Med. J. Cairo Univ., Vol. 90, No. 3, June: 755-769, 2022
www.medicaljournalofcairouniversity.net

Predictive Value of Serum Copeptin as a Severity Marker of Community-Acquired Pneumonia in Pediatrics

MAHMOUD MOHAMED FOUAD, M.B.B.CH.*; EMAN MAHMOUD FOUDA, M.D.*;
EMAN ABDEL-MONIEM EL-GOHARY, M.D.** and HEBA ALLAH AHMED ALI, M.D.*

The Departments of Pediatrics and Clinical Pharmacy**, Faculty of Medicine, Ain Shams University*

Abstract

Background: Community-acquired pneumonia is the most severe form of acute respiratory infections.

Aim of Study: This study aimed to assess the role of copeptin as an early predictor of severity of community-acquired pneumonia in children.

Patients and Methods: A case-control study was conducted on 53 children with community acquired pneumonia and another 40 children as controls with their gestational age, sex and weight matched, admitted to pediatric clinics from January 2021 to the end of December 2021. Blood samples for copeptin and procalcitonin were drawn and sent for analysis. Imaging techniques as X-ray, computed topography and ultrasound were used to assess the diagnosis of pneumonia.

Results: Blood levels of copeptin in children with pneumonia with a median of 65pmol/L were much higher than copeptin levels in controls with a median of 0.65pmol/L (P-value <0.001). Pneumonia complications were reported in 27 (50.9%) children. Higher severity scores as PRESS score, repertory illness score, bacterial pneumonia score, and PIRO score were reported in children with complicated pneumonia. Serum higher levels of copeptin and procalcitonin were reported in children with pneumonia compared to the control groups (*p*-value <0.001).

Conclusion: Serum blood levels of copeptin might be used as a diagnostic and prognostic biomarker for community-acquired pneumonia.

Key Words: *Community-acquired pneumonia – CAP – Copeptin – Procalcitonin.*

Introduction

COMMUNITY-acquired pneumonia (CAP) in childhood is defined as an acute infection of the pulmonary parenchyma in a child caused by a pathogen acquired as distinguished from hospital-acquired (nosocomial) pneumonia. CAP is a common and potentially serious illness with considerable morbidity [1].

Pneumonia has been the leading cause of death in children younger than 5 years for decades. Although there have been substantial decreases in overall child mortality and in pneumonia-specific mortality, pneumonia remains the major single cause of death in children outside the neonatal period, causing approximately 900,000 of the estimated 6.3 million child deaths in 2013 [2].

Substantial advances have occurred in the understanding of risk factors and etiology of pneumonia, in development of standardized case definitions, and in prevention with the production of improved vaccines and in treatment. Such advances have led to changes in the epidemiology, etiology and mortality from childhood pneumonia. However in many areas access to these interventions remains sub-optimal, with large inequities between and within countries and regions [3].

Copeptin is the c-terminal part of pre–provasopressin (pre-pro AVP) which is stored in neurohypophyseal vesicles together with AVP until they are secreted circulation in response to inflammation or hemodynamics changes [4].

Copeptin was reported to increase in CAP and due to its high negative predictive value (NPV), copeptin may help in identifying patients with low risk of death [5].

Early recognition of severe forms of CAP is vital for early hospitalization and appropriate treatment of the patients. The clinical status, oxygen saturation, and comorbidity mainly determine the need for hospitalization, while certain laboratory parameters can also facilitate the assessment of the severity of the disease [6].

Correspondence to: Dr. Mahmoud M. Fouad,
The Department of Pediatrics, Faculty of Medicine,
Ain Shams University

So in this study, we aimed to measure the serum copeptin levels in the patients with community acquired pneumonia to evaluate the relationship of serum copeptin levels with disease severity.

Patients and Methods

This was a prospective case-control study conducted on 53 children with a proven diagnosis of CAP and 40 children as controls who were admitted to pediatric clinics from January 2021 to the end of December 2021. The gestational age, sex and weight were matched between both groups. The children with CAP were categorized further into two groups based on the complications of CAP by clinical symptoms, signs, and imaging investigations as CT, US, and X-ray. This study was approved by an Ethical committee and a written consent was obtained from the parents and children aged more than 8 years prior to inclusion in the study.

Our inclusion criteria for CAP group were children admitted to the outpatient clinics and met the diagnostic criteria of CAP which are: The clinical findings of fever, cough, respiratory distress (e.g., tachypnea, intercostal/subcostal/suprasternal retractions, nasal flaring, grunting), and/or radiologic evidence of an acute pulmonary infiltrate/ consolidation. We excluded every children who had any major systemic illness such as chronic heart failure, chronic renal failure or other systemic diseases, or any immunodeficiency disorders such as severe combined immunodeficiency diseases or phagocytic defect diseases.

Both groups included in our study were subjected to full detailed history as follows: Personal history, social class, and family history. Besides a clinical examination included baseline data such as gender, gestational age, vital signs, and birth weight as well as any relative clinical findings. We used pneumonia severity scores as pediatric respiratory severity score (PRESS), respiratory illness score (PIS), PIRO score, and bacterial pneumonia score to outline the severity degree of pneumonia.

Regarding the investigations, blood samples were withdraw from children after delivery under complete aseptic condition. Routine lab investigations such as complete blood count (CBC), liver function, kidney function, random blood glucose, and arterial blood gases. The separation of serum blood samples of copeptin and procalcitonin were conducted by centrifuging the samples at 2000-3000 r.p.m for 10min then the samples were frozen at –20° C for further analysis.

Statistical analysis:

The data were coded, collected on an Excel sheet, and processed using SPSS 20 (Armonk, NY/USA). Descriptive statistics were represented by percent (%), and number (N). Mean, standard deviation (SD), range, minimum and maximum, and median were all used to describe quantitative data.

Chi-square test (χ^2): Was used to study the relation between two categorical variables. One-way analysis of variance (ANOVA) or (F test) was used to find any significant difference between different groups with a normally distributed quantitative variable, as well as comparison between pneumonia severities. A post hoc test with the least significant difference (LSD) was performed. For pairwise comparisons, Mann Whitney U test and Kruskual-Wallis (which are a non-parametric test of significance) was used to compare between two groups having quantitative variables but not normally distributed.

Receiver operating characteristic (ROC) curves were established to assess the sensitivity and specificity of parameters assessed by using SPSS. We used the combination of highest sensitivity and specificity which were determined at the apex of the ROC curve as the chosen clinical values. An ideal curve of a reasonable test should contain a larger area under the ROC graph. The p-value <0.05 was considered the cut-off value for significance.

Results

93 children were included in our study and were allocated intro two groups; the first group (pneumonia group) consisted of 53 children who were diagnosed as HIE cases according the diagnostic criteria of pneumonia, and the second group (control group) consisted of 40 gestational age, weight and sex-matched children with no risk factors of pneumonia.

The median age of pneumonic children was 3 years while for the controls was 2 years with insignificant difference between them regarding all demographic data (Table 1).

Serum copeptin was significantly higher among pneumonic children with a median of 65pmol/L compared to the healthy controls with a median of 0.65pmol/L ($p<0.001$) (Table 1).

We categorized pneumonic children into two subgroups; children with complicated pneumonia

as group A (50.9%), and children with uncomplicated pneumonia (49.1%) as group B. The complications reported in the current study were sepsis (32.1%), followed by pleural effusion (24.5%), and empyema (20.8%) (Table 2).

There was no significant difference between both two subgroups regarding baseline data except for socioeconomic level which was higher among children with uncomplicated pneumonia (p=0.026) (Table 3).

Table (1): Socio-demographic data and serum copeptin among the studied groups.

