A	43.05 (24-76) B	29.25 (5.6-76.8) A	0.013*
Platelets (10^3/ml)	266 (178 – 338)	303 (103-577)	297.5 (104-548)	0.286
CRP (mg/L) (Normal <10 mg/L)				
Positive (> 10 mg/L)	0 (0%)	30 (100%)	30 (100%)	< 0.001*
Negative (< 10 mg/L)	30 (100%)	0 (0%)	0 (0%)	
CRP	4 (2 – 8) A	48 (24-96) B	48 (24-96) B	< 0.001*
MPV (FL)				
Mean ± SD	7.94 ± 0.84 A	9.81 ± 0.97 B	10.7 ± 0.89 C	< 0.001*
Range	(6.8-10.3)	(7.7-12)	(7.4-12)	
Presepsin(pg/ml)				
Mean ± SD	141.14 ± 71.4 A	605.80 ± 176.11 B	1276.72 ± 1061.64 C	< 0.001*
Range	(51.8-309.10)	(51.9-977.10)	(207.5-5147)	

A, B, C: Similar results indicate no significant difference between adjacent groups

Different letters indicate a statistically significant difference between adjacent groups

Table (3): Correlation between MPV and presepsin with clinical and laboratory data in cases with pneumonia

		MPV	**Presepsin**
Age	r	0.192	-0.211
	P	0.382	0.254
Disease duration	r	**0.421**	0.619
	P	**0.001**	**< 0.001**
Hemoglobin	r	-0.314	-0.353
	P	0.003	0.001
WBCs	r	**0.541**	0.465
	P	**< 0.001**	**< 0.001**
Neutrophils	r	0.054	0.052
	P	0.616	0.628
Lymphocytes	r	-0.019	-0.031
	P	0.858	0.772
Platelets	r	0.065	0.163
	P	0.545	0.124
CRP	r	**0.478**	**0.391**
	P	**< 0.001**	**0.001**
Presepsin	r	0.643	
	P	**< 0.001**	
MPV	r		**0.643**
	P		**< 0.001**

The different cutoff points of MPV and presepsin in differentiating between control group and pneumonia cases and between pneumonia cases and severe pneumonia cases are shown in table (4). The best cutoff point of MPV to identify cases with pneumonia was > 8.75, with 86.7% sensitivity and 83.3% specificity. The AUC is 0.912 with high significant value (p< 0.001). The best cutoff point of presepsin to identify cases with pneumonia was > 265.5, with 93.3% sensitivity and 93.3% specificity. The AUC is 0.963 with high significant value (p< 0.001).

The best cutoff point of MPV to identify cases with severe pneumonia was > 10.25,

with 83.3% sensitivity and 70% specificity. The AUC is 0.789 with high significant value (p< 0.001). The best cutoff point of presepsin to identify cases with pneumonia was > 389.3, with 91.7% sensitivity and 89.6% specificity. The AUC is 0.877 with high significant value (p< 0.001).

Table (4): Validity (AUC, sensitivity, specificity) for of MPV and presepsin in differentiating between control group and pneumonia cases and between pneumonia cases and severe pneumonia cases

	AUC	p	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
Discriminate pneumonia patients (n = 30) from control (n = 30)								
MPV	0.912	<0.001[*]	0.837 – 0.987	> 8.75	86.7	83.3	84.5	82.4
Presepsin	0.963	<0.001[*]	0.900 – 1.0	> 265.5	93.3	93.3	95.4	91.2
Discriminate severe pneumonia patients (n = 30) from pneumonia patients (n = 30)								
MPV	0.789	<0.001[*]	0.669 – 0.910	> 10.25	83.3	70	75.0	81.4
Presepsin	0.877	0.004[*]	0.776 – 0.979	> 389.3	91.7	89.6	90.2	86.4

Discussion

The current study included 90 children who were divided into three age and sex matched groups, 30 clinically healthy children as a control group, 30 patients with pneumonia and 30 patients with severe pneumonia.

In the current study-regarding age of the study groups , there were no statistically significant differences between the three groups (p=0.875). there was slightly higher prevalence of male gender in the cases with pneumonia (53.3% and 56% in the pneumonia and severe pneumonia groups, respectively

This agreed with the study done in 2020 which revealed that male gender constituted a significant predictor of acquiring pneumonia in both bivariate and multivariate analysis [23].

In accordance to our finding, a meta-analysis reported that males are more likely than females to acquire pneumonia [24]. Gender variation can be explained by the stronger immune system in girls than boys. There is also evidence that the peripheral airways are narrower during the early years of life in boys, which may predispose them to LRIs [25].

