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Value of Granulocyte Colony Stimulating Factor in Mechanically Ventilated Children for Ventilator Associated Pneumonia Diagnosis and Mortality

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Abstract

Background: Granulocyte Colony Stimulating Factor (G-CSF) is a biomarker recommended for detection of Ventilator Associated Pneumonia (VAP).

Purpose: To assess G-CSF level in mechanically ventilated children to determine its cut-off point for VAP diagnosis and mortality.

Methods: A prospective research was performed on 122 children who were mechanically ventilated for more than 48 h at Pediatric Intensive Care Unit (PICU). All mechanical ventilated children were monitored for signs of VAP suspicion. 42 patients were without VAP suspicion and 80 suspected patients were subdivided regarding VAP confirmation by quantitative culture of non bronchoscopic Bronchoalveolar Lavage (BAL) into confirmed VAP (VAP group) and non-confirmed VAP group. Patients without VAP suspicion and non-confirmed VAP were considered as non-VAP control group. Clinical examination included estimation of Pediatric Risk of Mortality (PRISM), Pediatric Index of Mortality II (PIMII) and pediatric Sequential Organ Failure Assessment scores (pSOFA). Serum G-CSF was collected from the studied groups. The patients were monitored for 30 days.

Results: G-CSF was significantly elevated in VAP group than non-VAP control group (P=0.001). Among VAP group, G-CSF was positively correlated with duration of PICU stay, Mechanical Ventilation (MV) duration, pSOFA, PRISM and PIMII scores. Through logistic regression analysis, there was significant association between G-CSF level, PICU stay, MV duration, pSOFA score, shock and VAP risk (OR=1.794, 1.955, 1.955, 1.673, 5.67 respectively). The cut-off point G-CSF was 886.8 ng/ml for diagnosing VAP, while cut-off point for C-reactive protein was 20 mg/dl. G-CSF cut-off point for mortality was 1630 ng/ml, while cut-off points for PRISM, PIM, and pSOFA scores were (6.00, 2.50, 8.50) correspondingly.

Conclusion: High level of G-CSF is associated with VAP and its cut-off point can differentiate between confirmed VAP and non-confirmed VAP group.

Keywords: Granulocyte colony stimulating factor; Pediatric; Ventilator associated pneumonia

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Introduction

Ventilator Associated Pneumonia (VAP) is a kind of hospital-acquired pneumonia that develops in more than 48 h of mechanical ventilation [1]. VAP affects 3% to 19% of pediatrics who are ventilated and is linked with elevated rates of death and morbidity [2].

Common VAP causing pathogens include Gram negative bacteria involving *Klebsiella pneumoniae*, *Acinetobacter* species, *Pseudomonas aeruginosa*, and *Escherichia coli*, whereas *Staphylococcus aureus* as Gram-positive pathogens [3].

VAP is the most widespread cause for prophylactic antibiotic treatment initiation which comprises more than 50% of antibiotic days in PICU [4]. The precise detection of VAP in children and adults continues to be a challenge. In individuals with VAP, a delayed diagnosis and subsequent delay in starting adequate treatment may result in poorer results. Contrary to this, an erroneous diagnosis may result in unneeded treatment and following consequences of therapy [5]. Numerous diagnostic criteria for VAP have been provided, including clinical pictures, imaging studies, obtaining of bronchoalveolar specimens, and biomarkers measurements [5]. However, there is

currently no recognized gold standard method, and the diagnostic integrity of various modalities for VAP is questioned.

Colony Stimulating Factor 3 (CSF3), which was identified recently as Granulocyte Colony Stimulating Factor (G-CSF), is a glycoprotein that increases stem cell and granulocyte synthesis in the bone marrow and their release into the circulation [6]. G-CSF promotes neutrophil precursor survival, proliferation, and differentiating. CSF enhances the survival, multiplication, and differentiation of neutrophil precursors and mature neutrophils, so it increases during VAP and is utilized to evaluate the prognosis and diagnosis of suspected or confirmed individuals to have VAP [7]. No research has investigated the diagnostic effectiveness of G-CSF in pediatric VAP. Consequently, we conducted this research to evaluate the cut-off point of G-CSF for VAP diagnosis and mortality in Pediatrics.