	Pneumonia group (53)	Control group (40)	p-value	Sig.
Age (years):				
Median (IQR)	3 (1-4)	2 (0.75-3)	0.0731 *	NS
Gender:				
Female	19 (47.5%)	19 (35.8%)	0.260**	NS
Male	34 (64.2%)	21 (52.5.2%)		
Consanguity:				
+ve	20 (50%)	17 (32.1%)	0.082**	NS
Residency:				
Rural	16 (40%)	24 (45.3%)	0.612**	NS
Urban	24 (60%)	29 (54.7%)		
Socioeconomic score (Gilany score):				
Median (IQR)	43.5 (30-47)	45 (30-49.5)	0.467*	NS
Serum copeptin (pmol/L):				
Median (IQR)	65 (36.7-81)	0.65 (0.6-0.8)	<0.001 *	HS

IQR: Inter-quartile range. HS: Highly significant.
S : Significant. *Mann-Whitney's U test.
NS : Non-significant. **Chi square test.

Table (2): Etiology of complications among patients with complicated pneumonia.

Complicated pneumonia	27 (50.9%)
Sepsis	17 (32.1%)
Pleural effusion	14 (24.5%)
Empyema	11 (20.8%)
Hydro-pneumothorax	6 (11.3%)
Respiratory failure	6 (11.3%)
Lung abscess	2 (3.8%)
Myocarditis	1 (1.9%)

Table (3): Basic characteristics among the studied patient groups.

Socio-demographic data	Complicated pneumonia group (A) (27)	Un-complicated pneumonia group (B) (26)	p-value	Sig.
Age (years):				
Median (IQR)	3 (0.77-4)	3 (1-4)	0.512*	NS
Gender:				
Female	12 (44.4%)	7 (26.9%)	0.187**	NS
Male	15 (55.6%)	19 (73.1%)		
Consanguity:				
+ve	11 (40.7%)	6 (23.1%)	0.172**	NS
Residency:				
Rural	11 (40.7%)	13 (50%)	0.502**	NS
Urban	16 (59.3%)	13 (50%)		
Socioeconomic score (Gilany score):				
Median (IQR)	42 (28.5-45)	45 (37.7-54)	0.026*	S
Weight (Kg):				
Median (IQR)	13 (10.1-16.3)	14 (10-17)	0.532*	NS
Height (cm):				
Median (IQR)	88 (74.5-106)	90.5 (75-108)	0.708*	NS
Body mass index:				
Median (IQR)	15 (13.7-16.2)	15 (13.7-18)	0.6820*	NS

Regarding symptoms and signs, we reported higher significant rates in terms of exercise intolerance (92.6% vs 57.5%) (p=0.003), weight loss (63% vs 15.4%) (p=0.005), and recurrent hospital admissions (56.6% vs 15.4%) (p=0.002) in complicated children compared to un-complicated children. We also reported a higher duration of illness before hospitalization with median of 7 days in complicated children compared to 3.5 days in un-complicated children (p=0.01). Also, we reported higher respiratory rates and lower O_2 saturation in children with complicated pneumonia (p>0.05) (Table 4).

Regarding severity scores, we reported higher rates of PRESS score, bacterial pneumonia score, PIRO severity score and PIS score in children with complicated pneumonia compared to the children with uncomplicated pneumonia (p<0.001) (Table 5).

Regarding routine lab investigations, lower levels of hemoglobin and lymphocytes along with higher rates of total leukocytic count and neutrophils were reported in children with complicated pneumonia compared to children with uncomplicated pneumonia (p<0.05) (Table 6).

In relation to clinical findings, we reported higher levels of copeptin (medians of 79 vs 37pmol/L, $p<0.001$); higher serum levels of procalcitonin (medians of 860 vs 485pg/ml, $p=0.02$) and higher median rates of C-reactive protein (52 vs 20mg/L, $p=0.004$) in children with complicated pneumonia compared to children with uncomplicated pneumonia (Table 7).

We assessed the correlations between serum copeptin and other parameters in which it revealed positive correlations between copeptin and PRESS severity score, PIRO severity score, duration of hospital stay, inflammatory markers as CRP and PCT ($p<0.05$). A negative correlations between copeptin and hemoglobin and lymphocytes were reported ($p<0.05$) (Table 8).

We assessed multiple regression analysis which showed a statistical significance of serum copeptin levels and other parameters ($p<0.05$) (Table 9).

The best cut-off point of serum copeptin for identifying complicated pneumonia was >65pmol/L, with a sensitivity and specificity of 81.48% and 84.62% respectively and are under curve of 0.858 ($p<0.001$). As regard procalcitonin, the best cut-off point for diagnosis of complicated pneumonia was >630pg/mL, with a sensitivity and specificity of 62.96% and 73.08% respectively and are under curve of 0.685 ($p<0.001$) (Table 10).

Table (4): The presenting symptoms and signs among the studied patients' groups.

		Complicated pneumonia group (A) (27)	Un-complicated pneumonia group (B) (26)	*p*-value	Sig.
Dyspnea	+ve	26 (96.3%)	21 (80.8%)	0.077**	NS
Exercise intolerance	+ve	25 (92.6%)	15 (57.7%)	0.003**	HS
Cough	Dry	13 (48.1%)	14 (53.8%)	0.682**	NS
	Productive	14 (51.9%)	12 (46.2%)		
Weight loss	+ve	17 (63%)	4 (15.4%)	0.005**	HS
Abdominal pain	+ve	13 (48.1%)	7 (26.9%)	0.144**	NS
Recurrent hospital admissions	+ve	15 (56.6%)	4 (15.4%)	0.002	HS
Duration of illness (days) before hospitalization	Median (IQR)	7 (4-9.7)	3.5 (3-5)	0.01*	S
General condition	Bad	25 (92.6%)	8 (30.8%)	<0.0001*	S
	Fair	2 (7.4%)	18 (69.2%)		
O2 Saturation (%)	Median (IQR)	91 (89-93)	95 (93-96)	<0.001*	S
Degree of fever (º)	Median (IQR)	39 (38-40)	38.5 (38-39.5)	0.296*	NS
Respiratory rate (breath/min)	Median (IQR)	40 (36-42)	35 (32-38)	0.009*	S
Dullness on percussion	+ve	13 (48.1%)	0 (0.0%)	<0.001**	HS
	Unilateral	13 (48.1%)	0 (0.0%)		
	Bilateral	0 (0.0%)	0 (0.0%)		
Diminished air entry	+ve	27 (100%)	26 (100%)	0.004**	HS
	Unilateral	19 (70.4%)	8 (30.8%)		
	Bilateral	8 (29.6%)	18 (69.2%)		
Fine crepitations	+ve	27 (100%)	26 (100%)	0.004**	HS
	Unilateral	19 (70.4%)	8 (30.8%)		
	Bilateral	8 (29.6%)	18 (69.2%)		
Bronchophony	+ve	27 (100%)	26 (100%)	0.009**	HS
	Unilateral	19 (70.4%)	9 (34.6%)		
	Bilateral	8 (29.6%)	17 (65.4%)		
Wheezes	Positive	12 (22.6%)	8 (15%)	0.396**	HS
	Unilateral	7 (25.9%)	3 (11.5%)		
	Bilateral	5 (18.5%)	5 (19.2%)		
Grades of respiratory distress (RD)	Positive RD	25 (92.5%)	21 (80.7%)	0.018	S
	RD I	7 (25.9%)	15 (57.7%)	0.018	
	RD II	9 (33.3%)	4 (15.4%)	0.128	NS
	RD III	3 (11.1%)	1 (3.8%)	0.316	BS
	RD IV	6 (22.2%)	1 (3.8%)	0.048	S

S: Significant. NS: Non-significant. HS: Highly significant. *Mann-Whitney's U test. **Chi square test.

Table (5): Comparison between the studied patients groups regarding the clinical severity scores.