In the current study, previous hospital admission was reported in 70% and 53.3% of the patients with pneumonia and those with severe pneumonia respectively. However, the difference was not statistically significant.

In the study done in 2020 shown that around one-third of the children in the study had acquired pneumonia previously; 32.7% of these had experienced 3–5 episodes and 8.8% had experienced > 5 episodes who required hospital admission [23].

The higher percentage in our study could be explained due to difference in study centers. The high frequency of cases examined in our study (tertiary care center) could explain the higher percentage of more serious cases.

Common physical findings in CAP include fever, tachypnea, increasingly labored breathing, rhonchi, crackles, and wheezing. Hydration status, activity level, and oxygen saturation are important and may indicate the need for hospitalization [26].

In the current study, fast breathing and cough were detected in all the cases with pneumonia. Chest indrawing was reported in 56.1% in both the groups of patients. Difficult breathing was reported in 43.3% and 56.1% in the patients with pneumonia and severe pneumonia respectively while

fever was reported in 66.7% and 73.3% in the patients with pneumonia and severe pneumonia respectively with no statistically significant difference between the two groups.

The diagnostic challenge of childhood pneumonia lies in the broad range of presenting features. Children can present with pneumonia at different stages of illness and with clinical features that might be difficult to discriminate from other common paediatric conditions [27].

In the current study, that the mean hemoglobin levels of the cases with pneumonia were significantly lower than that of the controls (p< 0.001), but there was no statistically significant difference in the hemoglobin level between the cases with pneumonia and severe pneumonia.

These data came in agreement with several studies done among Egyptian children about anemia as a risk factor for acute lower respiratory tract infections.

For example, it was reported that low hemoglobin level was found to be a risk factor for acute lower respiratory tract infections as it was detected in 56.25% of bronchiolitis cases, 62.5% of pneumonia cases and 42.71% of the control group [28].

The same results were reported recently by other researchers (2021).

A group of researchers studied anemia and air pollution as risk factors for acute lower respiratory tract infections among Ecuadorian children it was shown; they studied anemia and air pollution as risk factors for acute lower respiratory tract infections. They found that anemic children are at increased risk of acute respiratory infection hospitalization compared to healthy non-anemic children. They explained their findings by that the central pathophysiological deficit in acute lower respiratory tract infections is poor tissue oxygenation and anemia independently decreases oxygen delivery [29].

Researchers found that any inadequate supply of iron to body tissues is detrimental to immunity, the effects of iron deficiency anemia on immune function, and increase in susceptibility to infections are well established [30].

On the other hand, a study reported that anemia was not found to be a risk factor for acute lower respiratory tract infections in 512 infants and children below 5 years of age [31].

The difference could be explained due to variations in the sample size between the

studies and variations in the population characteristics.

In the current study, the WBCs count and neutrophil count were statistically significantly higher in the cases with pneumonia as compared with the control group. Also, the WBCs count and neutrophil count were statistically significantly higher in the cases with severe pneumonia as compared with the cases with pneumonia.

This is in the same line with the study done in 2020, which showed that the WBCs count and neutrophil count were statistically significantly higher in the cases with pneumonia as compared with the control group [32]

Similar results were reported that WBC levels were significantly higher in CAP patients who were hospitalized (p<0.001) or followed-up as outpatients (p<0.001) than healthy controls [33]

In the current study, the lymphocytes were higher in the cases with pneumonia as compared with both the cases with severe pneumonia and the control group while the latter two groups didn't show a statistically significant difference. Similar results were reported before (32).

This agreed with the study that reported that there was an increase in the number of neutrophils but a decrease in the number of lymphocytes in the case group compared to the control group [34].

These findings are similar to the results which confirmed that abnormally low lymphocytes with elevated neutrophil count have good predictive power in pneumonia [35]

In the current study, there was no statistically significant difference in the mean platelets count between the cases within the three study groups.

This contradicts the results reported previously, that the mean platelets counts was statistically significantly lower in the cases with pneumonia as compared with the control group [32].

This disagreed with other researchers, who studied the platelet count as a marker of outcome in community-acquired pneumonia. They found that Lower platelet counts were associated with an increase of severity of pneumonia and more frequently complications in patients with community-acquired pneumonia [36].

It was reported that platelet count of the patients with pneumonia was statistically significantly higher in the patient group than in the control group (p< 0.05) [37].

