Presepsin level in children infected with community-acquired pneumonia

Article *in* International Journal of Health Sciences · April 2022

DOI: 10.53730/ijhs.v6nS1.5846

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Najm, R. A., AL-dujaili, A. N. G., & Hashim, J. M. (2022). Presepsin level in children infected with community-acquired pneumonia. *International Journal of Health Sciences*, *6*(S1), 4233–4244. https://doi.org/10.53730/ijhs.v6nS1.5846

Presepsin level in children infected with community-acquired pneumonia

Rana Ahmed Najm
Community Health Department, Kufa Technical Institute, Al-Furat Al-Awsat Technical University, Al-Najaf, Iraq
Email: kin.rna@atu.edu.iq

Arshad Noori Ghani AL-dujaili
Department of Biology, Faculty of Science, University of Kufa, Iraq
Email: arshad.aldujaili@uokufa.edu.iq

Jasim Mohammed Hashim
College of Medicine, University of Kufa, Iraq
Email: jasim.alghalibi@uokufa.edu.iq

***Abstract*---**Objective: To investigate the expression of Presepsin (P-SEP) in children infected with Community-acquired pneumonia and its correlation with total white blood cell count (WBC), gender and age. The current study included sixty (60) patient suffering from acquired community pneumonia aged range between one year to larger than 6 years, gander (30) female and (30) male Children in Al Zahara Teaching Hospitals in Najaf Provenance , during November 2020 – March 2021. The (30) control Child without suffering any of symptoms or criteria of acquired community pneumonia our results show significant elevation ($p<0.05$) in Total Leukocytes count and presepsin in pneumonia patient group in comparison with control group and non-significant ($p>0.05$) different in presepsin level between female and male pneumonia child patients. The results also indicate significant elevation ($p <0.05$) in serum presepsin level of pneumonia child patient among the age (1-3 y) when compare with among the ages (4-6 y) and (>6y) of pneumonia child patient .And there is no significant ($p>0.05$) different in presepsin between the ages (4-6y) when compare with ages (>6y).

***Keywords*---**presepsin level, children infected, community-acquired pneumonia.

Introduction

Pneumonia is a lung infection caused by an acute respiratory tract infection (ARTI). The lung's alveoli become clogged,when a person gets pneumonia, their lungs become filled with pus and fluid, making breathing difficult and oxygen intake limited. Pneumonia is caused by a number of different things, Bacteria and viruses are the most common pathogens, with *Streptococcus pneumoniae*, *Haemophilus influenzae* type b (Hib), and respiratory syncytial virus being the most prevalent causes (RSV). Under five-year-olds children are most frequently infected by *Streptococcus pneumoniae*, which is common in developing countries (Hema Latha *et al* ., 2017). Pneumonia was the greatest cause of mortality among children under the age of five in 2015, with an estimated 922,000 deaths, according to the World Health Organization. The majority of deaths occurred in the first two years of life, and most of them happen in impoverished areas, particularly in South Asia and Sub-Saharan Africa (World Health Organization *et al* ., 2015). There was a general consensus in 2010 that bacterial pneumonia was the most common cause of death from pneumonia (Zar *et al* ., 2013 ; Ali Imarah *et al* ., 2022).

Inflammatory biomarkers like white blood cell counts (WBCs) and C-reactive protein (CRP) Children with severe pneumonia can use these biomarkers to help diagnose the disease (Florin *et al* ., 2021). Patients with CAP may benefit from the use of these biological markers (Uwaezuoke *et al* ., 2017) . Clinical assessment and a panel of combined biomarkers need to be tested in further studies in order to see if they can significantly improve the treatment of pediatric CAP and minimize the disease's negative consequences (Al-Shemery *et al* ., 2019).