Patients and Methods

Patients

This research was performed between December 2019 and November 2020 on 122 mechanically ventilated children hospitalized at Menoufia University Hospital's Pediatric Intensive Care Unit (PICU). All involved children's parents obtained written parental consent for their children's participation in research. The ethics committees at Menoufia University approved the research. Inclusion criteria for the research included children aged 1 month to 18 years, patients who mechanically ventilated beyond forty-eight hours, and children whose parents consented to their participation. Criteria of exclusion included: Children whom mechanical ventilation is predicted to be required for ≤ than 48 h, children who without available samples, Lack of parental concept, immunosuppressed children, active infection on admission, and developing hospital associated infection except VAP during period of ventilation.

All mechanically ventilated patients monitored for development of signs of VAP which diagnosed based on the Centers for Disease Control and Prevention (CDC) [8] requiring the presence of two successive chest X-rays demonstrating fresh and persistent (or progressive and persistent) infiltration, cavitation, consolidation, or pneumatocele, in addition to specific clinical and biochemical criteria depending to age. Patients who had no signs of VAP suspicion were considered as without VAP suspicion group. After that the suspected patients were sub-grouped according to the confirmation of VAP that was determined by non-bronchoscopic bronchoalveolar lavage fluid quantitative culture containing ≥ 10^5 Colony Forming Units (CFU)/ml of a potentially pathogenic microorganism into confirmed VAP group and clinically suspected VAP group. The confirmed patients were defined as VAP group. The groups of without VAP suspicion and clinically suspected VAP were considered as Non VAP control group.

Methodology

All patients had a complete evaluation, including a medical history and a physical exam. Each individual was monitored by assessing vital signs and oxygen saturation. Hypoxia was defined as peripheral Oxygen Saturation (SPO_2) of less than 94% on a sustained basis [9]. For children admitted to the PICU, three severity scores were calculated: The Pediatric Risk of Mortality (PRISM) [10], the Pediatric Index of Mortality II (PIM II) [11] and the pediatric Sequential Organ Failure Assessment (pSOFA) score [12]. Each patient's PRISM score was computed within twenty-four hours after arrival, using 14 clinical and laboratory variables. Values for these variables were entered into the PRISM application (http://www.sfar.org/scores2/prism2.php), which calculates the expected death rate. PIM II is a more rapid technique for which scores are estimated within 1 h of in-person contact with the patient, and scores correspond to a predicted mortality rate. pSOFA utilized for evaluating organ malfunction. Depending on the patient's baseline risk level, a pSOFA score of 2 or greater corresponds to a 2- to 25-fold greater risk of death than patients with pSOFA scores less than 2.

The laboratory work-up of Complete Blood Count (CBC) using a Sysmex XN-1000 (Japan; 19723) was done *via* 1 ml of blood collected in EDTA-containing tubes, by venipuncture, 2 ml of venous blood was drawn from each patient and deposited in a plain tube then centrifuged at 4000 RPM after being allowed to clot for 10 min. The collected serum was used to measure C-reactive protein by Enzyme Linked Immunosorbent Assay (ELISA) using a Sun Red Elisa kit (catalogue No, 201-12-1799). Arterial Blood Gases (ABG) were measured by radiometer (ABL80, FLEX.) and blood culture by BACTECFX instrument. In addition, a chest X-ray and chest CT were performed. Other laboratory or radiological examinations were carried out when needed.

Non Bronchoalveolar Lavage fluid (BAL) fluid was collected through Endotracheal Tube (ET). The Mini-BAL sample was obtained by inserting a sterile 12 French long suction catheter *via* the Endotracheal Tube (ET) and blindly putting it into the distal airways until resistance is encountered, after which the catheter was wedged in place. NaCl 0.9% was given *via* the catheter, and aspirate was sucked into a sterile polypropylene collection tube (bronco collector; Cremer®, Brazil) [13]. Following these procedures, the probe was withdrawn carefully utilizing turning movements.

The group of controls was formed by matching children with non-VAP patients. Non-VAP control group was matched according to previous duration of mechanical ventilation until the infection, equal to previous ventilation duration in VAP group minus one and plus one day; if previous duration of ventilation was more than fourteen days in the VAP group. Serum biomarker level of VAP group on the day of VAP diagnosis was compared with the biomarker level on the matched ventilation day of control patients.

