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SERUM PROCALCITONIN CONCENTRATION VS. TOTAL AND DIFFERENTIAL WHITE BLOOD CELL COUNT IN IRAQI BURN INJURY PATIENTS

Meroj A. Jasem, Dr. Ayser E.Mahmood, Dr.Alia E. AL-Ubadi and Abbas AL-Bahadli*

Iraq.

***Corresponding Author: Abbas AL-Bahadly**
Iraq.

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ABSTRACT
White Blood Cell (WBC) count is an important test because it is easily available, and inexpensive laboratory marker already in use all over the world. Microbiological cultures of burn injury require time and among the newest biomarkers to detect bacterial infection is procalcitonin (PCT) which has the highest diagnostic accuracy. The present study aimed to determine the priority of PCT over the total WBC count and differential count in burn injury, infection detection for three time samples after burn occurrence. The results demonstrate that total and differential WBC count did not show any significant differences between survivor and non-survivor. There was no significant correlation between PCT and WBC in non-survivor group and survivor groups for the three times of samples, while PCT value rapidly increased in non-survivor group but in the survival group decreased due to successful treatment. As a conclusion procalcitonin would be a more useful biomarker for diagnosis the inflammation in burn injuries.

KEYWORDS: White Blood Cell, Procalcitonin, Burn Injury.

INTRODUCTION

Various therapeutic strategies are known to improve survival in patients with burn infection, therefore, rapid and accurate diagnosis is essential.

WBC count is an important test because it is easily available, and inexpensive laboratory marker already in use all over the world. Changes in laboratory values such as (WBC) count, neutrophil percentage, and C-reactive protein (CRP) level are of low yield in detecting or predicting burn infections because of the inflammatory response associated with the burn itself. Microbiological cultures require time, and the most common burn infection is leading to sepsis, which neither reflects the host response of systemic inflammation nor the onset of organ dysfunction, and may not be positive in sepsis patients for a number of reasons.

Greenhalgh *et al*., (2007) found that total WBC count is a proper diagnostic standard for sepsis in burn patients while (Murray *et al*., 2007) concluded that WBC count and neutrophil percentage, or any changes in these values were not clinically reliable in predicting bloodstream infection.Many studies outdated have documented impairments in neutrophil function after burn injury (Butler *et al*., 2010; Hasslen *et al*., 1993; Bjornson and Somers, 1993).

Moreover, (Butler *et al*., 2010) found that neutrophil is depressed as early as 24 hours after the burn injury due to inhibition of neutrophils migrate in burn patients and impaired neutrophil chemotaxis. It is known that burn injuries represent a great derangement of blood homeostasis (Alvarado *et al*., 2009; Kraft *et al*., 2012; Belba *et al*., 2015). Among the newest biomarkers to detect bacterial infection is PCT which has the highest diagnostic accuracy. The PCT became an important protein in the detection and differential diagnosis of inflammatory states (Monsef and Eghbalian, 2012)

MATERIAL AND METHODS

Patients: fifty burned patients were enrolled in the this study with an age ranging between (7 months to 85 years). All the patients were admitted to burn units in Al-Kennedy and Imam Ali hospitals in Baghdad, Iraq for the period from October 2015 to February 2016. The percentage of burns included in our study were between 10% to 95% of burns.

Samples: Three blood samples were collected from enrolled patients on three different times after burn occurrence, 48hrs, 5^{th} day and 10^{th} day and investigated within six hours of collection for total and differential WBC counts and the samples were stored for PCT investigation in later time. Wound swab samples were also collected at the mentioned three times for culturing.

Clinical Investigation:
WBC total and differential count were tested by Cell-Dyn Ruby Autoanalyzer, PCT by ELISA method and wound swab for bacterial identification Using Vitek 2 System.

Statistics: Data generated from this work were tabulated into Microsoft excel sheets and uploaded to Minitab version 13.0. The WBC and PCT were analyzed using ANOVA test *P*-value of <0.05 was considered as statistically significant Correlation coefficient.