Clinical severity scores	Complicated pneumonia group (A) (27)	Un-complicated pneumonia group (B) (26)	*p*-value	Sig.
	Median (IQR)	Median (IQR)		
PRESS score:	4 (3-4)	2 (1-3)	<0.001 *	HS
Mild (<2)	0 (0%)	9 (34.6%)		
Moderate (2-3)	11 (40.7%)	13 (50%)	0.003 *	HS
Severe (4-5)	16 (59.3%)	4 (15.4%)		
Respiratory illness score:	7 (5-8)	4 (2-4)	<0.001 *	HS
Mild (<4)	1 (3.7%)	10 (38.5%)		
Moderate (4-7)	16 (59.3%)	13 (50%)	0.003 *	HS
Severe (8-12)	10 (37%)	3 (11.5%)		
Bacterial pneumonia score:	8 (3.2-10)	3.5 (3-7)	0.006*	HS
Bacterial (>=4)	20 (74.1 %)	12 (46.2%)		
Non-bacterial (<4)	7 (25.9%)	14 (53.8%)	0.039*	S
PIRO score:	4 (3-5)	2 (1-3)	<0.001 *	HS
Low	1 (3.7%)	19 (73.1%)		
Moderate	18 (66.7%)	5 (19.2%)		
High	6 (22.2%)	1 (3.8%)	<0.001 *	HS
Very high	2 (7.4%)	1 (3.8%)		

S: Significant. NS: Non-significant. HS: Highly significant. *Mann-Whitney's U test.

Table (6): Comparison between the complicated, uncomplicated pneumonia groups regarding the laboratory data.

Laboratory data	Complicated pneumonia group (A) (27)	Un-complicated pneumonia group (B) (26)	*p*-value	Sig.
	Median (IQR)	Median (IQR)		
CBC:				
Hemoglobin (g/dL)	10.2 (9.4-12.2)	12 (10.6-12.9)	0.011 *	S
Mean corpuscular volume (fl)	74 (62-76.7)	75.5 (70-77)	0.292*	NS
Mean corpuscular hemoglobin (pg)	24 (23-26)	26 (24-27.8)	0.093 *	NS
Red cell distribution width (%)	15 (13-19)	14.5 (13-17)	0.452*	NS
Platelets (103/μL)	380 (249-516)	286.5 (250-350)	0.165*	NS
Total leucocytic count (103/μL)	16 (11.3-22.6)	10.5 (8-15)	0.002*	HS
Neutrophils (%)	60 (52.7-70)	55 (40-60)	0.032*	S
Lymphocyte (%)	30 (20-49.2)	34 (28-55)	0.049*	S
Routine tests:				
Urea (mg/dL)	22 (18-37)	21 (15-39)	0.470*	NS
Creatinine (mg/dL)	0.5 (0.3-0.6)	0.5 (0.4-0.8)	0.780*	NS
Alanine transaminase (U/L)	27 (22.2-43.7)	25 (20-35)	0.367*	NS
Aspartate transaminase (U/L)	22 (18-35)	22.5 (18-30)	0.865*	NS
Blood culture:				
Psoitive	9 (17%)	0 (0%)	0.001 **	HS
Streptococcus pneumonae	4 (7.5%)	0 (0%)		
Staphylococcus aureus	2 (3.7%)	0 (0%)		
Klebsiella	2 (3.7%)	0 (0%)		
Pseudomonas	1 (1.8%)	0 (0%)		

S: Significant. NS: Non-significant. HS: Highly significant. *Mann-Whitney's U test. **Chi square test.

Table (7): Comparison between complicated and uncomplicated pneumonia groups regarding the inflammatory markers.

Inflammatory markers	Complicated pneumonia group (A) (27)	Un-complicated pneumonia group (B) (26)	*p*-value	Sig.
	Median (IQR)	Median (IQR)		
Neutrophilia (%)	21 (77.8%)	10 (38.5%)	0.004*	HS
C-reactive protein, median (IQR)	52 (14.5-124.6)	20 (10-30)	0.013 *	S
Serum procalcitonin median (IQR):				
Normal (up to 500 pg/ml)	860 (452.5-1032.5)	485 (300-660)	0.02*	S
Serum copeptin:				
Normal (0.2-8 pmol/L)	79 (73.2-81.5)	37 (28-57)	<0.001 *	S

S: Significant. NS: Non-significant. HS: Highly significant. **Chi square test. *Mann-Whitney's U test.

Table (8): Spearman's correlation analysis for the study variables associated with serum copeptin level.

Associated factor	Serum copeptin level		
	r	*p*-value	Sig.
Clinical data:			
Age (years)	0.174	0.096	NS
Socioeconomic score (Gilany score)	–0.075	0.475	NS
Duration of illness (days)	0.253	0.067	NS
Weight (Kg)	0.111	0.429	NS
Height (cm)	0.086	0.538	NS
BMI	0.052	0.718	NS
Degree of fever (º)	0.259	0.061	NS
O^2 Saturation (%)	–0.556	<0.001 * *	S
Respiratory rate (breath/min)	0.212	0.139	NS
PRESS score	0.651	<0.001 * *	S
Respiratory illness score	0.647	<0.001 * *	S
Bacterial pneumonia score	0.401	0.003 * *	S
PIRO score	0.614	<0.001 * *	S
Laboratory data:			
Hemoglobin (g/dL)	–0.291	0.034*	S
Mean corpuscular volume (fl)	–0.0399	0.778	NS
Mean corpuscular hemoglobin (pg)	–0.206	0.1383	NS
Red cell distribution width (%)	0.156	0.265	NS
Platelets (103/μL)	0.183	0.189	NS
Total leucocytic count (103/μL)	0.408	0.004* *	S
Lymphocyte (%)	–0.353	0.009**	S
Neutrophils (%)	0.317	0.02*	S
pH	–0.398	0.003 * *	S
C-reactive protein (mg/dL)	0.338	0.013*	S
Serum procalcitonin (pg/ml)	0.394	0.035**	S
Outcome data:			
Hospital stay (days)	0.752	<0.001 * *	S
ICU days	0.191	0.353	NS

r: Spearman's rho (correlation coefficient).

Table (9): Multiple regression model for the variables affecting serum copeptin level using forward method.

	Unstandardized coefficients		Standardized coefficients	*t*	*p*-value	Sig.
	B	SE	Beta			
(Constant)	3.671	6.628				
PRESS score	9.767	2.176	0.515	4.488	<0.001	S
Serum procalcitonin (pg/ml)	0.021	0.007	0.274	3.076	0.003	S
Hospital stay (days)	1.366	0.605	0.267	2.259	0.028	S
Total leucocytic count	1.330	0.290	0.271	3.074	0.003	S

Table (10): ROC-curve to predict patients with complicated pneumonia.

Variables	Cut off point	AUC	Sensitivity	Specificity	+PV	–PV	*p*-value
Serum copeptin (pmol/L)	>65	0.858	81.48	84.62	84.6	81.5	<0.001
Serum procalcitonin (pg/ml)	>630	0.685	62.96	73.08	70.8	65.5	0.012

ROC = Receiver operating characteristic. AUC = Area under curve. SE = Standard error.

Discussion

The present study was conducted on 93 children who were categorized into two groups; 53 children with CAP and 40 children as controls in which the median age of pneumonic children was 3 years (IQR: 1-4 years); while for the controls was 2 years (IQR: 0.75-3 years) with insignificant difference between them regarding all demographic data ($p>0.05$).

In the current study, serum copeptin was significantly higher among pneumonic children with a median of 65pmol/L (IQR: 36.7-81) compared to the healthy controls with a median of 0.65pmol/L (IQR: 0.5-0.8) ($p<0.001$).

These findings come in alignment with a study conducted by Mohamed et al., [7] who found that serum concentration of copeptin was significantly elevated in pneumonic children compared to controls ($p=0.001$). Moreover, Abel-Fattah et al., [8] reported higher levels of copeptin in patients with pneumonia compared to controls (31.2 vs 25.3pg/mL; $p=0.03$).

Higher levels of serum copeptin in pneumonic children indicates a significant association between elevated copeptin level and the pathogenesis of CAP.

In the current study, we categorized pneumonic children into two subgroups; children with complicated pneumonia as group A (50.9%), and children with uncomplicated pneumonia (49.1 %) as group B. The complications reported in the current study were sepsis (32.1 %), followed by pleural effusion (24.5%), and empyema (20.8%).