Serum G-CSF measurement was performed for patients on the day of beginning of mechanical ventilation (D0), and on the day of Diagnosis of VAP (DV) and on the matched ventilation day of control patients. A 3-ml venous blood sample was taken then blood was left to clot for 5 min then centrifuged 10 min at 3000 rpm. Clear sera were separated and kept frozen at -80 until the time of the assay. Serum G-CSF was determined using (Human ELISA Kit for Granulocyte Colony-Stimulating Factor (G-CSF), Sun Red, Catalogue No, (201-12-0122).

Study outcomes

The cut-off point of G-CSF for VAP diagnosis was a primary outcome measure. The duration of mechanical ventilation, PICU stay, and hospital stay, and death were secondary outcome measures.

Statistical analysis

Results were collated and statistically analyzed on a personal computer using version 22 of Statistical Package for Social Science (SPSS) on an IBM personal computer (SPSS, Inc, Chicago, Illinois) Statistical analysis was performed utilizing: Descriptive: for example, percentage (%), mean and standard deviation (with range). Chi-Squared (χ^2), Student's t, and Mann-Whitney tests are analytical.

To determine the risk factors for VAP utilizing logistic regression models. Analysis of Receiver Operating Characteristics (ROC) was performed for the diagnostic and prognostic powers of the biomarker, and other variables and the ideal cut-off values were chosen using the Youden index. P-values of less than 0.05 considered to be statistically significant.

Results

Among the 122 eligible children, 80 children were with suspicion of VAP and 42 children were without VAP suspicion. Among 80 patients; 37 of them had confirmed VAP and 43 children had clinically suspected VAP. 43 children who clinically suspected VAP were included in the control group along with the 42 children without VAP suspicion (Figure 1).

Demographic and clinical features of the studied groups are shown in (Table 1)

Endotracheal quantitative cultures were positive (≥ 1 × 10^5 cfu/mL) in the VAP group. We found VAP group was more likely to have shock than non-VAP control group (p=0.001). Significant increase in MV duration, PICU and hospital stay was observed in VAP group compared to non-VAP group (p=0.001, 0.002, 0.001 respectively). Additionally, there was a significant raise in all mortality scores in the VAP group compared to the non-VAP group (pSOFA, PRISM and PIM II).

Laboratory characteristics of the studied groups were studied at (Table 2)

There was significant increase in WBCs count and CRP level in VAP group *vs.* non-VAP group (p=0.001, 0.034) but we showed significant decrease in platelet count and HCO_3 level in VAP group

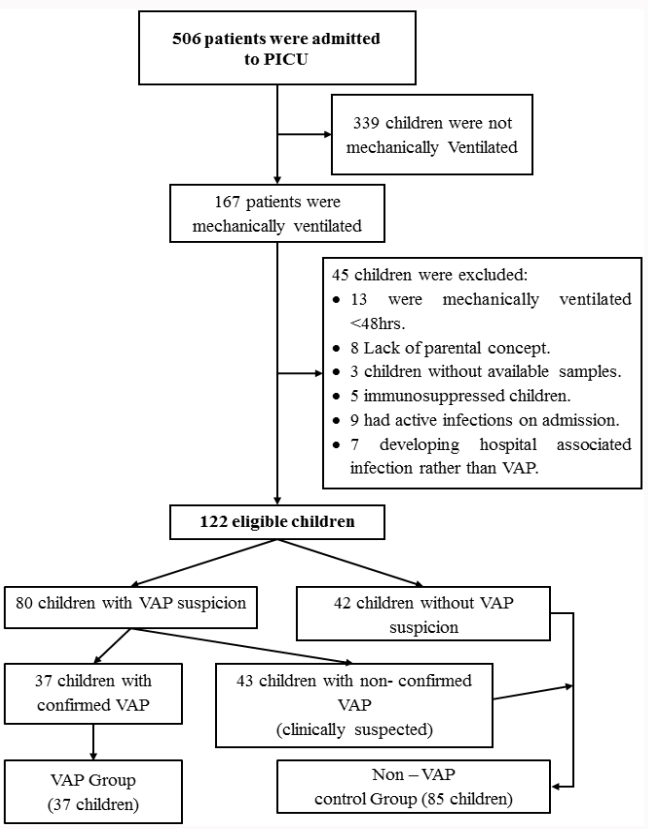

Figure 1: Flow chart of the studied groups.