RESULTS AND DISSCUTION

After a burn injury, most of the patients suffer from serious consequences of bacterial infections, which are the most common challenge to fight morbidity and mortality. The rupture of the skin barrier by burn injury leads to local and systemic immune responses and contribute in the complication of microorganism infection (Lederer *et al*., 1999). As table (1) show, the most frequent microorganisms are *Pseudomonas aeruginosa*, followed by *Klebsiella pneumonia* and then *Staphylococcus aureus*, while *Acinetobacter baumannii* has a significant percentage. Mixed culture have been also found within both survivor and non-survivor groups, especially *Pseudomonas aeruginosa* and *Klebsiella pneumonia*, which is a common result as it has been shown in many other studies (Dryden, 2010; Shahzad *et al.*, 2012; Saha *et al*., 2011).

Although both total and differential WBC counts are routinely performed in most infectious diseases, they are influenced by many other non-infectious diseases such as myocardial infarction, catecholamines, corticosteroids and acute bleeding. Thus, the leukocytosis value in the diagnosis of infection is very poor (Povoa, 2002) although the main function of White blood cells is to fight infection and defend the body by phagocytosis against invasion by foreign organisms and since neutrophils are the most common type of white blood cell, comprising about 50-70% of all white blood cells thus WBC counts and neutrophil (NEU) percentages still an important predictor for bloodstream infection. Burn injuries stimulate changes in hematopoiesis and induce the acute phase of the response (Belba *et al*., 2015) and burn injury causes systemic inflammatory response which increases WBC count (Lu *et al*., 2013). Furthermore WBC considers to be a biomarker for the detection of decreased oxygenation soon after a burn injury (Murray *et al*., 2007).

It has been claimed that no significant differences were found in the total WBC count, in burn patients with or without bacterial infection by (Barati *et al*., 2008). This result concordance with the present study, which declares that there are no significant differences in total WBC count ($p > 0.05$), for both survivor and non-survivor groups through the three times samples, contrariwise to (Belba *et al*., 2015). In a mouse model of thermal injuries done by (Calum *et al*., 2009), demonstrate decreases in the concentration of leukocytes in peripheral blood as well as reduced function of the PMNs that confirm an inhibition of the innate immune response like with observations in patients suffering from burn injuries, which lead to the increase in susceptibility to infections.

The present study demonstrates that the comparison neutrophils percentage between survivor and non-survivor showed a significant difference, especially during the 10^{th} day ($p< 0.05$), this agreed with (Murray *et al*., 2007), on the other hand, this result disagrees with (Lavrentieva *et al*., 2007), which did not find any significant differences between patients with non-infected and infected in WBC count and neutrophils percentage. Lymphocyte (LYM) percentage between survivor and non-survivor showed a significant difference, especially during the 10^{th} day ($p < 0.05$), while the monocytes (MON) percentage between the two groups showed a significant difference, especially during the 5^{th} day ($p < 0.05$). The present study shows a significant difference in eosinophils (EOS) percentage through the comparison between the two groups during the 10^{th} day ($p < 0.05$) table (2), figure (1).

Burn injuries cause anti-inflammatory response which leads to serious consequences as an immunosuppression, which leads to infectious complications (Church *et al*., 2006) which are characterized by the decrease of monocytes/macrophages after burn injury and sepsis (Gamelli *et al*., 1994). The increase of releasing of Prostaglandin E2 (PGE2) by inhibitory macrophages plays a remarkable role in immunosuppression of burn patients (Church *et al*., 2006), and the real events which follow the burn injury and lead to immunosuppression remain unknown.

The burn skin injury provides a rich environment of a vascular necrotic tissue that supplies microorganism with a rich medium of nutrient which cause suppuration. Sometimes, the formation of scars leads to reduce migration of immune cells into the burned area and impair local host immune responses which lead to limit distribution of antimicrobial agents which are produced by the host to the burned area (Nasser *et al*., 2003).

White Blood cell is important hallmarks in the evaluation of burn injuries. The total WBC count began to increase immediately after burn injury and reach the peak within 12 hours and then decreased at days 3 to 4 and then began increasing, this fluctuation in leukocyte count is due to dramatic changes within the first 72 hours after burn injury and it depends on burn size. (Kim *et al*., 2011).

