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ORIGINAL ARTICLE

Comparison of The Accuracy of Some Laboratory Parameters with Blood Culture for Early Detection of Neonatal Sepsis at Zagazig University Children Hospital

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ABSTRACT:

Background: The sepsis in neonates is a blood bacterial infection during the first 28 days of life. There are many common parameters that are widely used to diagnose this disease as levels of white blood cell (WBC), Procalcitonin (PCT) and C- reactive protein (CRP). This work aimed to compare the accuracy of some laboratory parameters with blood culture for early detection of neonatal sepsis at Zagazig university children hospital.

Methods: A case control study was carried out in the neonatal intensive care unit and clinical pathology department at Zagazig University Hospital, during the period from January 2019 to December 2019. This study was conducted on 15 cases had neonatal sepsis and 15 controls. All patients were subjected to the following: history talking, clinical examination, complete blood count with differential count done on peripheral blood film, quantitative measurement of the level of CRP, PCT level, blood culture and Hematological sepsis score (HSS).

Results: Respiratory dysfunction was the commonest clinical presentations of sepsis. There was a significant increase in WBCs among patients than controls. Mean count of platelets in the sepsis group was significantly lowered compared with the controls. There was significant increase in HSS in sepsis group than controls. The most common organism was E. coli. PCT is more accurate in diagnosis of cases followed by CRP and WBCs, respectively.

Conclusions: PCT seems to be an optimal sensitive marker for the diagnosis of neonatal sepsis.

Keywords: Sepsis, Neonatology, Culture

INTRODUCTION

The most serious disease affecting a significant number of newborns is neonatal sepsis which is a blood bacterial infection during the first 28 days of life. The incidence is low (1: 8 cases for every 1,000 live births) **[1]**, with an elevated incidence morbidity and mortality in fifteen to fifty per cent of the cases registered. **[2]**

Neonatal sepsis is divided into two groups based on the time of presentation after birth: early-onset sepsis (EOS) and late-onset sepsis (LOS). EOS refers to sepsis in neonates at or before 72 hours of life (some experts use seven days), and LOS is defined as sepsis occurring at or after 72 hours of life. **[3]**

Neonatal sepsis has symptoms that are mostly indifferent from any other transitional medical problems, like temporary hypothermia, a prolonged shift from fetal to postnatal physiology, temporary hypoglycemia, and transient tachypnea. **[4]**

The most prevalent bacterial organisms are Streptococcus agalactiae, Enterococcus sp., Staphylococcus aureus, Listeria monocytogenes, Escherichia coli, Staphylococcus epidermis **[5]** and Mycoplasmatales that influence the development of the children. **[6]**

There are many common parameters that are widely used to diagnose this disease as levels of white blood cell (WBC), Procalcitonin (PCT) and C- reactive protein (CRP) **[7]**. The aim of this work is to compare

the accuracy of some laboratory parameters with blood culture for early detection of neonatal sepsis at Zagazig university children hospital.

METHODS

Technical design: A case control study was carried out in the neonatal intensive care unit and clinical pathology department at Zagazig University Hospital, during the period from January 2019 to December 2019. This study was conducted on 15 cases had neonatal sepsis and 15 controls. Inclusion criteria included in sepsis group which is the study group (positive blood culture, negative blood culture who were clinically diagnosed with sepsis) and control group (15 apparently healthy subjects cross matched with age and sex) while exclusion criteria included neonatal asphyxia, neonatal respiratory distress syndrome, fetal fecal aspiration syndrome, pulmonary hemorrhage, congenital deformity, and antibiotic treatment before admission.