Table 1: Demographic and clinical characteristics of the studied groups.

Demographic and Clinical characteristics	VAP Group N=37	Non-VAP Control Group N=85		P Value
		Clinically suspected VAP Group N=43	Without VAP suspicion Group N=42	
Negative quantitative culture	0	38	42	**0.01***
Culture <1 × 10^5 (cfu/mL)	0	5	0	**0.01***
Culture ≥ 1 × 10^5 (cfu/mL)	37	0	0	**<0.01***
Age/months				
Median (IQR)	10 (1.50–84)	11 (2-85)		0.064
Sex	N (%)	N (%)		
Male	17 (45.0)	47 (55.0)		0.371
Female	20 (55.0)	38 (45.0)		
Weight (Kg)				
Median (IQR)	8.65 (2-23)	9(3.50 – 25)		0.357
Height (cm)				
Median (IQR)	75 (50-115)	79.5(50 - 120)		0.386
BMI(Kg/m^2)				
Median (IQR)	15.94 (5.20-17.4)	15.63 (11.7-17.6)		0.95
Primary diagnosis n (%)				
Respiratory	29 (78.6%)	57 (66.7%)		0.56
Cardiac	3 (8.5%)	13 (15.1%)		
Neurologic	3 (8.5%)	13 (15.1%)		
Others	2 (4.4%)	2 (3.1%)		
Shock N (%)				
Yes	21 (57.5)	15 (17.5)		**0.001***
No	16 (42.5)	70 (82.5)		
MV/hours				
Median (Range)	455 (144–2160)	168 (120-840)		**0.001***
PICU stay/day				
Median (IQR)	19 (6-90)	7(5-35)		**0.002***
Hospital stay/day				
Median (IQR)	25.5 (16–98)	15 (13-42)		**0.001***
pSOFA score				
Median (IQR)	9 (3–15)	6(2-11)		**0.001***
PRISM mortality risk %				
Median (IQR)	10 (3–29)	4 (2-19)		**0.001***
PIM mortality risk %				
Median (IQR)	14.1 (0.30–21.7)	1.8 (0.20-16)		**0.001***
Mortality				
Yes	24 (65%)	30 (35%)		**0.007***
No	13 (35%)	55 (65%)		

Data is expressed as number (%), median (IQR); BMI: Body Mass Index; MV: Mechanical Ventilation; PICU: Pediatric Intensive Care Unit; PRISM: Pediatric Risk of Mortality; PIMII: Pediatric Index of Mortality II; pSOFA: pediatric Sequential Organ Failure Assessment Score; *: Statistically Significant

than non-VAP group (p value =0.046, 0.013 respectively). There was significant increase in median of serum G-CSF level on Dv in VAP group (1693.2 ng/ml) compared with non-VAP group (304.4 ng/ml) (p=0.001) but there was no significant difference in median of serum

Table 2: Laboratory characteristics of the studied groups.

Laboratory Data	VAP Group N = 37	Non-VAP Control Group N = 85	P value
Hb (gm/dl)			
Median (IQR)	10.4 (6.50-13. 9)	10.5 (7.80-14.8)	0.814
WBCs (× 10^3/µl)			
Median (IQR)	23.75 (7.20-39)	11.2 (3.20-34.9)	**0.001****
Platelets count (× 10^3/µl)			
Median (IQR)	254.5 (52.0-575)	350 (70-605)	**0.046***
CRP (mg/dl)			
Median (IQR)	66.85 (24-160)	12 (10-96)	**0.034***
HCO3			
Median (IQR)	19 (11.3-29.3)	23.5 (10.5-32.8)	**0.013***
G-CSF (ng/ml) on D_0			
Median (IQR)	225.3 (93.8-344.8)	220.3 (87.9-336.5)	0.07
G-CSF (ng/ml) on Dv			
Median (IQR)	1693.2 (759.3-5401)	304.4 (97.2-545.6)	**0.001****
Isolated Organisms, n (%)			
Pseudomonas aeruginosa	14 (37.5%)	-	
Acinetobacter baumannii	9 (25.0%)	-	-
Coagulase -ve *Staph aureus*	8 (22.5%)	-	
Klebsiella pneumoniae	6 (15.0%)	-	

Data is expressed as number (%), median (IQR); WBCs: White Blood Cells; CRP: C-Reactive Protein; G-CSF: Granulocyte – Colony Stimulating Factor; D0: Day of beginning of mechanical ventilation; Dv: Day of diagnosis of VAP; *: Statistically Significant

Table 3: Correlation of G-CSF level on Dv with clinical and laboratory data of VAP group.