The average values of PCT concentrations have no significant differences among the non-survivor group and among the survivor group of three times samples, but there are a strong significant difference between non-survivor and survivor groups in the10^{th} day time post-

burn only (p=0. 000) as shown in table (3) and figure (2), with 2638 ± 3013pg/ml and 588 ± 364 pg/ml PCT concentrations, respectively and peak PCT levels are higher in non-survivor patients.

Results show that there is abnormal value in the biomarkers data on burn patients, perhaps there is another or mixed systemic infection like UTI, chest infections and etc. Recently, they found out that sometimes other non- infectious conditions may induce PCT for e.g. (cardiogenic shock, major surgery including cardiac surgery, accidental trauma, pancreatitis, or burn trauma) (Castelli *et al*., 2004; Zhao *et al*., 2014; Klingele *et al*., 2015).

On the 10th day the study corresponds with (Rosanova *et al*., 2015) who found that the PCT is elevated in the non-survivor patients, and (Barati *et al*., 2008; Castelli *et al*., 2004) who have indicated the higher levels of PCT in burn injury patient with infections as compared with burn injury patient without infection. (Kim *et al*., 2012) have found out that Procalcitonin levels could serve as a prognostic marker for burn patients and the concentrations ≥ 2 ng/ml provide a mortality marker. Secondary infection is a prevalent complication in burn injuries and late diagnosis is associated with increased morbidity and mortality. The secondary infection leads to sepsis, especially in burn injury patients and for being a reason early recognition of sepsis is important. However, the systemic inflammation signs, including changes in body temperature, tachycardia and leucocytosis are used for diagnosis of sepsis, but sometimes this can be misleading, because critically ill burn patients often manifest a systemic inflammatory response syndrome without infection (Mokline *et al*., 2015).

PCT rendering was better than WBC count, It was evinced that PCT value rapidly increased in non-survivor group while in the survivor group decreased due to successful treatment. In the present study, the correlation of plasma levels of PCT with WBC in patients with burn injuries were measured and compared. Correlation coefficients between PCT and WBC for the three times were determined as no correlation table (4).

Table (1): All The Isolated Bacteria According To Different Types

Groups	**Survivor group (35)**			**Non-survivor group (15)**		
Time of sampling	48hr (%)	5thday (%)	10thday (%)	48hr (%)	5thday (%)	10th day (%)
No Growth	40	14.285	25.714	66.666	13.333	40
Klebsiella pneumoniae	22.857	25.714	14.285	6.6666	13.333	20
Acinetobacter baumannii	8.571	5.714	8.571	0	6.666	0
Pseudomonasaeruginosa	8.571	22.857	31.428	6.6666	26.666	20
Staphylococcus aureus	8.571	5.714	2.857	6.6666	6.666	0
Enterococcus faecalis	2.857	0	0	6.6666	13.333	6.666
Proteus vulgaris	0	0	0	6.6666	13.333	6.666
Escherichia coli	0	0	0	0	0	6.666
Klebsiella pnumouiae + Enterococcus faecalis	2.857	0	0	0	0	0
Pseudomonas aeruginosa + Klebsiella pneumouiae	5.714	20	17.142	0	6.666	0
Pseudomonas aeruginosa+ Staphylococcus aureus	0	2.857	0	0	0	0
Klebsiella pnumouiae + Acinetobacter baumannii	0	2.857	0	0	0	0

Table (2): Total WBC And WBC Differentiatial Count

Group	**Test**	**NO**	**48hr**	**5th Day**	**10th Day**	**P**
Non Survivor	WBC	15	12.689±12.416	13.801±8.236	18.801±9.784	0.235
Survivor	WBC	35	16.979±10.584	14.391±6.855	14.910±6.797	0.387
P value			0.219	0.794	0.112	
Non Survivor	NEU%	15	75.16±11.99	68.80±21.52	74.43±16.21	0.539
Survivor	NEU%	35	66.49±18.40	63.59±16.73	62.91±13.40	0.623
P value			0.101	0.360	0.012	
Non survivor	LYM%	15	14.44±9.80	16.05±13.54	16.35±14.43	0.908
Survivor	LYM%	35	22.50±15.64	23.42±13.15	24.67±12.35	0.803
P value			0.072	0.078	0.043	
Non survivor	MON%	15	8.266±2.772	6.915±4.281	7.267±2.429	0.506
Survivor	MON%	35	9.101±3.072	9.993±4.871	8.727±3.810	0.397