PLT would increase against respiratory tract infections due to elevated levels of inflammatory cytokines so that the commonest cause of reactive thrombocytosis has been reported in respiratory infections [38 & 39]. In another study, an increase in PLT count was observed in children with pneumonia [40]. In a study by Sahin *et al.*, السنهthe number of PLT in the patient group was significantly higher than the control group [37]. The difference in our study could be explained due to small sample size in our study.

It has been reported that ESR, WBC count, and CRP, which are assumed as general indicators of infectious disease, are also valuable in the diagnosis of CAP [41]. Leukocyte count, ESR, and CRP are the most common acute phase reactants [37]. Changes in these indices can be used to diagnose infectious and inflammatory diseases [42].

In the current study, the median CRP levels of the patients groups were higher than that of the control group (p< 0.001) with an insignificant difference between the 2 groups of patients.

Thomas *et al*. السنهreported that the average CRP level was higher in patients with bacterial pneumonia than in patients with viral pneumonia [43].

In another study performed abnormally increased CRP in pneumonias patients was observed [44]

Furthermore, it was proved that CRP levels were significantly higher in CAP patients who were hospitalized compared to those who were followed-up as outpatients (p<0.001) [33]

In the current study, the mean presepsin level was highest in the severe pneumonia group followed by that of the pneumonia group and least in the control group with statistically significant differences between the 3 groups (P < 0.001).

This came in accordance with others who showed that there was statistically significant difference between case and control groups in presepsin level. In addition, there was statistically significant difference in presepsin level with disease severity in which presepsin is higher in sever than moderate and mild cases [32].

This come in agreement with those who found that plasma presepsin levels were significantly higher in severe community acquired pneumonia patients than mild and moderate cases [45].

The diagnostic and prognostic value of soluble Presepsin for sepsis and community acquired pneumonia in ICU patients, were investigated and it was found that plasma levels of presepsin was significantly higher in septic than in non-septic patients and in septic shock as compared to others [46].

Also in agreement with this, the diagnostic and prognostic value of presepsin in the management of sepsis in the emergency department were evaluated; and they found that elevated concentrations of presepsin at presentation were observed in septic patients compared to control patients [47].

In the current study, the mean MPV was highest in the severe pneumonia group followed by that of the pneumonia group and least in the control group with statistically significant differences between the 3 groups (P < 0.001).

In this regard, it was reported that MPV may be a useful predictor in the diagnosis of community-acquired pneumonia [33].

Another study of patients with community-acquired pneumonia presenting to the emergency department also concluded that MPV might be useful in determining

severity of disease and in predicting mortality [48].

Our results were in accordance some researchers demonstrated that the amount of MPV value was lower in CAP patients in comparison to the controls, although this difference was not statistically significant [34].

Also, in accordance with our results, one hundred and ninety child patients with pneumonia and 71 healthy children, were studied. They showed that the MPV value of the patients with pneumonia was statistically significantly lower than those of the control group (p< 0.05) [37].

Their findings showed that the amount of MPV varies depending on the severity of the infection suggesting it as a good indicator for CAP diagnosis [49].

Changes in both platelets count and morphology and the associated change in platelet indices might be caused by pathophysiological conditions, which inhibit platelets regeneration, increase their activation or accelerate their death [50]. It was postulated that the increased volume of platelets in critically ill children is related to the increased thrombocytosis with increased megakaryocyte ploidy [51].

It may be hypothesized that the bone marrow response to the infection is inadequate in CAP cases followed as outpatients, and that an increase in platelet size only occurs as a result of damage or consumption of peripheral circulating platelets due hyper stimulation. Considering that patients who require hospitalization tend to be brought to the hospital at a later stage of the disease, it may be postulated that MPV decreases during the earlier stages of CAP, which is followed by a significant increase in MPV as a result of bone marrow activation [33]

It was reported that changes in platelet size follow at least two distinct patterns: an early increase in MPV in severe infections (such as septicemia), and a late decrease in chronic bacterial infections, which may explain why patients with pneumonia have lower MPV levels than controls [52].

In the current study, the best cutoff point of presepsin to identify patients with pneumonia was > 265.5 pg/mL, with 93.3% sensitivity and 93.3% specificity. The AUC was 0.963 with a highly significant value (p< 0.001) and the best cutoff point to identify cases with severe pneumonia was > 389.3 pg/mL, with 91.7% sensitivity and 89.6% specificity. The AUC is 0.877 with a highly significant value (p< 0.001).

In the study conducted in 2020, it was proved that the best cutoff point of presepsin 0.8 (ng/ml) was detected for diagnosis of the community acquired pneumonia calculated from ROC curves , and the area under the curve of presepsin was 0.833 with sensitivity 97.8% and specificity 72% [32].