Variables	G-CSF on Dv	
	Spearman correlation coefficient (r_s)	P value
Age (months)	-0.373	**0.018***
Weight (kg)	-0.387	**0.014***
PICU stay (day)	0.32	**0.044***
MV duration (hours)	0.382	**0.037**
Hb (gm/dl)	0.19	0.241
WBCs (× 10^3/µl)	0.32	**0.044***
Platelet count (× 10^3/µl)	-0.012	0.941
CRP (mg/dl)	0.461	**0.003****
pSOFA score	0.817	**0.001****
PRISM mortality risk %	0.714	**0.001****
PIM mortality risk %	0.713	**0.001****

PICU: Pediatric intensive care unit; WBCs: White blood cells; CRP: C-reactive protein; PRISM: Pediatric Risk of Mortality; PIMII: Pediatric Index of Mortality II; pSOFA: pediatric Sequential Organ Failure Assessment Score; G-CSF: Granulocyte – Colony Stimulating Factor; *: Statistically Significant

G-CSF level on D_0 between two groups. *Pseudomonas aeruginosa* was the most frequently isolated microorganisms from non-bronchoscopy BAL samples in the VAP group (36.3%).

Correlation of G-CSF level on Dv with clinical and laboratory data of VAP group

We detected a negative correlation between G-CSF and age and weight, but a positive correlation between G-CSF and length of PICU stay, MV duration, WBCs, CRP, pSOFA, PRISM, and PIM II in the VAP group (p=0.044, 0.037, 0.044, 0.003, 0.001, 0.001, 0.001, 0.001) (Table 3).

Table 4: Multivariate regression analysis for risk factors for VAP.

Predictors	P value	OR	95% CI (lower – upper)
Hb (gm/dl)	0.937	0.009	0.798 – 1.27
Platelet count (×10^3/µl)	0.376	0.001	0.997- 1.00
WBCs (×10^3/µl)	0.152	0.903	0.786 – 1.03
CRP (mg/dl)	0.757	1.007	0.983 – 1.01
HCO_3	0.095	0.923	0.841 – 1.01
G-CSF level (ng/ml)	**0.040***	1.794	1.638 – 1.989
PICU stay/days	**0.001****	1.955	1.914 – 1.997
MV duration (hours)	**0.001****	1.995	1.993 – 1.998
PRISM %	0.672	0.959	0.992 – 1.16
PIM %	0.258	0.977	0.999 – 1.10
pSOFA	**0.002****	1.673	1.538 – 1.860
Shock	**0.006****	5.67	1.62 – 19.8

PICU: Pediatric intensive care unit; WBCs: White blood cells; CRP: C-reactive protein; PRISM: Pediatric Risk of Mortality; PIMII: Pediatric Index of Mortality II; pSOFA: pediatric Sequential Organ Failure Assessment Score; G-CSF: Granulocyte – Colony Stimulating Factor; *: Statistically Significant

Table 5: Values of serum G-CSF level on Dv and other variables for VAP diagnosis and mortality.

	VAP diagnosis			Mortality prediction			
	G-CSF	CRP	WBCs	G-CSF	PRISM	PIM	pSOFA
AUC	0.993	0.588	0.557	0.76	0.687	0.684	0.768
Cut off point	886.8	20	6.9	1630	6	2.5	8.5
Sensitivity	97%	90%	75%	65%	81%	73%	73%
Specificity	95%	47%	13%	64%	21%	36%	64%
PPV	95%	69%	46%	77%	66%	68%	79%
NPV	97%	78%	33%	50%	38%	42%	56%
Accuracy	96%	71%	44%	65%	60%	60%	70%

G-CSF: Granulocyte colony stimulating factor; Dv: Day of diagnosis of VAP; WBCs: White Blood Cells; CRP: C Reactive protein; PRISM: Pediatric Risk of Mortality; PIM: Pediatric Index of Mortality II; pSOFA: pediatric Sequential Organ Failure Assessment

Multivariate regression analysis showed that increased G-CSF level, long duration of PICU stay and MV, high pSOFA score and presence of shock are risk factors for VAP (OR=1.794, 1.955, 1.995, 1.673, 5.67 respectively) (Table 4).