An early indicator of various infections has recently been identified as Presepsin (PSP) (Marazzi *et al* ., 2018 ; Al-Shemery *et al* ., 2019). PSP is a part of the soluble form of the CD14 subtype (sCD14-ST). CD14 is a member of the Toll-like receptor (TLR) family, which helps identify ligands from Gram-positive and Gram-negative bacteria and triggers an inflammatory response. CD14, in particular, can exhibit two distinct types: membrane bound (mCD14), which is expressed on the membrane of monocyte/macrophage cells, and soluble (sCD14), which is present in plasma and is cleaved by cathepsin D into a 13 kDa fragment known as PSP (Zou *et al* ., 2014). Activation of immune cells as a result of an invading pathogen is indicated by an increase in PSP levels in plasma, which decrease following antibiotic treatment. PSP secretion has also been linked to monocyte phagocytosis, implying that PSP could be measured in healthy, non-infected individuals. Since an increase in PSP above the physiological cutoff value correlates with the immune response activity, and therefore with the severity of the infection, a specific and sensitive method for measuring PSP is essential (Arai *et al* ., 2015 ; Al-Fatlawi *et al* ., 2020).

Presepsin has been shown in numerous studies around the world to be an excellent inflammatory marker for sepsis (Zhang *et al* ., 2015). The purpose of this study is to assess the diagnostic value of presepsin as a tool for children infected with community-acquired pneumonia.

Material and Methods

The current study included sixty (60) patient suffering from acquired community pneumonia aged range between one year to larger than 6 years, gander (30) female and (30) male Childs with Cough, sputum production, Dyspnea, leukocytes count > 100000 / mm^3, positive sputum culture with more than 25 polymorphonuclear leukocyte for bacterial infection only with 10 squamous cells in field also chest radiography and ultrasonography. Male and female patients Childs diagnose by specialized physician in Al Zahara Teaching Hospitals in Najaf Provenance, during November 2020 – M arch 2021. The (30) control Child were selected from same hospital without suffering any of symptoms or criteria of acquired community pneumonia.

Blood samples

Three milliliters of venous blood were drawn from each patient and control using a disposable needle and plastic syringes. The blood was train into EDTA tube for estimated of total leukocyte and procalcitonin, The surm was suctioned after centrifugation at3000 pm for 15 min, divided into aliquots in epindroff tubes and stored at 20 c°.

Total white blood cell count

According to this question, a blood cells counter and Turks fluid were used to determine the total leucocyte count by microscope:
Total Leucocytes count /mm3 = The count cells ×50

Determination presepsin concentration

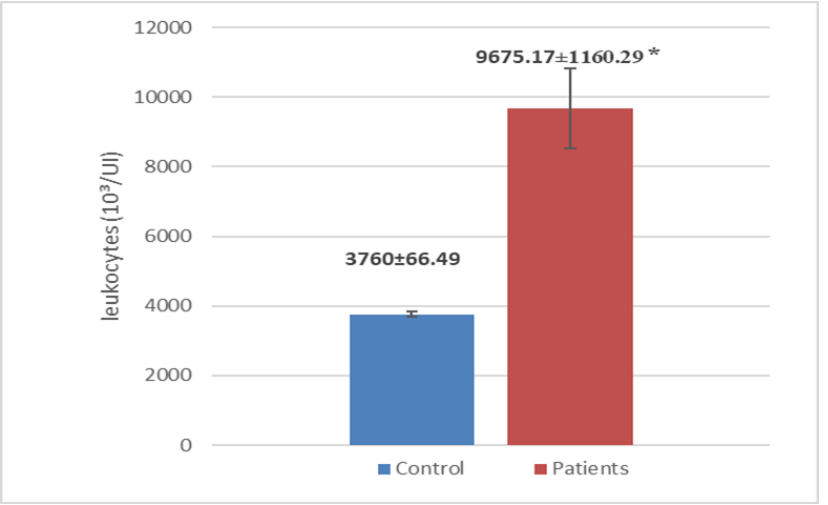
Presepsin concentrations in the serum of patients and control was examined by using ELISA according to prepare processed from Bioassy Technology Lbaratory, China-Cat-No. E3754Hu.