This result come in accordance with a previous study conducted Qin and Shen, [9] who reported that the complications of bacterial pneumonia included pleural effusion, empyema, pneumatoceles, necrotizing pneumonia, and lung abscesses.

Compared to our results, a recent study conducted by Alcoba et al., [10] including 88 children with CAP which reported that only (12.5%) of the studied patients presented with complicated CAP as follows: Empyema (10.2%), and bacteremia (4.5%), and 2 children had both complications.

The higher prevalence of complicated pneumonia among the studied patients compared to other studies could be attributed to the low socioeconomic level, delayed diagnosis and lack of proper management which led to this higher percentage of complications.

Our results found no statistical difference between children with complicated pneumonia (median age=3 years) and un-complicated ones (median age=3 years) in terms of age ($p=0.512$).

On the same hand, a study by Musolino et al., [11] reported a non-significant difference between children with complicated pneumonia with a median age of 57 months (IQR: 16-162.5) when compared to children with uncomplicated pneumonia with a median of 44 months (IQR: 20-70).

This finding also come in alignment with a study by Elemraid et al., [12] who found that the age was similar between children with empyema and those with pneumonia only. On the other hand, a study by Masarweh et al., (2021) [13] found that children with complicated pneumonia were older than un-complicated ones; a possible explanation is that younger children with pneumonia are more likely to be hospitalized even with a mild clinical course.

Also a study by Du et al., [14] reported a significant difference of age between complicated and un-complicated children in which complications were much among lower age group (8 months vs 32 months).

The varying contribution of age to complicated pneumonia may be related to different populations, lower rates of vaccination, smaller sample size, and variable definition of complications or intervention criteria [13].

In the current study, the socioeconomic status using Gilani score was significantly higher among children with uncomplicated pneumonia (median= 45) compared to complicated ones (median=42) (p=0.026) suggesting that low socioeconomic levels may increase the potential of the complications of pneumonia.

This result come in accordance with a study conducted by Azab et al., (2014) [15] who found that lower socioeconomic level, a young maternal age, a low maternal education level, parents' smoking habits, rural residency, a low family income, and unavailability of adequate medical care were significantly associated with the risk of severe complicated community acquired pneumonia (all p<0.01) when compared to mild community acquired pneumonia.

In the current study, we investigated symptoms and signs between patient's subgroups. We reported a higher significant rate in terms of exercise intolerance (92.6% vs 57.5%) (p=0.003), weight loss (63% vs 15.4%) (p=0.005), and recurrent hospital admissions (56.6% vs 15.4%) (p=0.002) in complicated children compared to un-complicated children. We also reported a higher duration of illness before hospitalization with median of 7 days in complicated children compared to 3.5 days in un-complicated children (p=0.01).

These findings come in accordance with a study Huysentruyt et al., [16] by who found a reduction in weight and recurrent hospital admissions in children with complicated pneumonia with pleural effusion or empyema.

On the contrary, Musolino et al., [11] reported non-significant difference between complicated and un-complicated in term of duration of illness before emergency department admission (4 vs 3 days).

Most of our children with complicated pneumonia were not severe cases, so the median duration of illness before hospitalization was higher than that reported by Musolino et al., [11].

Moreover, majority of children with complicated pneumonia showed bad general condition (92.6%) when compared to children with uncomplicated pneumonia who showed (30.8%) as bad general condition (p<0.001).

This finding come in accordance with a study by Buonsenso et al., [17] who found that there was a significantly higher rate of consolidation (52.2%) in children with complicated pneumonia having a surgical procedure when compared to children with uncomplicated pneumonia (10.2%) suggesting a bad general condition in children with complicated pneumonia.

Regarding O_2 saturation, children with uncomplicated pneumonia showed higher rates with median of 95% compared to complicated ones with a median of 91% (p<0.001). Respiratory rate was significantly higher in children with complicated pneumonia with a median of 40 breath/min compared to uncomplicated ones with a median of 35 breath/min (p=0.009).

These results come in accordance with a study by Masarweh et al., [13] who found that O_2 saturation was higher in un-complicated children with a mean of 91.94% compared to complicated children with a mean of 90.15%.

Another study by Pabary et al., [18] who reported that respiratory rate was reported to be <50 breath/min in children with complicated pneumonia.

On the other hand, Musolino et al., [11] reported a lower oxygen saturation in children with complicated pneumonia with a mean of 96.5% compared to children with uncomplicated pneumonia with a mean of 97.3%, however the result was insignificant (p>0.05).

In the current study, several clinical severity scores were compared between children with complicated pneumonia and un-complicated ones, where PRESS score was severe among (59.3%) of

complicated pneumonia compared to (15.4%) of un-complicated children with a significant statistical difference (p=0.003).

In complicated pneumonic group, the prevalence of bacterial pneumonia score was (74.1%) compared to uncomplicated group (46.25%) with a statistical significance (p=0.03).

Our study revealed that a higher PIRO score was significantly observed among children with complicated pneumonia with a median of 4 compared to un-complicated children with a median of 2. Moreover, the majority of PIRO scores was moderate to severe in complicated children (88.9%) compared to un-complicated ones (23%) (p<0.001).

This result comes in accordance with a study conducted by Araya et al., (2016) **[19]** who reported that higher PIRO scores were associated with children with complicated pneumonia and admitted to hospital (p<0.001).

To our knowledge, we are the first to mention severity scores of pneumonia between complicated and un-complicated children, so further studies should be applied to confirm the diagnostic abilities of such scores.

In the current study, we reported lower levels of hemoglobin in complicated children (10.2g/dL) compared to uncomplicated children (12g/dL). Regarding total leukocytic count, we reported higher total leukocytic count in complicated children with a median of 16 (IQR: 11.3-22.6) compared to uncomplicated children with a median of 10.5 (IQR: 8-15) (p=0.002).

Also, lower levels of lymphocytes were associated with complicated children (30%) compared to uncomplicated (34%). Additionally, higher levels of neutrophils were detected in complicated children (60%) compared to uncomplicated ones (55%).

On the same hand, Mohamed et al., **[7]** reported lower levels of Hb in pneumonic children when compared to controls, and much lower Hb levels in complicated children compared to uncomplicated ones, they also reported a significantly increased total leukocytic count (p=0.001).

Our results are in agreement with another study conducted by Sheb et al., **[20]** whofound that Hb count was much lower in severe children with complicated pneumonia (median=9, IQR: 8.5-9.5) compared to uncomplicated children (median= 10, IQR: 9-10.5). Also, they reported higher total leukocytic count in severe complicated children with a median of 14 (IQR: 13-15) compared to uncomplicated with a median of 13 (IQR: 11-13).

On the contrary, Masarweh et al., **[13]** reported that the total leukocytic count did not differ in both complicated and uncomplicated pneumonia groups.

Lower rates of Hb and total leukocytic count were attributed to the severe infection caused by S. pneumoniae in children with complicated pneumonia compared to the less severe infection caused by viral pneumonia in children with uncomplicated pneumonia.

In the current study, we reported higher serum levels of copeptin (79 vs 37pmol/L, p<0.001) in children with complicated pneumonia compared to children with uncomplicated pneumonia.

Our findings coincide with previous studies conducted by Du et al., **[14]**, Mohamed et al., **[7]** who reported thathigher levels of serum copeptin were also in association with CAP-related complications compared to uncomplicated children (p=0.001).

On the same hand, another study conducted by Sheb et al., **[20]** reported higher levels of serum copeptin in severe complicated children with medians of 5.6 compared to uncomplicated children with medians of 0.97 (p<0.001).

On the contrary, Alcoba et al., **[10]** found that serum copeptin did not differ between children with complicated and uncomplicated pneumonia (p=0.9). The possible explanations of that indifference were the sample size which might limit such conclusions. This could also be due to the low prevalence of severe CAP in their population compared to that observed in other studies, and the absence of mortality, even in cases with bacteremia and empyema.

