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Correlation Study Between C-Reactive Protein, Procalcitonin with Hematological Parameters Of Children with Pyrexia of Unknown Origin (PUO) in Karbala Pediatric Teaching Hospital

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Abstract:

A case control hospital based selective study was done on 100 children with PUO who admitted to the Karbala Pediatric Teaching Hospital in Karbala city, during the period from 1st of March 2018 to the last of March 2019 aged from 2 months-5 years. A comparable group of similar number of cases of apparently healthy children was taken as a control group. This study aimed to evaluate the diagnostic value of CRP and PCT pyrogenic of unknown origin (PUO) in relation to some hematological parameters.

The study included the collection of 3 ml of blood from each patient and control for assessment of PCT and CRP by immunofluorescence and hematological parameters by general auto-analyzer hematology. This case control study included 100 children with PUO (60 males and 40 females), their age range was 3-48 months (mean: 17.12±8.2 month), the study also included 100 healthy children (as control group) with the same characteristics of the patient. The study revealed that the highest mean level of PCT was recorded among children with PUO (17.36 ng/ml) and the lowest level mean level was found in healthy children (3.56 ng/ml). The study also exposed that the highest mean level of CRP was recorded among children with PUO (22.6 ng/ml) and the lowest level mean level was found in healthy children (2.11 ng/ml). The study showed that WBCs, neutrophils and lymphocytes counts were elevated significantly among children with PUO as compared with healthy children. The study revealed a significant positive correlation between PCT and CRP among children with PUO (r: 0.84, P<0.001), and a significant positive correlation of PCT and CRP with each of WBCs, neutrophils and lymphocytes counts among children with PUO. It was concluded that there a significant positive correlation between PCT and CRP and significant positive correlation of PCT and CRP with each of WBCs, neutrophils and lymphocytes counts among children with PUO

Keywords: Fever; PCR; CRP; PUO; Children
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Introduction

Fever is one of the most common reasons for emergency department and outpatient clinic visits by these patients; many of which have no diagnostically reliable signs and symptoms and receive a diagnosis of fever without a source (FWS) after an initial clinical evaluation [1]. Bacterial infection represents one of the most frequent complications in patients with cirrhosis and ascites, as a result of multiple abnormalities in the defensive mechanisms against bacteria [2]. The infection caused by multidrug resistance (MDR) organisms is more likely to prolong the hospital stay, increase the risk of death, and require treatment with more expensive antibiotics [3]. Cytokines have been implicated in the pathogenesis of sepsis. Macrophages phagocytose bacteria and produce a range of proinflammatory cytokines, which initiate the innate immune system's response to the bacterial pathogen [4,5]. The clinical significance of serum PCT in discriminating between bacterial infections and nonbacterial infections, such as systemic inflammatory response syndrome (SIRS), has been compared with that of other markers including endotoxin, *β*-D-glucan, interleukin (IL)-6, C-reactive protein (CRP), and white blood cell (WBC) count(3). Serum PCT levels in patients with systemic or localized bacterial infections were significantly higher than those in patients with nonbacterial infections or noninfectious diseases [6,7]. This study aimed to evaluate the diagnostic value of CRP and PCT pyrogenic of unknown origin (PUO) in relation to some hematological parameters.

Materials and Methods

The study cases (children with PUO) were taken from the general Pediatric ward. A case control hospital based selective study was done on 100 children with PUO who admitted to the Karbala Pediatric Teaching Hospital in Karbala city, during the period from 1st of March 2018 to the last of March 2019 aged from 2 months-5 years. The consent of the parents of the participating children was obtained in addition to their data in the study. A comparable group of similar number of cases of apparently healthy children was taken as a control group. The anthropometric measurements were measured for each case included in the study (malnourished cases).These include Wt/age, Ht/age, OFC/age, Wt/Ht. Each case was assessed for weight using the Unicef weight scale for children who cannot stand and a digital scale for older children who can stand. Each case weighed with minimum clothes with 2 measurements at least and the mean were taken, the weight taken to the minimum of 5 gram. The study included the collection of 3 ml of blood from each patient and control for assessment of PCT and CRP by immunofluorescence (I-chroma, Korea), and hematological parameters by general auto-analyzer hematology, (Celtac G, Japan).