Statistical analysis

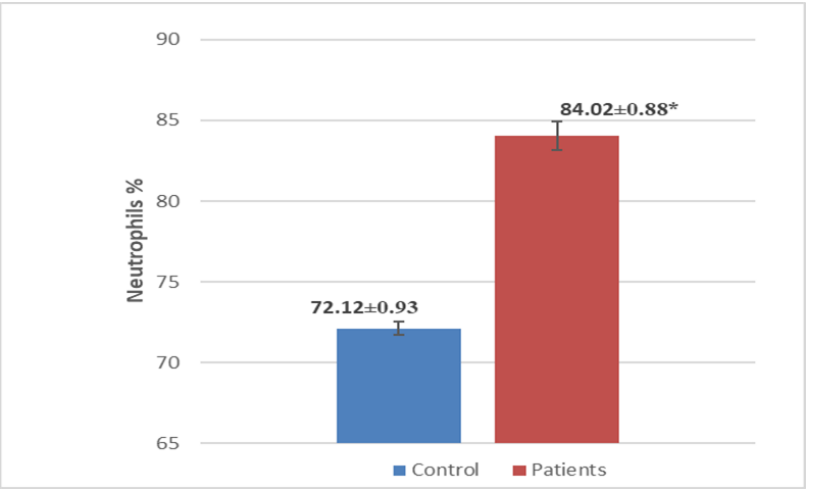
All values were expressed as means ± standard Error (SE). The computerized SPSS application was used to examine the data. Student's t-test was used to investigate differences between and within groups. Firstly a comparisons between patients and control was done by using un paired t-test. The unpaired t-test and ANOVA test were used to make comparisons between and within patient groups. A statistically significant p value < 0.001.

Result
Comparison of hematological parameters between patient and control

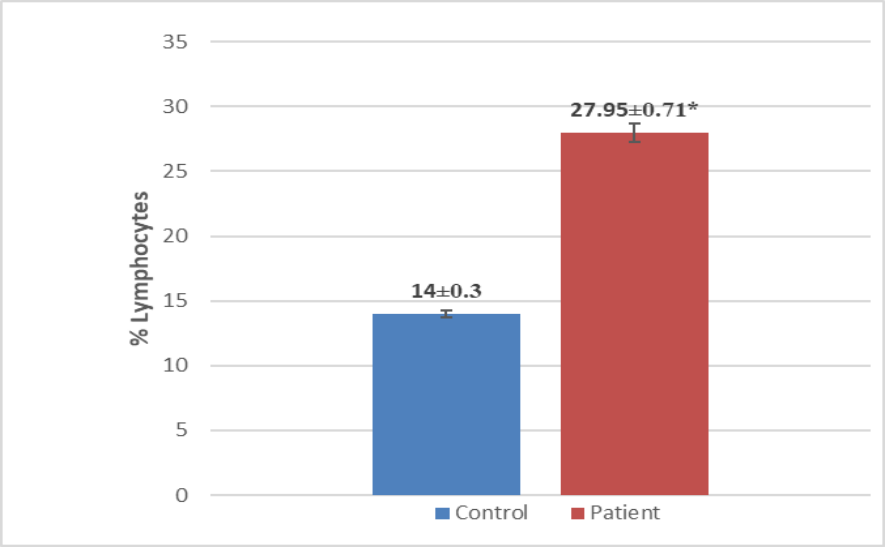
The result in figures (1,2, 3, 4) exhibit a significant elevation ($p<0.05$) in Total Leukocytes count, Neutrophils, Monocytes (%), Platelets (10^9/ L) Neutrophils (%) ,lymphocytes (%) and lymphocytes(10^9/L) in Pneumonia patients group in comparison with control group respectively.