Regarding diagnostic power for VAP, we discovered that G-CSF on Dv was a more accurate predictor of VAP than WBCs and CRP. G-CSF cutoff value of 886.8 ng/ml demonstrated a sensitivity of 97% and specificity 95% for VAP diagnosis. A WBCs cutoff point of 6.90 had a sensitivity of 75% and a specificity of 13%, but a CRP cutoff point of 20 had a sensitivity of 90% and a specificity of 47% (Table 5 and Figure 2).

Concerning the ability for mortality prediction; this ability was studied by the ROC curve and showed that a cutoff point of G-CSF of 1630 had a sensitivity of 65% and specificity of 64% in mortality prediction. A pSOFA cutoff point of 8.5 exhibited a 73% sensitivity and 64% specificity. A cutoff point of PRISM of 6 had a sensitivity of 81% and a specificity of 21%, whereas a cutoff point of PIM II of 2.50 showed a sensitivity of 73% and a specificity of 36% (Table 5 and

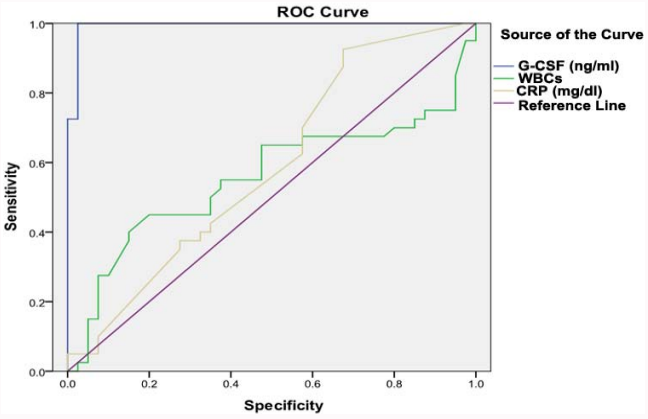

Figure 2: ROC curve of G-CSF level on Dv, CRP, and WBCs for VAP diagnosis.

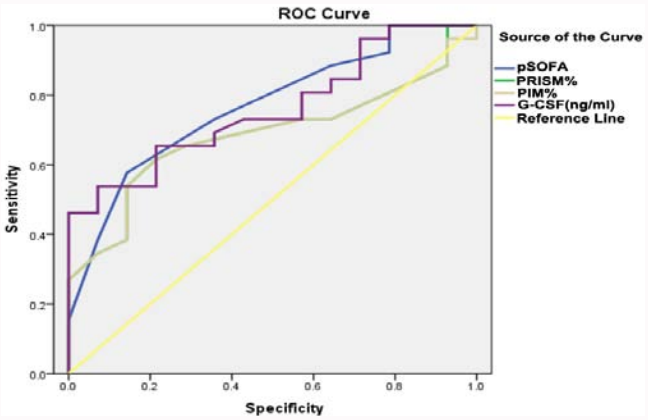

Figure 3: ROC curve of G-CSF level on Dv, pSOFA, PRISM and PIM for mortality prediction.

Figure 3).

Discussion

Nosocomial infections are accountable for high rates of morbidity and death in PICU and also are the main cause of high cost of healthcare resources utilization. VAP is the second leading cause of nosocomial infections in PICU and is associated with increased duration of PICU and hospitalization [14]. PICU mortality increased 3-fold according to multicenter prospective analysis of pediatric VAP [2].

A definitive VAP diagnostic approach for children remains dubious. The investigators used non-bronchoscopic techniques because the bronchoscopic techniques are invasive and expensive. Non-bronchoscopic and bronchoscopic VAP diagnostic techniques were evaluated and authors demonstrated that non-bronchoscopic bronchial sample methods were the most accurate for VAP diagnosis [15]. So, our research favored non-bronchoscopy BAL sampling due to its simplicity, lower risk of complications, and reliability.

