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

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Abstract

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

Aim of Study: This study aimed to assess the level of copeptin in community- acquired pneumonia in children.

Patients and Methods: A cross- sectional study was conducted on 40 children with community acquired pneumonia and another 30 healthy children as controls. Imaging techniques as X-ray, and computed topography were used to assess the diagnosis of pneumonia.

Results: Blood levels of copeptin in children with pneumonia with a median of 55 pmol/L were much higher than copeptin levels in controls groups (*p*-value <0.001). Pneumonia complications were reported in 15(50.0%)

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

Key Words: *Community-acquired pneumonia – CAP*

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 **[4-6]**.

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]**.

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

Patients and Methods

This was a cross-sectional study conducted on 30 children with a proven diagnosis of CAP and 20 children as controls who were admitted to pediatric clinics from January 2021 to the end of December 2021. The 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, and X-ray. This study was approved by an Ethical committee and a written consent was obtained from the parents 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.

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, age, vital signs, and birth weight as well as any relative clinical findings.

Regarding the investigations, blood samples were withdrawn from children under complete aseptic condition. Routine lab investiga- tions such as complete blood count (CBC), liver function, kidney function,and random blood glucose were collected.

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. Forpairwise comparisons, Mann Whitney U test andKruskual-Wallis (which are a non-parametric test of significance) was used to compare between two groups having quantitative variables but not normally distributed.

Results

50 children were included in our study and were allocated intro two groups; the first group (pneumonia group) consisted of 30 children who were diagnosed according the diagnostic criteria of pneumonia, and the second group (control group) consisted of twenty age, weight and sex-matched children.

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 55pmol/L compared to the healthy controls ($p<0.001$) (Table 1).

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

as group A (50.0%), and children with uncomplicated pneumonia (50.0%) as group B. The complications reported in the current study were sepsis (26.6%), followed by pleural effusion (26.6%), and hydro-pneumothorax (20.0%) (Table 2).

There was no significant difference between both two subgroups regarding baseline data (Table 3).

Table (1): Socio-demographic data amongthe studied groups.

	Pneumonia group (30)	Control group (30)	*p*-value	Sig.
Gender:				
Female	11 (36.6%)	13 (43.3%)	0.150**	NS
Male	19 (63.3%)	17 (56.6%)		
Age (years):	3 (0.7-4)	2 (0.65-3)	0.0621 *	NS
Consanguity:				
+ve	11 (36.6%)	14 (46.6%)	0.071**	NS
Residency:				
Rural	11 (36.6%)	13 (43.3%)	0.411**	NS
Urban	19 (63.3%)	17 (56.6%)		
Serum copeptin:				
Median (IQR)	55 (40.7-79)	0.55 (0.4-0.7)	<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	15 (50.0%)
Sepsis	4 (26.6%)
Pleural effusion	4 (26.6%)
Empyema	1 (6.7%)
Hydro-pneumothorax	3 (20.0%)
Respiratory failure	1 (6.7%)
Lung abscess	2 (13.3%)

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

Socio-demographic data	Complicated pneumonia group (A) (15)	Un-complicated pneumonia group (B) (15)	*p*-value	Sig.
Age (years):				
Median (IQR)	3 (0.7-4)	3 (1-4)	0.511	NS
Gender:				
Female	5 (33.3%)	6 (40.0%)	0.177	NS
Male	10 (66.6%)	9 (60.0%)		
Consanguity:				
+ve	6 (40.0%)	5 (33.3%)	0.161	NS
Residency:				
Rural	4 (26.6%)	7 (46.6%)	0.401	NS
Urban	11 (73.3%)	8 (53.3%)		
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

Discussion

The present study was conducted on 50 children who were categorized into two groups; 30 children with CAP and 20 children as controls in which the median age of pneumonic children was 3 years (IQR: 0.7-4 years); while for the controls was 2 years (IQR: 0.65-3 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 55pmol/L (IQR: 40.7-79) compared to the healthy controls with a median of 0.55pmol/L (IQR: 0.4-0.7) (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).

In the current study, we categorized pneumonic children into two subgroups; children with complicated pneumonia as group A (50.0%), and children with uncomplicated pneumonia (50.0 %) as group B. The complications reported in the current study were sepsis (26.6 %), followed by pleural effusion (26.6%), and hydro-pneumothorax (20.0%).

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, pneumatoce- les, necrotizing pneumonia, and lung abscesses.

Conducted a retrospective study including 80 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.

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=0.511).

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.

In the current study, we reported higher serum levels of copeptin (p<0.001) in children with pneumonia compared to control children.

Our findings coincide with previous studies conducted by Du et al., **[14,17-19]** , Mohamed et al., **[7]** who reported that higher levels of serum copeptin were also in association with CAP-related compli- cations compared to uncomplicated children (p=0.001).

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).

Moreover, majority of children with complicat- ed pneumonia showed bad general condition (60.0%) when compared to children with uncom- plicated pneumonia who showed (20.0%) as bad general condition (*Data not shown*).

This finding come in accordance with a study by Buonsenso et al., **[15-17]** 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.

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 thatserum copeptin did not differ between children with complicated and uncomplicated pneumonia (p=0.9).

Conclusion:

Serum copeptin was helpful in diagnosis of children with CAP.

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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.