Endotoxins produced by bacteria that cause pneumonia were found to stimulate vasopressin and copeptin release directly, independently of baroreceptor activity and osmotic stimuli. Also acute phase cytokines (i.e. IL-1 0, IL-6, TNF-(x) were also shown to enhance vasopressin and copeptin production. In addition, copeptin plays not only a critical role in osmo-regulation, but also in the regulation of the hypothalamo-pituitary-adrenal (HPA) axis and, thus, reflects the individual stress response. 'Stressors' such as severe pneumonia are strong stimulators of the release of copeptin which reflects its high serum level in CAP **[21]**.

In the current study, we reported higher serum levels of procalcitonin (860 vs 485pg/ml, p=0.02).

The elevated serum levels of procalcitonin (PCT) in our study comes in accordance with previous studies conducted by Johansson et al., [22], Colak et al., [23] who found that higher levels of PCT were significantly reported among pneumonic children with medians of (1.18, 0.07ng/mL respectively).

Furthermore, Creamer et al., [24] statedthatplasma PCT concentrations have recently been shown to be an easy to determine, stable parameter, and are markedly elevated in patients with CAP.

Systemic inflammatory response to severe infection as pneumonia induce production of PCT by endotoxins and possibly by other bacterial or inflammatory products. Serum levels of PCT increases with increasing severity of the inflammatory response to infection [25].

In the current study, we reported higher median rates of C-reactive protein (52 vs 20mg/L, p=0.004).

On the same hand, Mohamed et al., [7] reported higher rates of CRP levels in children with complicated pneumonia compared to children with uncomplicated pneumonia (p=0.001).

Similarly, a previous study conducted by Masarweh et al., [13] foundreported higher CRP levels with a median of 18.5 (IQR: 5.8-6.5) in children with complicated pneumonia compared to uncomplicated children with a median of 5.05 (IQR: 1.7-12.1).

Moreover, Sheb et al., [20] reported higher levels of CRP in severe complicated children with medians of 38 compared to uncomplicated children with medians of 36 (p<0.001).

The same results were reported by Du et al., [14] who found higher levels of CRP in complicated children compared to uncomplicated ones (8.1mg/dL vs 6.2mg/dL) (p<0.001).

Elevated CRP levels in children with complicated pneumonia might be attributed to an ongoing inflammatory process that could be associated with a failure of initial antibiotic therapy as well as with a septic complication such as an empyema or an abscess [26].

In the current study, there was a statistically significant positive correlation found between serum copeptin and PRESS severity score (p< 0.001).

This comes in agreement with a study conducted by Mohamed et al., [7] which reported that serum copeptin was directly correlated with PRESS severity score (p=0.002).

On the contrary, another study by Du et al., [14] reported that copeptin is known to reflect the severity of pneumonia and it seems to correspond with complications of pneumonia in children. However, they found no correlation between copeptin and pneumonia severity based on clinical and laboratory features. Their explanation of this insignificance is the small sample sized of children with complications and similar clinical and laboratory features of the complicated and uncomplicated children.

PRESS is a score of pneumonia severity and this correlation may may reflect the value of serum copeptin in identification of high risk patients with severe complicated pneumonia.

In the current study, there was a statistically significant positive correlation found between serum copeptin and PIRO severity score (p<0.001).

Our findings go parallel with a previous study conducted by Araya et al., [19] who stated that PIRO score could be a reliable tool to identify children with severe pneumonia and to select patients for admission to ICU and for adjunctive therapy.

Severe CAP is associated with serious complications and PIRO severity score comprise these complications as variables such as organ dysfunction, or response (multilobar or complications of pneumonia). So higher scores of PIRO severity score is associated with severe form of CAP.

In the current study, serum copeptin levels correlated positively with the duration of hospital stay (p<0.001).

This result comes in accordance with Tiewsoh et al., [27] who found a positive correlation between prolonged hospital stay and elevated serum copeptin levels in children with complicated pneumonia.

In this work, serum copeptin levels significantly correlated with inflammatory markers including CRP and PCT (p=0.013 and 0.035 respectively).

Similarly, a previous study conducted by Müller et al., [28] reported a significant correlation of copeptin levels with other laboratory parameters as PCT (r=0.57, p<0.001), CRP (r=0.46, p<0.001) among pneumonic patients.

In the present study, serum copeptin levels correlated negatively with hemoglobin levels and

lymphocytic counts (r=0.291 and 0.353; p=0.034 and 0.009).

Similarly, a previous study conducted by shebl et al., [20] reported a negative correlation between serum copeptin and hemoglobin level (p=0.04) which may be attributed to the relation between serum copeptin and severe pneumonia with negatively affect hemoglobin level.

In the current study, there were significant relations betweenserum copeptin and clinical, radiological findings of severe pneumonia, and the need for ICU admission (p<0.05).

This comes in agreement with a study by Kolditz et al., [29] who reported increased copeptin levels are associated with early clinical deterioration resulting in ICU-admission (p<0.005).

Higher levels of copeptin are associated with the need for ICU admission which indicates the higher prognostic value of monitoring copeptin levels in children with CAP.

We also reported that the higher levels of serum copeptin were significantly observed among patients with complicated pneumonia compared to uncomplicated ones (p<0.001).

Our results come in accordance with Principi and Esposito, [30] who found that lobar consolidation was significantly correlated with serum copeptin in complicated pneumonic children (p<0.05). In addition, elevated serum copeptin correlated positively with poor outcome and severe complications of pneumonia.

These results support the use of suchbiomarker for identifying children at high risk for potential pooroutcomes, and for monitoring of disease progression. Principi and Esposito, [30].

In the current study, multiple regression analysis showed that the increase in PRESS score, total leukocytic count and hospital stay had an independent effect onincreasing serum copeptin level with significant statistical difference (p<0.05 for all), indicating a significant association between serum copeptin level and the severity of pneumonia.

It is important to note that, this is one of fewest studies that had examined the relationships between serum copeptin and the fore mentioned several pneumonia severity scores, clinical, radiological pneumonia parameters and evaluated the independent effects of these parameters on the serum copeptin levels.

In the current study, the best cut-off point of serum copeptin for identifying complicated pneumonia was >65pmol/L, with a sensitivity and specificity of 81.48% and 84.62% respectively and are under curve of 0.858.

Our results go parallel with another study conducted by Abdel-Fattah et al., [8] whostated that the best cut-off point of copeptin for diagnosis of pneumonia was 56pg/mL with a sensitivity and specificity of 39% and 85% respectively with area under curve of 0.62. Furthermore, Du et al., (2013) [14] reported an area under curve of 0.87 and a cut-off point of copeptin for diagnosis of CAP was 62.7pmol/L with a sensitivity and specificity of 77.1% and 81.5% respectively.

Similar to our study, Mullar et al., [28], reported that cut-off points for diagnosis of pneumonia of the serum copeptin were 53pmol/L with sensitivities and specificities of 58% and 80% with area under curve of 0.75.

On the other hand, a previous study conducted by Mohamed et al., [7] who reported a copeptin best cut-off point for CAP diagnosis was 52.7pg/mL with a sensitivity and specificity of 70% and 85% respectively with area under curve of 0.62.

The difference between current study and other studies that mentioned that cutoff value of serum copeptin for the diagnosis of CAP was primarily due to the wide varieties of CAP complications assessed by these studies, as well as the sample sized included.

The explanation of different cutoff values among various studies might be attributed to the sizeable overlap in copeptin values among patients with varied etiologies of pneumonia.

In the current study, the best cut-off point of serum procalcitonin for diagnosis of complicated pneumonia was >630pg/mL, with a sensitivity and specificity of 62.96% and 73.08% respectively and are under curve of 0.685.

Comparable to our study, Mullar et al., [28] reported that cut-off points for diagnosis of pneumonia of procalcitonin were 330pg/mL with sensitivities and specificities of 76% and 50% with area under curve of 0.68 respectively.