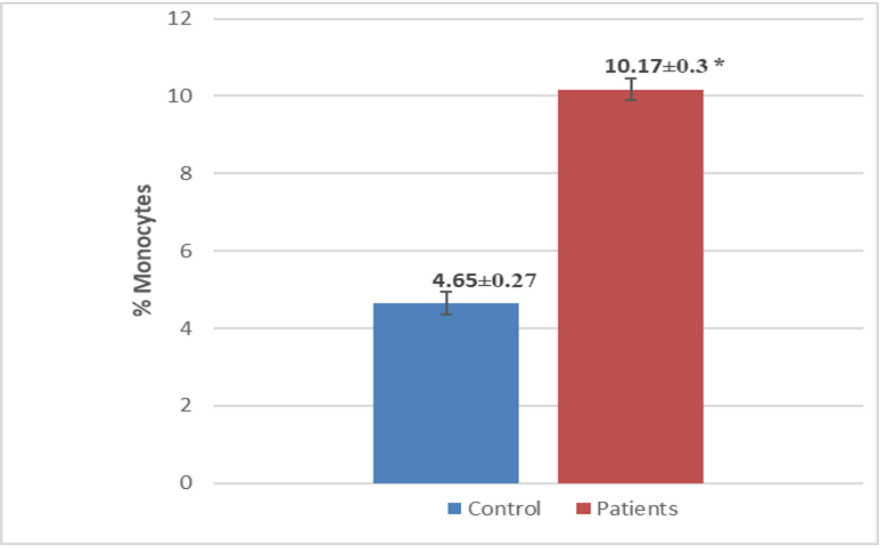
(*): Statistically significant differences ($p<0.05$) mean± stander Error
(Fig. 1): Total Leukocytes count in healthy controls and Pneumonia patients group



(*): Statistically significant differences ($p<0.05$) mean± stander Error
(Fig. 2): Comparison of Neutrophils between healthy controls and Pneumonia patients group



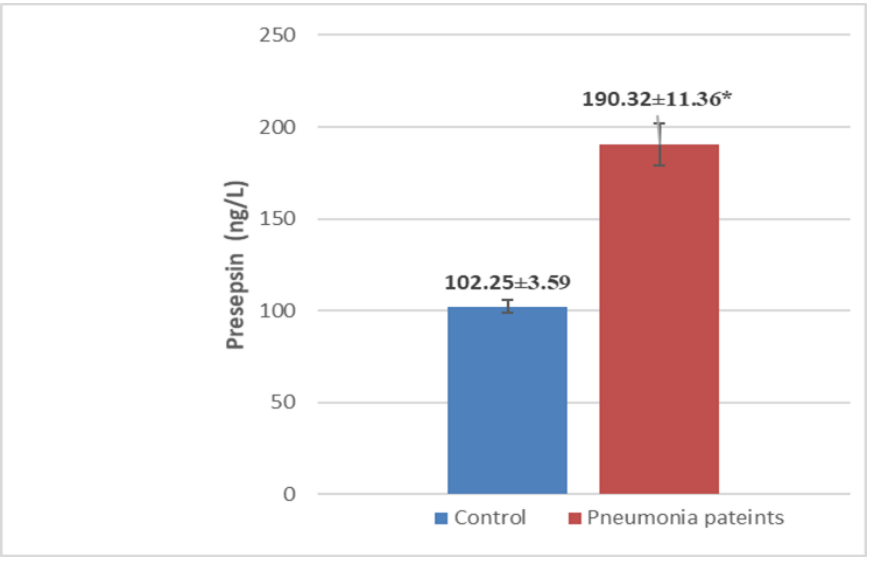
(*): Statistically significant differences (p<0.05) mean± stander Error
(Fig. 3): Distribution of Lymphocytes % in healthy controls and Pneumonia patients group



(*): Statistically significant differences (p<0.) mean± stander Error
(Fig. 4): Distribution of Monocytes (%) in healthy controls and Pneumonia patients group