Upon suspicion of neonatal sepsis, all patients were subjected to the following: history talking, clinical examination, complete blood count with differential count done on peripheral blood film, quantitative measurement of the level of CRP, PCT, blood culture and Hematological sepsis score (HSS). which is assigns a score of one for each of the seven criteria which were total WBC , abnormal total polymorphonuclear neutrophil (PMN) count , abnormal Immature (PMN) count , Immature to total PMN ratio, Immature to mature PMN ratio, Degenerative changes in PMN and Platelet count) found to be significantly associated with sepsis and all scored 1 except the abnormal total count is assigned of 2 instead of 1 if no mature polymorphs are seen on the peripheral. **[8]**. Total score ≥ 3 suggestive of sepsis. Complete blood count was done on automated cell counter by Sysmex XS_500i device with the differential count done on Leishmania - Giemsa stained peripheral. Then, quantitative measurement of the level of C-reactive protein (CRP) using Roche Cobas c 501 device, and Procalcitonin (PCT) levels were analyzed by using Roche Cobasc -411 device. Both are using dedicated reagents from analyzer vendor (Roche diagnostics, Switzer land). The total volume of blood required for CBC is 1.5 ml in tube with EDTA and 1.5 ml blood for CRP and PCT in plain tube. 1 ml blood for Blood culture were systematically collected before initiation of any treatment and done on BaCT/ ALERT 3D 60. CRP levels start in raising within 6 to 8 hours during the infectious episode in neonates and peak at about 24 hours and repeating CRP at 18_24 hours.

Administrative considerations: Written informed consent was obtained from all participants after clear explanation of the study and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (Institutional Research Board "IRB"). The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

STATISTICAL ANALYSIS

The collected data were tabulated and analyzed using SPSS version 24 software (Spss Inc, Chicago, ILL Company). Categorical data were presented as number and percentages. Chi square test (X2) were used to analyze categorical variables. Quantitative data were expressed as mean ± standard deviation, median and range. Student "t" test was used to analyze normally distributed variables among 2 independent groups. Spearman's correlation coefficient (rho) was used to assess correlation between nonparametric variables. ROC curve was used to detect cutoff values with optimum sensitivity and specificity. The accepted level of significance in this work was stated at 0.05 (P <0.05 was considered significant). AUC = area under the curve, the greater the area, the more accurate is the curve, 95% CI of AUC= confidence interval = it is an interval at which the investigator is 95% confident that the true AUC lies. AUC <0.5 → bad. AUC: 0.5-0.69 → fair. AUC: 0.7-0.8 → good. AUC: 0.8- 0.9 → Very good. AUC >0.9 → excellent. **[9]**

RESULTS

There was no statistically significant difference between cases and control regarding Gestational Age (weeks), Postnatal Age, Sex and mode of delivery as shown in (Table 1). On examination there was no statistically significant difference between cases and control regarding Hypothermia. On examination there was statistically significant difference between cases and control regarding prolonged capillary refill rate, Hyperventilation, Tachycardia, Activity as shown in (Table 1). There was no statistically significant difference between cases and control regarding HB, RBCs and HCT. There was statistically significant increase in WBCs and Haematological sepsis score among cases than control. There was statistically significant decrease in platelets among cases than control. There was statistically significant increase in CRP, PCT among cases than control as shown in (Table 2). There was statistically highly significant difference between cases and control regarding culture as shown in

(Table 3). PCT is more accurate in diagnosis of cases followed by CRP and WBCs respectively; however, blood culture seems to be the "gold standard" for infection identification as shown in (Table 4). Accuracy of Blood culture in diagnosis of cases was 100%. the percentage of Sensitivity (100%), Specificity (100%), Positive predictive value % (100%), Negative predictive value % (100%). Accuracy of PCT of cases was 100%. the percentage of Sensitivity (80%), Specificity (100%), Positive predictive value % (100%), Negative predictive value % (83.3%). Figure 1 demonstrated a ROC curve for PCT, CRP and WBCs in diagnosis of cases. Figures 2 and 3 demonstrates a comparison between cases and controls regarding CRP and PCT respectively.