In accordance with this study, it was found that the AUCs (area under the curve) calculated from ROC curves were 0.75 for presepsin, at a cutoff value of 466.5 pg/mL, sensitivity and specificity of Presepsin to severe sepsis and septic shock diagnosis were 90 and 55 %, respectively. While others found that the area under the curve (AUCs) calculated from the ROC curve were 0.701 for presepsin, the best diagnostic cutoff for presepsin was 600 pg/ml. At that level, sensitivity and specificity were 78.95% and 61.90% respectively [46].

The pooled diagnosis sensitivity and specificity of presepsin for sepsis were 0.84 and 0.76 respectively and AUC was reported to be 0.88 [10].

In neonates, it was shown that the best cut-off plasma presepsin to predict early-onset neonatal pneumonia was 605 pg/mL with 70% sensitivity, 73.3% specificity, 72.4%

PPV, and 71% NPV with a fair AUC 0.74 (p .001) [53].

Similarly, it was reported that presepsin measured in blood with values more than 788 pg/mL have a 93% sensitivity and 100% specificity as an early marker for infection [54].

Our results are in agreement with others who reported that at cutoff value 686 pg/mL presepsin achieved the highest specificity which could be documented by a univariate marker in their study (95.5%), in addition to sensitivity 82.7%, PPV 95.4%, NPV 83.1%, efficacy 88.7%, and AUC 0.887, respectively [55].

On the other hand, in a research conducted to examine Presepsin as a diagnostic marker for sepsis, they found that sensitivity and specificity of presepsin were 0.83 ng/ml and 0.81 ng/ml, respectively, with a relatively high rate of missed diagnosis (17%) and misdiagnosis (19%). AUC was 0.89, indicating good diagnostic performance [56].

A possible source of heterogeneity came from the use of different specimen types. Our subgroup analysis result suggested that the use of whole blood had higher specificity than plasma, with statistical significance [10].

In the current study, the best cutoff point of MPV to identify patients with pneumonia was > 8.75 femtoliter, with 86.7% sensitivity and 83.3% specificity. The AUC was 0.912 with a high significant value (p< 0.001) and the best cutoff point of MPV to identify the patients with severe pneumonia was >10.25, with 83.3% sensitivity and 70% specificity. The AUC is 0.789 with high significant value (p< 0.001).

It was suggested by ROC curve analysis that MPV level cut-off point for making a diagnosis of CAP was 8.1 fL, with a sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 91%, 51%, 80.8% and 70.5%, respectively **[33]**

In the current study, there was a statistically significant positive correlation between presepsin level and MPV (r= 0.643, P < 0.001), disease duration (r= 0.619, P < 0.001), WBCs count (r= 0.465, P < 0.001) and CRP level (r= 0.391, P= 0.001).

It was reported that there was low positive correlations between the plasma presepsin level and serum C-reactive protein level (rs =0.375, P<0.001) **[57]**.

The authors explained the association as C-reactive protein is an acute-phase protein synthesized in hepatocytes responding to infection, inflammation, tissue damage, and malignant neoplasm. Presepsin is also an acute inflammatory protein synthesized in monocytes and macrophages during systemic bacterial infection. The present study cohort mainly comprised of patients with bacterial infection. This may explain the positive correlation between C-reactive protein and presepsin.

In the current study, there was a statistically significant positive correlation between MPV with presepsin level (r= 0.643, P < 0.001), disease duration (r= 0.421, P < 0.001), WBCs count (r= 0.541, P < 0.001) and CRP level (r= 0.478, P < 0.001).

It was shown that in the pneumonia and control groups included in their study, MPV was found to be significantly positively correlated with age and hemoglobin, but had a significant negative correlation with platelet count (pneumonia group p= 0.046, p= 0.008, p< 0.001; control group p= 0.002, p= 0.019, p= 0.003, respectively) **[37]**

We must acknowledge some limitations of this study. First, the study included a small number of patients because it was a single-center study. To establish the clinical significance of plasma presepsin level in patients with pneumonia, a multi-center

clinical study with a larger patient group is required.

We also didn't follow up the cases to determine the pattern of outcome. This could provide additional diagnostic validity of presepsin and MPV in relation to different outcomes.

Conclusion

Based on our findings, both serum presepsin and mean platelet volume (MPV) could be used as non-invasive biomarkers in diagnosis of pneumonia together with assessment of the degree of pneumonia severity.

Moreover, we concluded that serum presepsin showed higher diagnostic ability as compared to MPV in assessment pf CAP and determination of severity

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