P value			0.370	0.039	0.179	
Non survivor	EOSN%	15	0.616±0.803	0.728±0.796	0.555±0.631	0.815
Survivor	EOSN%	35	0.951±1.549	1.354±1.399	1.537±1.477	0.241
P value			0.434	0.112	0.017	
Non survivor	BASO%	15	1.742±1.023	2.128±1.630	1.342±0.811	0.216
Survivour	BASO%	35	1.434±1.0121	1.675±1.317	1.998±2.748	0.446
P value			0.330	0.305	0.371	

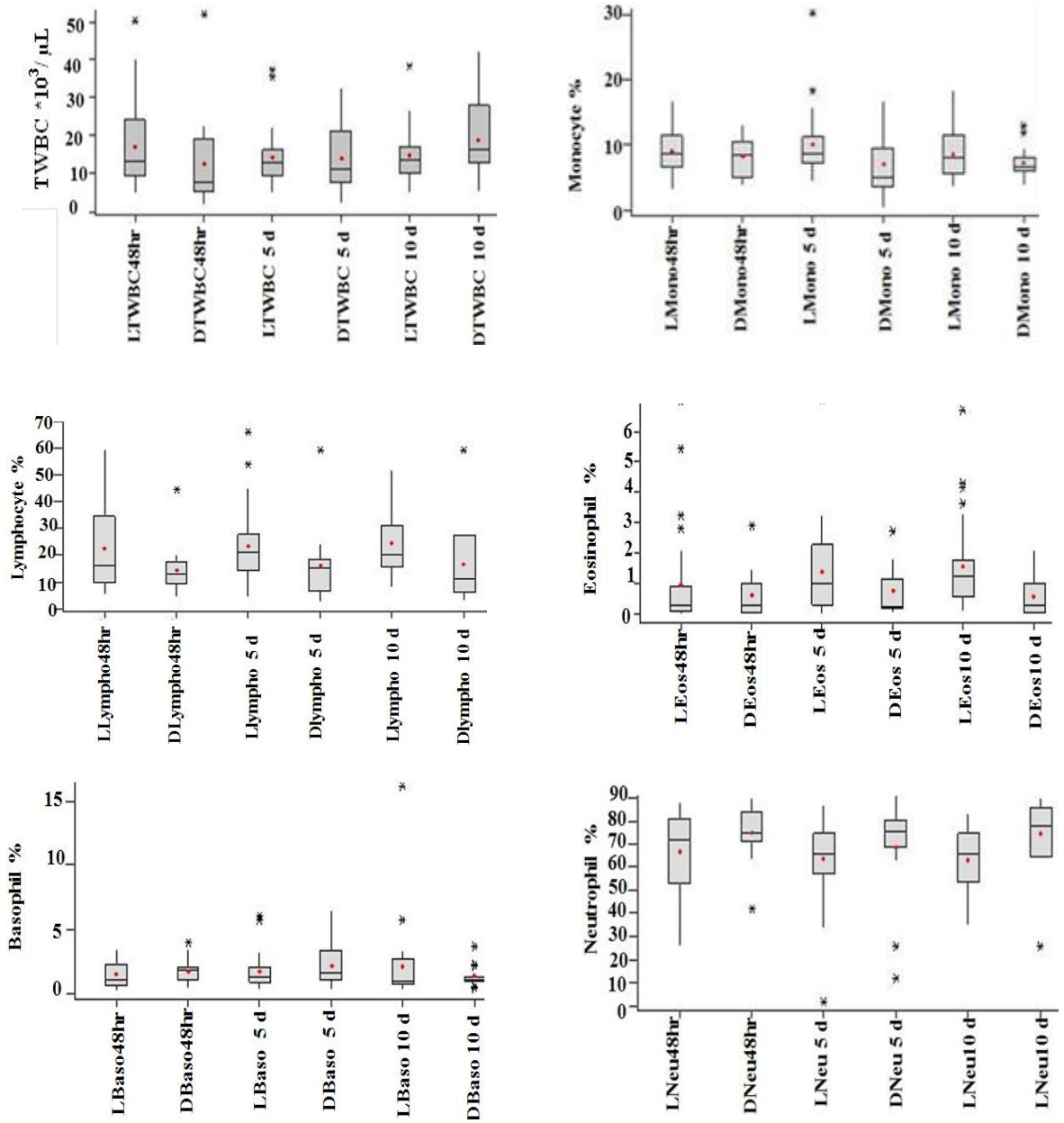

Figure (1): Comparison Of WBC For Survivor And Non-Survivor Groups

Table (3): Mean Of PCT Concentration (Pg/ml) In Survivor And Non-Survivor Groups.

Group	NO.	Mean Of PCT Concentration (pg/ml) ± SD			
		48hr	5thDay	10thDay	P value
Non Survivor	15	773 ± 799	1383± 1972	2638 ± 3013	0.061
Survivor	35	827± 852	724± 573	588 ± 364	0.258