Similarly, in a study by Bafadhel et al., [31], they reported the optimal threshold value calculated for procalcitonin was 80pg/mL, of which a level greater than this had a sensitivity of 89% and specificity of 78% for identifying patients with pneumonia.

Based on our findings, copeptin has a higher sensitivity and specificity and AUC than PCT indicating that copeptin has more accuracy in discriminating complicated from uncomplicated pneumonia.

Conclusion:

Serum copeptin was helpful in diagnosis of children with CAP; also provided a good manner prognostic value along with PCT and other radiological investigations as CT and US. So, we conclude that serum copeptin might play a critical role in diagnosis of CAP and also might be considered as a prognostic biomarker for complications of pneumonia.

References

1- LEUNG A.K., WONG A.H. and HON K.L.: Community-acquired pneumonia in children. Recent Patents on Inflammation & Allergy Drug Discovery, 12 (2): 136-144, 2018.

2- KYU H.H., PINHO C., WAGNER J.A., BROWN J.C., BERTOZZI-VILLA A., CHARLSON F.J., et al.: Global and national burden of diseases and injuries among children and adolescents between 1990 and 2013: Findings from the global burden of disease 2013 study. JAMA Pediatrics, 170 (3): 267-287, 2016.

3- LE ROUX D.M. and ZAR H.J.: Community-acquired pneumonia in children-A changing spectrum of disease. Pediatric Radiology, 47 (11): 1392-1398, 2017.

4- TASEVSKA I., ENHORNING S., PERSSON M., NILSSON P.M. and MELANDER O.: Copeptin predicts coronary artery disease cardiovascular and total mortality. Heart, 102: 127-2, 2016.

5- LYNCH T., BIALY L., KELLNER J.D., OSMOND M.H., KLASSEN T.P., DUREC T., et al.: A systematic review on the diagnosis of pediatric bacterial pneumonia: When gold is bronze. PloS One, 5 (8): e11989, 2010.

6- WUNDERINK R.G.: Community-Acquired Pneumonia. Infectious Diseases, 251-257. e1. doi: 10.1016/B978-0-7020-6285-8.00028-9, 2017.

7- MOHAMED G.B., SAED M.A., ABDELHAKEEM A.A., SALAH K. and SAED A.M.: Predictive value of copeptin as a severity marker of community-acquired pneumonia. Electron Physician, 9 (7): 4880-4885. Published 2017 Jul 25. Doi:10.19082/4880, 2017.

8- ABDEL-FATTAH M., MELIGY B., EL-SAYED R. and EL-NAGA Y.A.: Serum Copeptin Level as a Predictor of Outcome in Pneumonia. Indian Pediatr., 52 (9): 807-808. Doi: 10.1007/s13312-015-0723, 2015.

9- QIN QIANG and KUN-LING SHEN: "Community-acquired Pneumonia and its Complications." Indian Journal of pediatrics, Vol. 82, 8: 745-51. doi: 10.1007/s12098-015-1785-4, 2015.

10- ALCOBA G., MANZANO S., LACROIX L., et al.: Proadrenomedullin and copeptin in pediatric pneumonia: a prospective diagnostic accuracy study. BMC Infect Dis 15, 347. https://doi.org/10.1186/s12879-015-1095-5, 2015.

11- MUSOLINO A.M., TOMÀ P., SUPINO M.C., et al.: Lung ultrasound features of children with complicated and noncomplicated community acquired pneumonia: A prospective study. Pediatr. Pulmonol., 54 (9): 1479-1486. doi:10.1002/ppul.24426, 2019.

12- ELEMRAID M.A., THOMAS M.F., BLAIN A.P., RUSHTON S.P., SPENCER D.A., GENNERY A.R., et al.: North East of England Pediatric Respiratory Infection Study Group Newcastle upon Tyne, UK. Risk factors for the development of pleural empyema in children. PediatrPulmonol. Jul;50 (7): 721-6. doi: 10.1002/ppul.23041. Epub 2014 Apr 1. PMID: 24692118, 2015.

13- MASARWEH K., GUR M., TOUKAN Y., BAR-YOSEPH R., KASSIS I., GUT G., et al.: Factors associated with complicated pneumonia in children. Pediatr. Pulmonol. Aug. 56 (8): 2700-2706. doi: 10.1002/ppul.25468. Epub 2021 May 25. PMID: 33991059, 2021.

14- DU J.M., SANG G., JIANG C.M., HE X.J. and HAN Y.: Relationship between plasma copeptin levels and complications of community-acquired pneumonia in preschool children. Peptides, 45: 61-65. doi: 10. 10 1 6/j.peptides.2013. 04.015, 2013.

15- AZAB S.F., SHERIEF L.M., SALEH S.H., ELSAEED W.F., ELSHAFIE M.A. and ABDELSALAM S.M.: Impact of the socioeconomic status on the severity and outcome of community-acquired pneumonia among Egyptian children: a cohort study. Infect Dis. Poverty, 3: 14. Published 2014 Apr 24. doi: 10. 1186/2049-9957-3-14, 2014.

16- HUYSENTRUYT K., ALLIET P., RAES M., WILLEKENS J., DE SCHUTTER I., et al.: Nutritional Status of Children Hospitalized for Parapneumonic Effusion. PLOS ONE, 9 (4): e94242. https://doi.org/10.1371/journal.pone . 0094242, 2014.

17- BUONSENSO D., TOMÀ P., SCATENI S., CURATOLA A., MORELLO R., VALENTINI P., et al.: Lung ultrasound findings in pediatric community-acquired pneumonia requiring surgical procedures: A two-center prospective study. Pediatric Radiology, 50 (11): 1560-1569, 2020.

18- RISHI PABARY and IAN M. BALFOUR-LYNN: Complicated pneumonia in children Breathe Mar., 9 (3): 210-222; DOI: 10.1183/20734735.04301, 2013.

19- ARAYA S., LOVERA D., ZARATE C., et al.: Application of a Prognostic Scale to Estimate the Mortality of Children Hospitalized with Community-acquired Pneumonia. Pediatr Infect Dis. J., 35 (4): 369-373. doi:10.1097/INF. 0000000000001018, 2016.

20- SHEBL A., SOBIEH A., ELSAYED Y. and MOHAMED M.: Copeptin as an Inflammatory Marker in Diagnosis and Prognosis of Community Acquired Pneumonia in Children. Benha Journal of Applied Sciences, 5 (1): 141-150. doi: 10.21608/bjas.2020.136639, 2020.

21- MULLER B., MORGENTHALER N., STOLZ D., SCHUETZ P., MÜLLER C., BINGISSER R., et al.: Circulating levels of copeptin, a novel biomarker, in lower respiratory tract infections. Eur. J. Clin. Investig., 37 (2): 145-52, 2007.

22- JOHANSSON N., KALIN M., BACKMAN-JOHANSSON C., LARSSON A., NILSSON K. and HEDLUND J.: Procalcitonin levels in community-acquired pneumonia - correlation with aetiology and severity. Scand J. Infect

Dis., 46 (11): 787-791. doi: 10.3109/00365548.2014.945955, 2014.

23- ÇOLAK A., YıLMAZ C., TOPRAK B. and AKTOĞU S.: Procalcitonin and CRP as Biomarkers in Discrimination of Community-acquired Pneumonia and Exacerbation of COPD. J. Med. Biochem., 36 (2): 122-126. Published 2017 Apr. 22. doi: 10. 1515/jomb-2017-0011, 2017.

24- CREAMER A.W., KENT A.E. and ALBUR M.: Procalcitonin in respiratory disease: Use as a biomarker for diagnosis and guiding antibiotic therapy [published correction appears in Breathe (Sheff). 2019 Dec., 15 (4): e152]. Breathe (Sheff), 15 (4): 296-304. doi:10.1183/20734735.0258-2019, 2019.

25- HEDLUND J. and HANSSON L.O.: Procalcitonin and C-reactive protein levels in community-acquired pneumonia: Correlation with etiology and prognosis. Infection, 28 (2): 68-73. doi:10.1007/s150100050049, 2000.