Results

This case control study included 100 children with PUO (60 males and 40 females), their age range was 3-48 months (mean: 17.12±8.2 month), the study also included 100 healthy children (as control group) with the same characteristics of patient. Further features of patients and control were mentioned in Table 1

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Table 1:General characteristics of the studied groups

Variables		Malnutrition children		Healthy control		P. value
		No.	%	No.	%	
Age groups (months)	3-12	46	46	44	44	NS*
	13-24	34	34	33	33	NS
	25-36	12	12	13	13	NS
	37-48	8	8	10	10	NS
	Total	100	100	100	100	NS
	(Mean±SD)	17.12±8.2		17.34±8.1		NS
Gender	Males	60	60	59	59	NS
	Females	40	40	41	41	
Residence	Rural	62	62	60	60	NS
	Urban	38	38	40	40	
The educational level of a mother	Illiterate	52	52	45	45	NS
	Read and write	14	14	15	15	
	Primary school	18	18	20	20	
	Secondary school	11	11	14	14	
	Higher educate	5	5	6	6	

* P. value >0.05 = non-significant (NS)

The study revealed that the highest mean level of PCT was recorded among children with PUO (17.36 ng/ml) and the lowest level mean level was found in healthy children (3.56 ng/ml), Table 2

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Table 2: Levels of PCT in the study groups

PCT	Children with PUO (n:100)	Control groups (n:100)
Mean	17.36	3.56
S.D	1.12	0.52

The study also exposed that the highest mean level of CRP was recorded among children with PUO (22.6 ng/ml) and the lowest level mean level was found in healthy children (2.11 ng/ml), Table 3

Table 3: Levels of CRP in the study groups

CRP	Children with PUO (n:100)	Control groups (n:100)
Mean	22.6	2.11
.D	1.92	0.13

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The study showed that WBCs, neutrophils and lymphocytes counts were elevated significantly among children with PUO as compared with healthy children (Table 4)

Table 4: Levels of hematological parameters in the study groups

Hematological parameters	Children with PUO	Control group	P. value
WBCs count ($x10^9$/L)	14.6	4.8	<0.01
Neutrophils ($x10^9$/L)	8.4	3.22	<0.01
Lymphocytes ($x10^9$/L)	3.81	1.57	<0.01
Platelets ($x10^9$/L)	3.76	3.83	NS
Hemoglobin (g/dl)	11.7	12.5	NS

The study revealed a significant positive correlation between PCT and CRP among children with PUO (r: 0.84, P<0.001), and a significant positive correlation of PCT and CRP with each of WBCs, neutrophils and lymphocytes counts among children with PUO, Table 5.

Table 5: Correlation of PCT and CRP with hematological parameters of Children with PUO

Parameters	CRP	PCT
CRP	1	0.84
PCT	0.84	1
WBCs	0.56	0.64
Neutrophils	0.57	0.73
Lymphocytes	0.22	0.34
Platelets	0.07	.12
Hemoglobin	0.11	0.1

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Discussion

The study revealed that the highest mean level of PCT and CRP were recorded among children with PUO and the lowest level mean level was found in healthy children. The study also revealed a significant positive correlation between PCT and CRP among children with PUO (r: 0.84, P<0.001), and a significant positive correlation of PCT and CRP with each of WBCs, neutrophils and lymphocytes counts among children with PUO. A previous study expressed that PCT is beneficial in defining bacterial infection in children and adults, and in determining the severity of the underlying disease, guiding treatment, and predicting the result (8). Meta-analyses suggested that PCT useful in differentiating bacterial infection from other causes of infection in critical patients (9). Similar other studies conducted previously demonstrated that PCT was elevated in children with positive blood cultures and it is reliable in differentiating bacteremia from non-bacteremia (10-12). In a meta-analysis study, authors reviewed 351 researches and reported that PCT has elevated in bacteremic patients compared with no bacteremic persons (13). Uusitalo-Seppälä (14) reported that CRP and PCT are a helpful marker for the clinician in detecting severe sepsis, bacteremia and local infection due to its elevation in these diseases. Kofoed et al (15) reviewed that PCT levels were significantly higher in bacteremia cases than in healthy individuals. Andreola *et al.*, (16) study revealed that the highest mean level of PCT and CRP were recorded among children with PUO and the lowest level mean level was found in healthy children and revealed a significant positive correlation between PCT and CRP among children with PUO.