P value		P=0. 837	P = 0.074	P = 0.000**	

*P<0.05= Significant**:** **P<0.01= High Significant**:** P>0.05= Non Significant

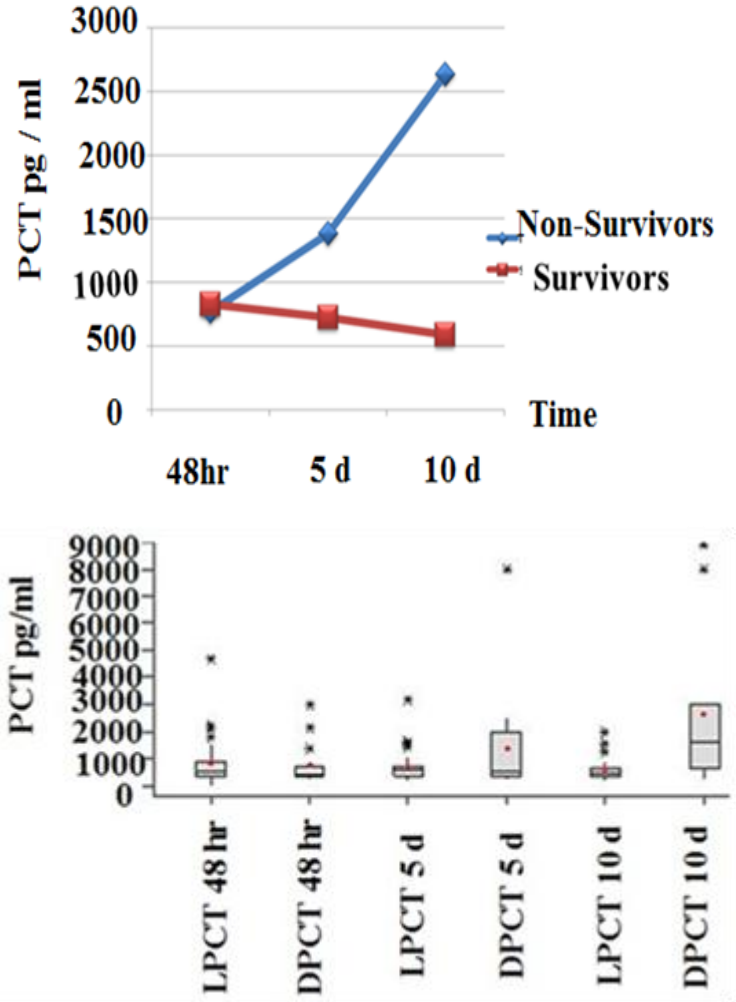

Figure (2): The PCT Concentration (pg/ml) In Correlation With Sampling Time In Survivor And None-Survivor Groups

Table (4): Correlation Coefficient Between PCT And WBC Count In Survivor And Non-Survivor After Burn Injuries For Three Times

	48hr		5th day		10th day	
	Correlation coefficients	P	Correlation coefficient	P	Correlation coefficient	P
Survivor Group	-0.088	0.614	-0.212	0.222	0.064	0.717
Non-Survivor Group	0.298	0.281	-0.163	0.562	-0.193	0.562

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