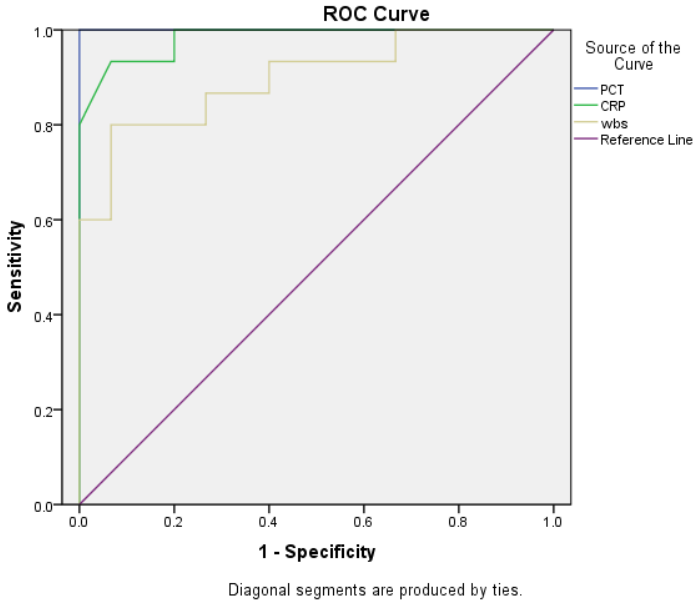

Figure 1: ROC curve for PCT, CRP and WBCs in diagnosis of cases. Quantitative data were expressed as mean ± standard deviation.

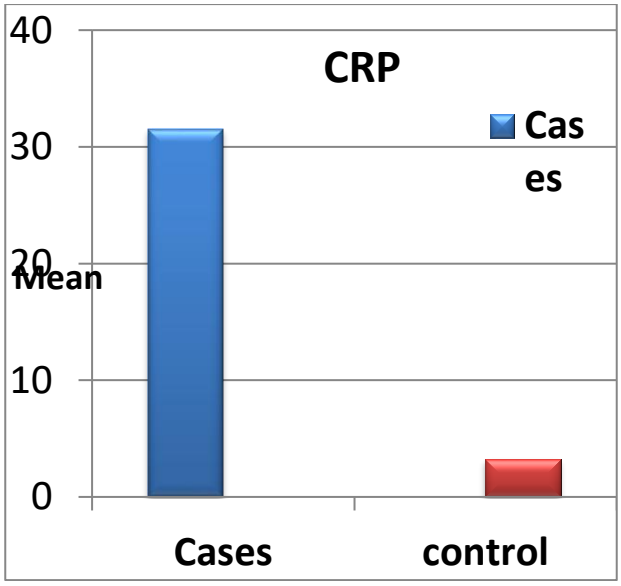

Figure 2: Comparison between cases and control regarding CRP. There was statistically significant increase in CRP among cases than control.

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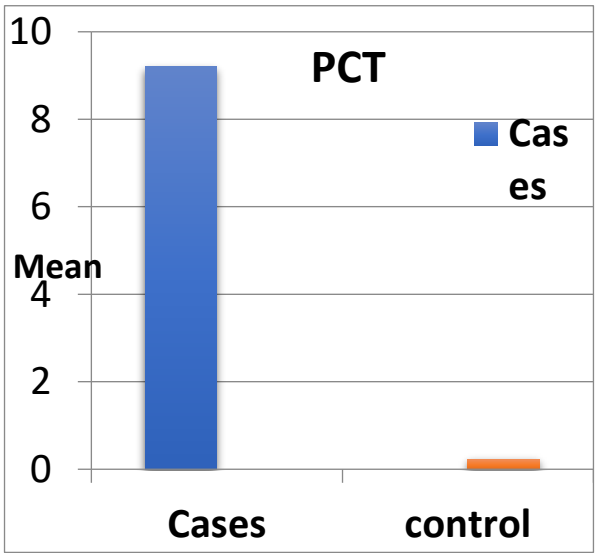

Figure 3: Comparison between cases and control regarding PCT**.** Quantitative data were expressed as mean ± standard deviation. There was statistically significant increase in PCT among cases than control

Table (1): Comparison between cases and control regarding demographic data and finding in clinical examination.