Compere chemical presepsin biomarker between pneumonia patient and control group

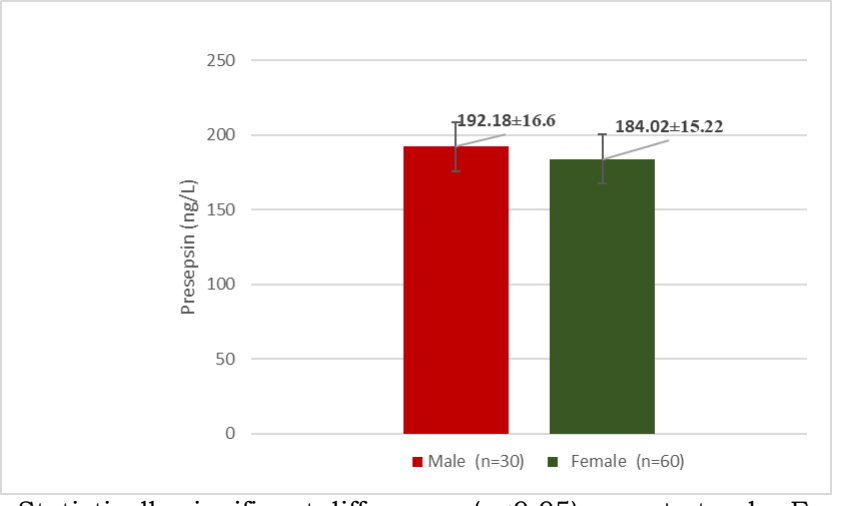
The results in figures (5) showed a significant increment (p<0.05) in chemical biomarker presepsin in pneumonia patient group in comparison with control group.



(*): Statistically significant differences (p<0.05) mean± stander Error
(Fig. 5) Comparison of serum presepsin level between pneumonia patient and control group

Estimation of presepsin biomarker in pneumonia child patients according to gander

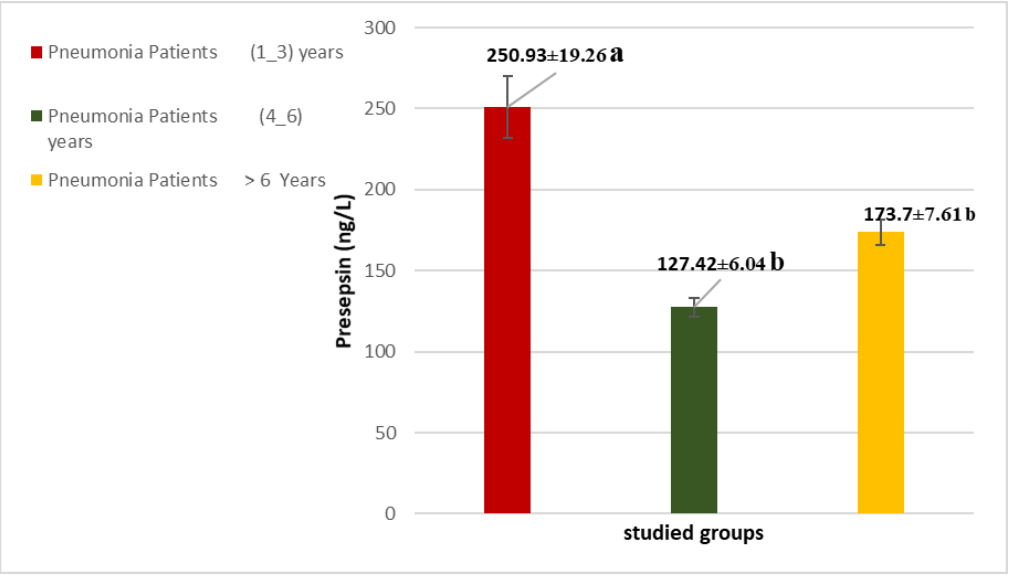
The result in figures (6) showed non significant (p>0.05) different in biomarker presepsin level between female and male pneumonia child patients respectively.



(*): Statistically significant differences (p<0.05) mean± stander Error
(Fig. 6) Comparison of serum presepsin level between male and female pneumonia patient

Estimation of presepsin biochemical markers in pneumonia child patient according to age