The biggest advantage of using the biomarker is to diagnose VAP and additionally, to possibly increase the efficiency of existing diagnostic methods, several biological indicators for assessing the diagnosis and prognosis of individuals with suspected VAP have been evaluated [16].

G-CSF is a promising biomarker that is used for VAP diagnosis. In this research, we measured G-CSF in VAP group and non-VAP control group; it was significantly greater in the VAP group than non-VAP group., denoting that G-CSF has been shown to have diagnostic relevance for pediatric VAP suggesting that T lymphocytes and macrophages are the primary cells that produce G-CSF; it may stimulate granulocyte aggregation by attaching to certain cell receptors [17].

Hoshina et al. showed G-CSF may enhance the life cycle of eosinophils in inflammatory regions by increasing their aggregation and adsorption on vascular endothelium. Also, it activates eosinophils in the body releasing chemical agents leading to damage of tissue and increasing lung susceptibility [18,19].

The VAP group was more likely to have shock than non-VAP group; this can be explained by nearly half of patients with VAP suffering septic shock. In these individuals, septic shock is an independent predictor of death [20]. During VAP, certain clinical indicators such as lymphocytopenia and blood glucose levels more than 120 mg/dL, and advancing age, might indicate septic shock [21].

There was significant increase in MV duration in VAP group compared to non-VAP group, this agree with the result of Tirpathi et al., who stated the mean duration of MV in infants with VAP was (12.5+0.9) days and *vs.* non-VAP group was (5.4+0.8) days [22].

In our result; there was a significant rise in mortality scores (pSOFA score, PRISM and PIMII) in VAP group compared to non-VAP group. A previous study found no significant elevation of mortality scores among patients who later developed VAP [23]. Another study found association between mortality scores and VAP [24].

We found a significant decrease in platelet count in VAP group than non-VAP group. Thrombocytopenia caused by the following factors; direct toxic injury to platelets, megakaryocyte suppression, increased peripheral consumption, or the presence of an immune component due to high level of platelet-associated immune globulins [25].

The CRP level increased significantly in VAP group than non-VAP group. This was in line with the results of the studies of [26,27]. CRP is a component of the acute-phase response, a physiological and metabolic reaction to an acute tissue injury of diverse etiologies in which the goal is to neutralize the inflammatory agent and to stimulate the healing of the injured tissue [28].

In our research, we showed that long duration of PICU stay and MV are risk factors for VAP. According to Safdar et al., longer duration of ventilation step-up, the danger of infection caused by exposure to numerous equipment, as nebulizers, humidifiers, and ventilator circuits, which have been shown to be a significant source and medium for microorganisms [29] and Apisarnthanarak et al. showed that the risk of VAP rose by 11% for each additional ventilator week [30]. Afify et al. observed that extended hospitalization to PICU was a major risk factor for VAP because it increases the risk of infection and exposure to inadequate infection control methods such as hand washing [31] and Tirpathi et al. showed that patients with VAP had an average duration of stay in the PICU of (32.7+34.7) hours, compared to (19.7+23.3) hours for patients without VAP [22].

Serum level of G-CSF rose significantly when comparing the VAP group to non-VAP group with an excellent power for diagnosing of VAP versus than WBCs and CRP. This can be explained by G-CSF

stimulate neutrophil precursors and mature neutrophils' survival, proliferation, and differentiation, consequently, it rises during VAP and may be utilized to evaluate the diagnosis and prognosis of individuals with suspected or confirmed VAP [7].

There was positive correlation between G-CSF and PRISM, PIMII and pSOFA scores. G-CSF has low sensitivity in prediction of mortality than other mortality scores while it has a good specificity similar to pSOFA score and more than other mortality scores (PRISM and PIMII scores).

Future research required to investigate the function of G-CSF in prediction of mortality in VAP patients.

Conclusion

Serum G-CSF is an excellent biomarker for pediatric VAP diagnosis and to a lesser extent importance in prediction of mortality among VAP patients. The cut-off points of G-CSF at 886.8 ng/ml has excellent sensitivity and specificity for pediatric VAP diagnosis.

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