			Cases (No.= 15)	Control (No.= 15)	t.test	P. value
Gestational Age(wks)	**Mean ± SD**		35.67 ± 3.44	37.27 ± 1.67	-1.622-	0.116
Postnatal Age	**Mean ± SD**		11.93 ± 7.06	12.40 ± 9.09	-.157-	0.876
Sex	**Female**	**No.**	8	8	X^2 0.00	1
		%	53.3%	53.3%		
	Male	**No.**	7	7		
		%	46.7%	46.7%		
mode of delivery	**cs**	**No.**	9	8	X^2 0.136	0.713
		%	60.0%	53.3%		
	vaginal	**No.**	6	7		
		%	40.0%	46.7%		
prolonged capillary refill rate	**no**	**No.**	0	15	X^2 30.00	0.000
		%	.0%	100.0%		
	yes	**No.**	15	0		
		%	100.0%	.0%		
Hypothermia	**no**	**No.**	10	13	X^2 1.677	0.195
		%	66.7%	86.7%		
	yes	**No.**	5	2		
		%	33.3%	13.3%		
Hyperventilation	**no**	**No.**	3	15	X^2 20.000	0.000
		%	20.0%	100.0%		
	yes	**No.**	12	0		
		%	80.0%	.0%		
Tachycardia	**no**	**No.**	3	15	X^2 20.000	0.000
		%	20.0%	100.0%		
	yes	**No.**	12	0		

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			Cases (No.= 15)	Control (No.= 15)	t.test	P. value
		%	80.0%	.0%		
Activity	**active**	**No.**	6	0		0.000
		%	40.0%	.0%		
	hypoactive	**No.**	8	0	X^2 26.250	
		%	53.3%	.0%		
	normal	**No.**	1	15		
		%	6.7%	100.0%		

T test was used. P value was set at <0.05 for significant results. Chi square test (X2).

Table (2): Comparison between cases and control regarding CBC and Hematological sepsis score, CRP and PCT.

		Cases (No.= 15)	control No.= 15)(	t.test	P. value
HB	**Mean ± SD**	11.99 ± 3.21	10.79 ± 1.46	1.317	0.198
WBCs	**Mean ± SD**	18.99 ± 6.36	9.68 ± 3.78	4.875	0.000
platelet	**Mean ± SD**	304.87 ± 158.74	387.93 ± 171.27	-1.378-	0.017
RBCs	**Mean ± SD**	3.68 ± 0.91	3.9753 ± 0.63	-1.035-	0.310
HCT	**Mean ± SD**	35.27 ± 9.48	32.71 ± 4.28	0.950	0.350
Hematological sepsis score	**Mean ± SD**	3.67 ± 0.617	1.07 ± 0.79	9.975	0.000
CRP	**Mean ± SD**	31.53 ± 21.18	3.26 ± 3.84	Mann-Whitney U 4	0.000
	Median	23	1		
PCT	**Mean ± SD**	9.20 ± 3.19	0.23 ± 0.13	10.88	0.000

T test was used. P value was set at <0.05 for significant result

Table (3): Comparison between cases and control regarding culture**.**

			cases	control	X^2	P. value
culture	**Acinetobacter**	**No.**	1	0	30.000	.000
		%	6.7%	.0%		
	CONS	**No.**	2	0		
		%	13.3%	.0%		
	E.coli	**No.**	3	0		
		%	20.0%	.0%		
	GPS	**No.**	1	0		
		%	6.7%	.0%		
	klebseilla	**No.**	2	0		
		%	13.3%	.0%		
	MRSA	**No.**	2	0		
		%	13.3%	.0%		
	No Growth	**No.**	0	15		
		%	.0%	100.0%		
	Psaudomonus	**No.**	2	0		
		%	13.3%	.0%		
	staph. Aureus	**No.**	2	0		
		%	13.3%	.0%		

Chi square test (X2).

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Table (4): Accuracy of PCT, CRP and WBCs in comparison with blood culture in diagnosis of neonatal sepsis.