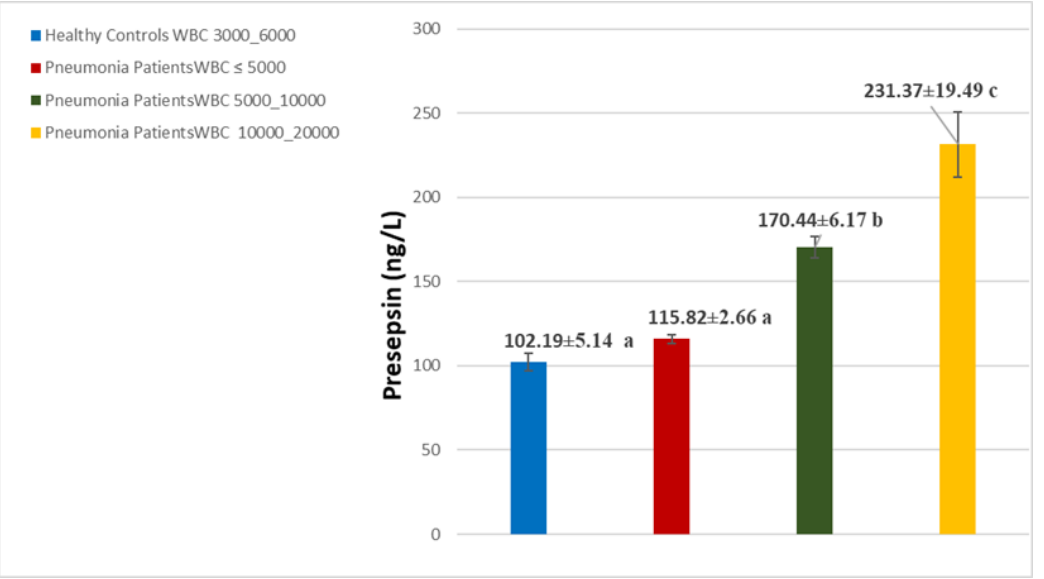
The results in figure (7) showed significant increment (p <0.05) in serum presepsin level of pneumonia child patient among the age (1-3 y) in comparison with among the ages (4-6 y) and (>6y) of pneumonia child patient .And there is no significant (p>0.05) different in presepsin between the ages (4-6y) when compare with ages (>6y).



The different letters mean significant differences (p<0.05) mean± stander Error
(Fig. 7) Comparison of serum presepsin level in pneumonia child patient at different age

Estimation of presepsin biochemical markers in pneumonia child patient and control group according to total count of leukocytes

The results of figure (8) indicate there is a significant increase (p<0.05) in serum presepsin at leukocyte count (5000-10000) and (10000-20000) of pneumonia child patient as compare with control group. And there is no significant (p> 0.05) different in presepsin at leukocyte count ≤5000 of pneumonia child patient as compare with control group.



The different letters mean significant differences ($p<0.05$) mean± stander Error
(Fig. 8) Comparison of serum presepsin level in pneumonia child patient and control group according to total of leukocytes

Discussion

Community Acquired Pneumonia (CAP) is the biggest cause of mortality in children under five years old. In 2015, WHO projected that 920136 children died of CAP, accounting for 16% of all deaths in children under the age of five (Jain *et al* ., 2018). Many bacteria, viruses, and their combinations can cause this infection, but most agents lack quick and commercially available diagnostic tests, which may explain why the etiology is rarely detected in clinical practice and why antibiotic therapy is mostly empirical in the majority of cases. Approximately 60 percent of the cases are viral infections, therefore unnecessary and ineffective antibiotic therapy may be given (Kartal *et al.*, 2017). Rapid detection and treatment of systemic bacterial infections in children is critical. Indeed, delaying treatment of severe bacterial infections can have negative consequences. When it comes to treatment options, It is critical to distinguish between a serious bacterial illness and a minor bacterial or viral infection (Don *et al.*, 2007).

The result indicated significant increase in total leukocyte count in CAP patients, and this is consistent with prior research showing that neutrophil, lymphocyte, monocyte, and platelet levels play an important role in systemic inflammation and infection, and that they are massively increased in CAP, implying that they can be used as predictors of CAP's presence (Adler-Shohet *et al.*, 1998).

Infections (particularly sepsis), trauma, a poor diet, physiologic stress, or even chronic psychological stress can cause a significant increase in total leukocyte count. Despite previous research indicating that a high leukocyte count may be a true sign of chronic systemic inflammation and subclinical diseases (Leli *et al.*, 2016).