26- EISENHUT M.: A persistently elevated C-reactive protein level in pneumonia may indicate empyema. Crit Care, 12, 409. https://doi.org/10.1186/cc6204, 2008.

27- TIEWSOH K., LODHA R., PANDEY R.M., BROOR S., KALAIVANI M. and KABRA S.K.: Factors determining the outcome of children hospitalized with severe pneumonia. BMC Pediatr., 9: 15. Published 2009 Feb. 23. doi:10.1186/1471-2431-9-15, 2009.

28- MULLER B., MORGENTHALER N., STOLZ D., SCHUETZ P., MÜLLER C., BINGISSER R., et al.: Circulating levels of copeptin, a novel biomarker, in lower respiratory tract infections. Eur. J. ClinInvestig., 37 (2): 145-52, 2007.

29- KOLDITZ M., HALANK M., SCHULTE-HUBBERT B., BERGMANN S., ALBRECHT S. and HÖFFKEN G.: Copeptin predicts clinical deterioration and persistent instability in community-acquired pneumonia. Respir Med., 106 (9): 1320-1328. doi:10.1016/j.rmed.2012.06.008, 2012.

30- PRINCIPI N. and ESPOSITO S.: Biomarkers in pediatric community-acquired pneumonia. International Journal of Molecular Sciences, 18 (2): 447, 2017.

31- BAFADHEL M., CLARK T.W., REID C., et al.: Procalcitonin and C-reactive protein in hospitalized adult patients with community-acquired pneumonia or exacerbation of asthma or COPD. Chest., 139 (6): 1410-1418. doi:10.1378/chest. 10-1747, 2011.

القيمة التنبؤية لنسبة الكوبيبتين بالدم كمؤشر لشدة المريض فى حالات الالتهاب الرئوى المكتسب من المجتمع فى الأطفال

المقدمة: كان ولا يزال الالتهاب الرئوى هو المسبب الاول والرئيسى لوفاة الأطفال تحت سن الخامسة لعقود عديدة، وبالرغم من الجهود المكثفة لتقليل نسب هذه الوفاة فى الاطفال الا أنه لا يزال الالتهاب الرئوى هو المتسبب الرئيسى لوفاة الاطفال الأقل عمراً من خمس سنوات بما يُقارب ٩٠٠ الف من أصل ٦.٣ مليون طفل توفوا خلال عا م ٢٠١٣.

الالتهاب الرئوى المكتسب من المجتمع يعّرف على أنه التهاب حاد يصيب الهيكل الداخلى لرئة الطفل بسبب ميكروب مكتسب من المجتمع وهذا يختلف عن الاصابة بهدا الالتهاب داخل المستشفيات. كما يعد الالتهاب من هذا النوع هو مرض خطير بل ولديه القدرة على احداث مضاعفات عديدة.

تعد مستويات الكوبيبتن علامة على وجود التهاب شديد فى مختلف الأمراض البيولوجية مثل أمراض القلب. أيضاً قد تم دراسة مستويات الكوبيبتن حديثاً فى أمراض مثل الازمة التى تنتج عن تسمم الدم بالبكتريات فى الأطفال والكبار أيضاً.

كما يعد التعرف على المستويات العالية من الكوبيبتن دليل واضح على وجود عدوى شديدة مثل الالتهاب الرئوى المكتسب من المجتمع وعلاوة عليه، قد يتم حجز هؤلاء المرضى فى المستشفيات وعلاجهم بشكل سليم. كما أن هناك عوامل من خلالها نستطيع أن إذا كان الطفل يحتاج إلى الرعاية الصحية فى المستشفى أم لا مثل الحالة الاكلينيكية ونسبة تشبع الاوكسجين فى الدم وأيضاً المضاعفات التى حدثت نتيجة الاصابة بهذه العدوى، كما أن هناك اختبارات معملية محددة قد تساعد على تقييم خطورة المرض.

الهدف من الدراسة: لقياس نسبة الكوبيبتن بالدم وتقييم علاقته بشدة الإلتهاب الرئوى المكتسب من المجتمع فى الأطفال.

المنهج وطرق البحث: تم تنفيذ هذه التجربة السريرية التداخلية فى مستشفيات الأطفال التخصيصة بجامعة عين شمس فى الفترة من بداية شهر يناير لسنة ٢٠٢١ حتى نهاية شهر ديسمبر لسنة ٢٠٢١.

تمت هذه الدراسة على ٩٣ طفل وتم تقسيمهم على النحو الآتى: المجموعة (١) ٥٣ طفل تم تشخيصهم التهاب رئوى عن طريق الأعراض والعلامات التى توحى بالإلتهاب الرئوى مثل (السعال، وضيق التنفس، والحمى، وعلامات صعوبة التنفس) وتقسم هذه المجموعة إلى طفل يعانون من مضاعفات الإلتهاب الرئوى و٢٦ طفل بدون مضاعفات. المجموعة (٢) ٤٠ طفل لا يعانون من أعراض الإلتهاب الرئوى متطابقين فى السن والجنس مع مجموعة (١).

هؤلاء الأطفال قيد الدراسة قد تم لهم الآتى:

١- التاريخ المرضى الكامل والذى يشتمل على الاسم والعمر والجنس والتاريخ المرضى أيضاً تم تقيم المستوى الإجتما عى لدى الابوين أيضاً تم تقييم أعراض الإلتهاب الرئوى والتى تتمصل فى (الكحة والحم وألم البطن ونقصان الوزن وعدم القدرة على ممارسة الرياضة) وتقييم مدة المرض وتناول المضادات الحيوية قبل دخول المستشفى. كما تم عمل الفحص الجسدى والذى اشتمل على المقاييس الجسدية الكاملة مثل الطول والوزن، كما تم أيضاً فحص الجهاز التنفسى فحصاً كاملاً.

٢- الاختبارات المعملية والتى اشتملت على صورة الدم الكاملة، كما تم قياس مستويات السى ار بى فى هؤلاء الأطفال. أيضاً تم عمل فحوصات تصويرية على الصدر مثل الأشعة السينية لاستبعاد وجود مضاعفات وأيضاً الموجات الصوتية على الصدر لتقيم السائل الموجود داخل الغشاء البلورى، كما تم عمل أشعة مقطعية لاستبعاد وجود مضاعفات. أيضاً تم عمل فحوصات معملية خاصة للمرض مثل قياس مستويات الكوبيبتن ومستويات البروكالسيتونين فى الدم.

٣- قياسات تمت قبل الدراسة: مثل قياس مستويات الخطورة لهذا المرض.

معايير الاشتمال:

- الفئة العمرية من شهرين إلى ٥ سنوات
- الأطفال الذين تم تشخيصهم بمرض الإلتهاب الرئوى.

معايير الاستبعاد:

- الأطفال الذين لديهم أمراض رئوية مزمنة مثل مرض الدرن.
- الأطفال الذين لديهم أمراض فى أجهزة متعددة مثل الفشل الكبدى والفشل القلبى.
- الأطفال الذين لديهم أمراض نقص مناعة.

الاعتبارات الأخلاقية:

تم الحصول على الموافقة خطية قبل الانضمام للدراسة من أولياء أمور الأطفال المشاركين فى الدراسة بعد توضيح هدف الدراسة، كما تم الحصول على الموافقة من لجنة أخلاقيات البحث العلمى بكلية الطب - جامعة عين شمس.

النتائج: كان متوسط عمر الأطفال المصابين بالإلتهاب الرئوى ٣ سنوات ويتراوح أعمارهم ما بين ١-٤ سنوات، أما متوسط عمر الأطفال الاصحاء سنتين فقط ويتراوح أعمارهم ما بين ٩ شهور إلى ٣ سنوات بالرغم من عدم وجود فرق إحصائى بين المجموعتين.