Test Result Variable(s)		Cut off value	Area Under the Curve	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value %
dimension	Blood culture	-	1	100%	100%	100%	100%
	PCT	6.5	1	80%	100%	100%	83.3%
	CRP	12	.981	93.3%	93.3%	93.3%	93.3%
	wbs	13.5	.894	80%	80%	80%	80%

DISCUSSION

In the current study, there was no significant difference between both groups concerning age or sex (p>0.05). These results were in accordance with Bassuoni and colleagues who revealed that the both sex have the same chance of developing neonatal sepsis in their study (male to female ratio is 1:1). **[10]** But Klein demonstrated that the risk of developing sepsis in male infants is more than female ones. **[11]**

In our study, we found that there were no significant differences in gestational age. This was in accordance with that reported by El-Gendy and colleagues who cleared that there were no significant differences in gestational age in his study. **[12]**

In contrast to these results, Bizzarro and colleagues who revealed that most cases of neonates with sepsis had a gestational age that is estimated less than thirty days. **[13]**

This study showed that, there was no statistically significant difference between cases and controls regarding mode of delivery. This agreed with Rass and colleagues who found there was no significant difference between the two groups concerning the method of delivery. **[14]**

On clinical evaluation of the septic group, respiratory dysfunction and hyperventilation, poor suckling and lethargy were the commonest clinical presentations of sepsis (80%, 53.3% and 53.3% respectively). This comes in agreement Payaslı and colleagues who demonstrated that respiratory dysfunction was the widely found symptom of sepsis (eighty per cent in cases). **[15]**

Also, Fathy and colleagues cleared that poor Moro-reflex, poor suckling and lethargy represent 65%, 60%, and 55% respectively between the manifestations of sepsis in their study. **[16]**

Regarding CBC, our results revealed that, there were significant increase in WBCs among patients than controls. Our results agree with El-Mazary and colleagues who found that there was significant increase of WBCs in the group of septic neonates in comparison with control group. **[17]**

In the present work, the mean count of platelets in the sepsis group was significantly lowered compared with the controls. This agrees with El-Mazary and colleagues who studied the platelets in neonatal sepsis. They found a statistically significant decrease in sepsis group than the control one **[17]**. Thrombocytopenia is known to be among the hematological markers of intensity of neonatal sepsis, but a typical number of platelets doesn't exclude the disease. **[18]**

In our study there was significant increase in HSS in sepsis group than controls group. This was in accordance with El-Gendy and colleagues who conducted results that revealed that HSS was notably higher in septic neonates than healthy ones. **[12]**

Regarding, CRP was found significant increase in patients than controls. This agrees with Mondal and colleagues who cleared an increase in CRP level in septic patients. **[19]**

In our study E. coli (20%) Klebsiella was (13.3%), pseudomonas (13.3%), staph aureus (13.3%), CONS (13.3%), MRSA (13.3%) and Acinetobacter (6.7%). This agrees with El-Mashad and colleagues who found that (23.3%) had negative blood cultures and (76.6%) of the case group had positive blood cultures; (36.7%) of these were positive for Klebsiella spp., (16.7%) were positive for Staphylococcus aureus and (13.3%) were positive for E. coli. **[20]**

Boseila and colleagues found that Klebsiella dominated the organisms isolated from the blood

culture in thirty-five per cent of cases followed by Pseudomonas. **[21]**

According to Hashim and colleagues, the difference between results and other studies could be due to the various infection control strategies and limited sample size. **[22]**

In our study showed that, there were statistically significant increase in PCT among cases than control. We also found that PCT is more precise in diagnosis of sepsis followed by CRP and WBCs, respectively. This came to agree with the previous studies by Vercauteren and colleagues that found that PCT had a valuable diagnostic power compared with CRP. **[23]**

In our study we found that Blood culture seems to be the "gold standard" for infection identification. Which come in accordance with Mirrett S, Hanson KE, Reller LB. Who found that blood culture is An ideal diagnostic test for neonatal sepsis should be rapid, sensitive and specific, while providing detection of all organisms relevant in neonatal sepsis and limiting the effects of maternal exposure to antibiotics. **[24]**

CONCLUSIONS AND RECOMMENDATIONS

Blood culture seems to be the "gold standard" for infection identification. PCT seems to be an optimal sensitive marker for the diagnosis of neonatal sepsis. Further studies on large geographical scale and larger sample size to emphasize our conclusion. Many research is necessary to prevent and treat neonatal sepsis to improve clinical outcomes in the susceptible neonates.

Conflict of Interest: None
Financial Disclosure: None declared

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