The result also indicated significant increase in Presepsin in CAP patients as compare with control group. for more clarity, Presepsin is the 13 KDa N-terminal fragment of soluble form of CD14, which is cleaved by cathepsin D in plasma and involved in activating the innate immune system (P-SEP), a subtype of CD14 (sCD14-ST) (Memar *et al* ., 2017). Previous research, particularly in the last decade, has demonstrated rises during and after the healing or effective treatment of bacterial infections (Iskandar *et al.*, 2019), so P-SEP is regarded as a novel biomarker beneficial for detecting various types of infections at an early stage (Yokose *et al.*, 2021).
P-SEP has been studied for its diagnostic and prognostic value in a variety of pediatric illnesses, including early (EOS) and late (LOS) onset sepsis in preterm infants, including meningitis and pneumonia, as well as infections in febrile neutropenic patients with onco-hematological neoplasms (Ham *et al* .,2019).

According to previous research, presepsin levels rise in direct proportion to the severity of infection (Hayashi *et al.*, 2017). In another report, presepsin levels were discovered to be an independent predictor of severity, and when combined with traditional severity grading systems, presepsin levels increased their potential to detect more severe disease status and mortality, particularly in CAP patients (Arai *et al* .,2015).

No different in presepsin level between female and male of current study may be explained by presence of similar immune system in both male and females that activate macrophage also all biomarkers to resist of bacterial infection also hormonal system were not developed so the concentration of testosterone and estrogen at low level to contribute a differences between two gender in addition to same exposure to risk and environmental factor also bacterial infection.

The current study showed increase of presepsin at early age, because the translocation of intestinal microbial flora influences P-SEP, several pathophysiological factors, such as age (newborns and the elderly), are significant in the formation of highly P-SEP (Qi *et al* ., 2018).

Plasmatic PSP levels have been demonstrated to rise in response to bacterial infection and to decline following antibiotic therapy, therefore it can be regarded a marker of immune cell activation in reaction to an invading pathogen. When PSPs are secreted, monocytes can phagocytose them (Klouche *et al.*, 2016). Community-acquired pneumonia (CAP) is commonly caused by bacteria, however culture detection of bacteria from blood and sputum takes several days and leads in a significant proportion of false – negative results (Munger *et al* ., 2015). Bacterial CAP was successfully diagnosed and prognosticated using plasmatic PSP levels (BCAP) (Sato *et al.*, 2016).

The results indicate there was significant increase in serum presepsin at leukocyte count (5000-10000) and (10000-20000) of pneumonia child patient as compare with control group. It was discovered that CD14, a presepsin substrate, is a glycoprotein that is formed in a glycosylphosphatidylinositol (GPI)-anchored membrane form on the membrane surfaces of innate immune response cells related to monocytes (mCD14) (Unay-Demirel *et al* ., 2020). After binding to the LPS/LPS-binding protein (LBP) complex, CD14 has been shown to be involved in

the recognition of a wide range of bacterial products, it activates the toll-like receptor (TLR) 4-specific pro-inflammatory signaling, by the LPS/LBP-CD14 complex, when the cell membrane sheds its CD14, allowing soluble CD14 to be released into the bloodstream (sCD14), and these events are linked to immune cell activation, particularly monocyte (Ciesielska *et al* ., 2021) .

One experiment in rabbits found that granulocytes were the predominant source of presepsin. The requirement for presepsin secretion was demonstrated by the rabbit cecal ligation and puncture (CLP) sepsis model and an in vitro study using rabbit peritoneal granulocytes, which play a role in granulocyte phagocytosis rather than inflammatory stimuli (Unay-Demirel *et al* ., 2020).

In humans, phagocytosis by monocytes was discovered to be the initial stimulation that induced presepsin production. Induced by a variety of microorganisms as well as sterile phagocytic stimuli such as Monosodium urate (MSU) crystals (Ciesielska *et al.*, 2021).

Conclusions

1. Highly level of presepsin in pneumonia child patient related with inflammation represented by high leukocytes count in comparison with healthy child.
2. Presepsin in present study related with younger age than other without dependent on gander

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