Several studies found that procalcitonin levels were dramatically different in patients with and without bacteremia and its levels were elevated markedly in patients with bacteremia (17,18). Previous studies have investigated the usefulness of using procalcitonin as a positive predictive marker for BSI or sepsis with varying outcomes regarding its clinical suitability(3,4). Procalcitonin can also accurately discriminate between true bacteremia and coagulase-negative staphylococci-contaminated blood cultures (6). Another study demonstrated that bacteremia is unlikely when procalcitonin levels are low (19). Some meta- analyses focused on the diagnostic value of procalcitonin for microbiologically confirmed local infection or bacteremia (20-23).

Conclusions: It was concluded that, there significant positive correlation between PCT and CRP and significant positive correlation of PCT and CRP with each of WBCs, neutrophils and lymphocytes counts among children with PUO

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دراسة الارتباط بين البروتين النشط نوع C والبروكالسيتونين مع المتغيرات الهيماتولوجيه للأطفال المصابين بالحمى المجهولة المنشأ في مستشفى كربلاء التعليمي للأطفال

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الخلاصة:

تم إجراء دراسة انتقائية على 100 طفل مع PUO الذين أدخلوا مستشفى كربلاء التعليمي لطب الأطفال في مدينة كربلاء ، خلال الفترة من 1 مارس 2018 إلى آخر مارس 2019 الذين تتراوح أعمارهم من 2 أشهر إلى 5 سنوات. تم أخذ مجموعة مماثلة من عدد مماثل من حالات الأطفال الأصحاء على ما يبدو كمجموعة سيطرة. كان الهدف من هذه الدراسة هو تقييم القيمة التشخيصية للـ CRP و PCT Pyrogenicمن أصل غير معروف (PUO) فيما يتعلق ببعض متغيرات الدم. تضمنت الدراسة جمع 3 مل من الدم من كل مريض والتحكم في تقييم PCT و CRP عن طريق التألق المناعي والمعايير الدموية بواسطة محلل الدم العام الذاتي.

شملت الدراسة على جمع 3 مل من الدم من كل مريض ومجموعة سيطرة لتقييم PCT و CRP عن طريق التألق المناعي والمعايير الدموية عن طريق تحليل الدم التلقائي العام ، وشملت دراسة الحالة هذه 100 طفل مع PUO (60 ذكر و 40 أنثى) ، تراوحت أعمارهم بين 3-48 شهرًا (17.12 ± 8.2 شهرًا) ، وشملت الدراسة أيضًا 100 طفل سليم (كمجموعة سيطرة) مع نفس خصائص المريض.

أوضحت الدراسة أن أعلى مستوى لمتوسط الـ PCT سُجل بين الأطفال الذين يعانون من PUO(17.36 نانوغرام / مل) وأن أدنى مستوى كان عند الأطفال الأصحاء (3.56 نانوغرام / مل).أظهرت الدراسة أيضًا أنه تم تسجيل أعلى مستوى لمتوسط CRP بين الأطفال الذين يعانون من PUO (22.6 نانوغرام / مل) ووجد أدنى مستوى متوسط عند الأطفال الأصحاء (2.11 نانوغرام / مل). وبينت الدراسة أن عدد كرات الدم البيضاء والعدلات والخلايا الليمفاوية ارتفع بشكل ملحوظ بين الأطفال المصابين بـ PUO مقارنة بالأطفال الأصحاء.

كشفت الدراسة عن ارتباط إيجابي معنوي بين PCT و البروتين النشط بين الأطفال المصابين بـ PUO (r: 0.84 ، P <0.001)، ووجود ارتباط إيجابي معنوي بين PCT و CRP مع عدد كرات الدم البيضاء ، العدلات والخلايا الليمفاوية بين الأطفال المصابين بـ PUO. استنتج أن هناك علاقة إيجابية معنوية بين PCT و CRP وعلاقة إيجابية معنوية بين PCT و البروتين النشط مع كل من كرات الدم البيضاء ، العدلات والخلايا الليمفاوية بين الأطفال الذين يعانون من.PUO

الكلمات الرئيسية: حمى؛ PCR ؛ البروتين النشط ؛ الأطفال