أيضاً أظهرت النتائج فرقاً إحصائياً بين المجموعة الأولى فى الأطفال المصابين بالإلتهاب الرئوى فى مستويات الكوبيبتن بمتوسط pmol/L 65 مقارنة بمجموعة الأطفال الأصحاء بمتوسط 0.65 pmol/L.

فى هذه الدراسة، تم تقسيم المجموعة الأولى إلى مجموعتين، المجموعة الأولى هم الأطفال الذين أصيبوا بمضاعفات ناتجة عن الإلتهاب الرئوى والمجموعة الثانية أطفال لديهم إلتهاب رئوى ولكن لم يظهر عليهم مضاعفات. هذه المضاعفات تمت دراستها وتقسيمها على النحوى الآتى: تعفن الدم بشكل رئيسى وأساسى فى ٣٢.١٪ من أطفال المجموعة الأولى.

لم يكن هناك فرق إحصائى بين أطفال الإلتهاب الرئوى أصحاب المجموعة الأولى والثانية فى العمر (٣ سنوات لكلتا المجموعتين).

فى هذه الدراسة، دراسة المستوى الإجتماعى استناداً إلى جيلان أظهر فرق إحصائى حيث كان المستوى الاجتماعى أعلى فى الأطفال الذين لم يظهر عليهم مضاعفات مقارنة بالأطفال الذين ظهرت عليهم مضاعفات مقترحاً أن المستوى الإجتماعى المتدنى قد يكون له عامل أساسى ومباشر فى ظهور مضاعفات الإلتهاب الرئوى.

دراستنا أظهرت نسب عالية من عدم القدرة على اداء التمارين بإنتظام وخسارة الوزن والزيارات المتكررة للمستشفيات فى الأطفال الذين ظهرت عليهم مضاعفات المرض مقارنة بالأطفال الذين لم تظهر عليهم أى مضاعفات. كما أفدنا أيضاً بطول مدة المرض قبل زيادة المستشفى بمتوسط ٧ أيام فى مجموعة المضاعفات مقارنة بـ ٣.٥ أيام فى مجموعة الأطفال الذين لم يظهر عليهم مضاعفات.

الأطفال الذين لم يظهر عليهم مضاعفات افادوا بنسب عالية من تشبع الدم بالأكسجين بمتوسط ٩٥٪ مقارنة بالأطفال الذين ظهرت عليهم مضاعفات بمتوسط ٩١٪. أيضاً معدل التنفس الرئوى أظهرت نسباً عالية فى الأطفال أصحاب المضاعفات بمتوسط ٤٠ مرة عدد تنفس فى الدقيقة مقارنة بـ ٣٥ عدد مرات التنفس فى الدقيقة فى الأطفال الذين لم يظهر عليهم مضاعفات.

فى هذه الدراسة، صعوبة القدرة على التنفس تم تقريرهم بنسبة ٩٢.٥٪ فى أطفال المضاعفات من المستوى الأول والثانى ومقارنة بالأطفال الذين لم يظهر عليهم مضاعفات، فقد أفدنا بوجود فرق إحصائى بين المجموعتين.

فى هذه الدراسة، عوامل الخطورة للإصابة بمرض الإلتهاب الرئوى كانت أكثر فى الأطفال الذين ظهرت عليهم مضاعفات بنسبة ٧٤.١٪ مقارنة بـ ٣٨.٥٪ فى مجموعة الأطفال الذين لم يظهر عليهم مضاعفات، كما تم تقرير هذه العوامل على النحوى التالى الأطفال عرضة للتدخين بنسبة ٣٣.٣٪، والنظام الغذائى السئ بنسبة ٣٣.٣٪، والمستويات الاجتماعية المتدينة بنسبة ٢٩.٦٪.

فى هذه الدراسة، استخدمنا العديد من قياسات خطورة المرض والتى تم تقريرها بنسب عالية فى الأطفال ذوى المضاعفات بنسبة ٥٩.٣٪ على المقياس الأول وهو مقياس خطورة الجهاز التنفسى لدى الأطفال مقارنة بـ ١٥.٤٪ فى الأطفال الذين لم يظهر عليهم مضاعفات. كما تم تقرير مقياس خطورة المرض قياساً على العدوى البكتيرية، والذى أفاد بنسبة ٧٤.١٪ فى الأطفال ذوى المضاعفات مقارنة بـ ٤٦.٢٥٪ لدى الأطفال الآخرين.

فى هذه الدراسة، كان هناك نسبة قليلة من مستويات الهيموجلوبين وعدد الخلايا الليمفاوية فى الأطفال ذوى المضاعفات، كما أن هناك أيضاً مستويات عالية من إجمالى عدد كرات الدم البيضاء فى الأطفال ذوى المضاعفات مقارنة بالأطفال الذين لم يظهر عليهم مضاعفات مع وجود فرق إحصائى بين المجموعتين.

كان هناك مستويات عالية من الكوبيبتن فى الدم بمتوسط 79 pmol/L فى الأطفال ذوى المضاعفات مقارنة بـ 37 pmol/L فى الأطفال الذين لم يظهر عليهم مضاعفات، أيضاً كان هناك مستويات عالية من البروكالسيتونين فى الدم بمتوسط 860 pg/ml فى الأطفال ذوى المضاعفات مقارنة بـ 485 pg/ml فى الأطفال الآخرين. أيضاً مستويات السى ار بى كانت أعلى فى الأطفال ذوى المضاعفات بمتوسط 52 mg/L مقارنة بـ 20 mg/L 860 فى الأطفال الاخرين.

فى هذه الدراسة، كانت هناك علاقة إيجابية بين مستويات الكوبيبتن فى الدم والعلامات الحيوية الأخرى مثل مستويات الخطورة الخاصة بالجهاز التنفسى ومدة المكوث فى المستشفى والسى ار بى والبروكالسيتونين، و لكن كانت هناك علاقة سلبية بين مستويات الكوبيبتن والهيموجلوبين والخلايا الليمفاوية.

فى هذه الدراسة، تحليل الانحدار المتعدد اثبت أن زيادة مستويات الخطورة وإجمالى عدد كرات الدم البيضاء ومدة المكوث فى المستشفى كان له ارتباط وثيق وفعال بزيادة مستويات الكوبيبتن فى الدم مع وجود فرق إحصائى والذى يدل على وجود علاقة وثيقة بين مستويات الكوبيبتن فى الدم وخطورة الإلتهاب الرئوى.

فى هذه الدراسة، كانت أفضل نقطة انقطاع لمستويات الكوبيبتن فى الدم للقدرة على التعرف على مضاعفات الإلتهاب الرئوى هى أكبر من 65 pmol/L بنسبة حساسية ٨١.٤٨٪ ونسبة نوعية ٨٤.٦٢٪، ومساحة تحت المنحنى بقدر ٠.٨٥٨. كما كانت أفضل نقطة انقطاع لمستويات البروكالسيتونين فى الدم لتشخيص مضاعفات الإلتهاب الرئوى هى أكبر من 630 pg/mL بنسبة حساسية ٦٢.٩٦٪ ونسبة نوعية ٧٣.٠٨٪ ومساحة تحت المنحنى بقدر ٠.٦٨٥.

\الخاتمة: فى الختام، أظهرت دراستنا أن نسبة الكوبيتبن بالدم قد زادت بشكل ملحوظ فى جميع المرضى الذين يعانون من الإلتهاب الرئوى لمكتسب من المجتمع مقارنة بالأطفال الأصحاء، علاوة على ذلك فقد كان مفيداً فى تشخيص الأطفال الذين يعانون من الإلتهاب الرئوى الحاد والمعقد. كما أنها قدمت قيمة تنبؤية جيدة أعلى من مستويات البروكالسيتونين بالدم مقارنة مع الفحوصات الإشعاعية الأخرى مثل التصوير المقطعى للصدر والأشعة المقطعية، لذلك نستنتج أن الكوبيتين قد يمثل علامة بيولوجية جديدة للتنبؤ بالمضاعفات المرتبطة بالإلتهاب الرئوى فى الأطفال.