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ORIGINAL ARTICLE

Prognostic and Diagnostic Value of Pancreatic Stone Protein (PSP) in Septic Intensive Care Unit (ICU) Patients

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ABSTRACT

Keyword: Procalcitonin; CRP; Pancreatic stone protein.

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Background: Sepsis is a condition caused by the dysregulation of the host response to infection, and known as life-threatening organ dysfunction. **Objectives:** To estimate of the pancreatic stone protein level in intensive care unit septic manifestation and prognostic and diagnostic value of pancreatic stone protein. **Subject and methods:** This prospective case control research has been performed at Aswan University Hospital. **Results:** Pearson's correlation coefficients (r) between procalcitonin level and C- reactive protein (CRP) was 0.348, with a strong positive relationship between the two variables. Pearson's correlation coefficients (r) between procalcitonin level and blood culture (positive) were 0.197, with a strong positive relationship between the two variables. Pearson's correlation coefficients (r) between pancreatic stone protein level and blood culture (positive) were -0.098, with a weak negative relationship between the two variables. **Conclusion:** Procalcitonin is a reliable predictor of mortality and a marker for sepsis, while pancreatic stone protein is limited in critically sick cases for diagnosing sepsis, but its performance is comparable to other biomarkers like CRP and PCT.

INTRODUCATION

Sepsis is a condition caused by the dysregulation of the host response to infection, and known as life-threatening organ dysfunction.[1]

This definition integrates the present knowledge of the pathophysiological processes of sepsis and assists in the identification of a subset of infected cases who are at an elevated probability for mortality because of organ damage.

The pathophysiology of sepsis is complex and is influenced by a combination of factors that are correlated to both the microorganism and the host's immune response. The most frequent sequence of events is a hyperinflammatory phase, a persistent inflammation phase, and, subsequently, a suppressive of immunity and catabolic phase. These phases are normally distinguished by a greater susceptibility to nosocomial infections, reactivation of latent viral infections, multiple organ dysfunction, cognitive decreases and long-term functional. [2]

Sepsis remains correlated with recorded death rates of approximately thirty percent, regardless of significant advancements in the treatment of septic shock, organ failures, and sepsis. However,

death rates may be significantly greater based on the healthcare facility's accessibility and geographical location.[3]

At present, the diagnosis of sepsis is primarily determined by nonspecific clinical signs, laboratory results, and medical scores, that are typically obtained following the onset of sepsis. No indicator was determined that has the ability to identify sepsis with an elevated level of diagnostic precision and in a timely manner, regardless of extensive study.[4]

C-reactive protein (CRP) is a well-defined inflammatory biomarker that is frequently utilized to assist in the diagnosis of infection.

In the past two decades, procalcitonin (PCT) was extensively investigated as an indicator for bacterial infection. Although C-reactive protein and procalcitonin are both frequently utilized in the context of sepsis diagnosis, both have demonstrated suboptimal efficacy.[5]

Pancreatic stone protein (PSP) is a C-type lectin protein that has been demonstrated to have proinflammatory activity in vitro and to activate polymorphonuclear cells. [6]

In an unselected cohort of severely sick adults, pancreatic stone protein was determined to be more effective than procalcitonin and other sepsis indicators in determining the precise presence of sepsis. [7]

The objective of this research was to estimate of the pancreatic stone protein concentration in ICU septic manifestation and prognostic and diagnostic value of pancreatic stone protein.

SUBJECT AND METHODS

This prospective case control research has been performed at Aswan university hospital, study duration was 1 year, carried on100 cases which has been classified divided into 2 groups: **Group A**: 50 cases with positive blood culture and **group B** (Control): 50 cases with negative blood culture.

Inclusion criteria: Intensive care unit (ICU) patients with, both sexes, fever, positive blood culture and patients with hospital acquired infection.

Exclusion criteria: cases with community acquired infection.

Methods

All cases have been exposed to Complete history taking, complete physical investigation and laboratory investigation.

Technique

Prepare all reagents, samples, and standards according to the manual's instructions, then add 100 microliters of standard or sample to each well. Incubated for 2.5 hours at room temperature or overnight at four degrees Celsius, then add one hundred microliters of the prepared biotin antibody to each well and incubated for one hour at room temperature. Add one hundred microliters of the prepared streptavidin solution into each well and incubate for forty-five minutes at room temperature. Add one hundred microliters of TMB one-step substrate reagent into each well and incubation for thirty minutes at room temperature. Subsequently, add fifty microliters of stop solution to each well and measure the absorbance at 450 nanometers immediately.

Ethical consideration

The present investigation followed to all regulations set forth by the ethical committee of the Faculty of Medicine at Aswan University. The case has been required to sign an informed consent document containing all required information regarding the research. Enrollment in the investigation was restricted to individuals who provided consent. Participants retained the entire right to withdraw from this investigation at any moment with no providing cause.

Statistical Analysis

All data have been collected, tabulated and statistically examined utilizing SPSS 26.0 for windows (SPSS Inc., Chicago, IL, USA). Qualitative data have been presented by utilizing percent and number. Quantitative data have been presented by utilizing mean, standard deviation, range (minimum and maximum), and median. All statistical comparisons were two-tailed with significance. A $p < 0.001$ represents a highly significant variance, $P > 0.05$ represents a insignificant variance whereas P-value of ≤ 0.05 represents significance. The used tests were: **Chi-square (X2) test of significance** : has been utilized for comparing proportions among qualitative variables. **Independent T-test**: has been utilized for comparing among 2 independent groups with parametric quantitative data. **Pearson correlation coefficient**: utilized to determine the strength of an association is among 2 parameters. **Kruskal wallis test subsequently Dunnes post hoc analysis** for comparison between more than two groups

RESULTS

This table show that age in cases group varied between 7 and 81 with mean ± standard deviations = 54.74 ± 18.65 whereas in control group the age varied between 18 and 85 with mean ± standard deviations = 64.36 ± 15.7 with statistically significant difference (p = 0.006) among both groups. According to sex, statistically insignificant variance was observed among both studied groups (p= 1). (Table 1)

This table show that regarding cause of sepsis, a significant variance was observed among both examined groups (p= 0.021). Hospital stays before sepsis in cases group varied between 3 and 38 with mean ± standard deviations = 10.04 ± 8.04 while in control group the hospital stays before sepsis varied between 3 and 28 with mean ± standard deviations = 8.42 ± 5.15 with statistically insignificant variance (p= 0.233) among both groups. (Table 2)

This table show that procalcitonin in cases group varied between 0.02 to 101 with mean ± standard deviations = 13.02 ± 27.64 while in control group the procalcitonin varied between 0 to 96.4 with mean ± standard deviations = 4.29 ± 14.11 with statistically insignificant variance (p-value = 0.051) among both groups. Pancreatic stone protein in cases group ranged between 0.07 and 0.92 with mean ± SD = 0.21 ± 0.17 while in control group the pancreatic stone protein varied between 0.04 and 0.98 with mean ± standard deviations = 0.25 ± 0.25 with statistically insignificant variance (p= 0.334) among both groups. (Table 3)

This table demonstrated correlation coefficients (r) of the Pearson between procalcitonin level and CRP were 0.348, with a strong positive relationship between the two variables. The correlation coefficients (r) of Pearson between procalcitonin level and blood culture (positive) were 0.197, with a strong positive relationship between the two variables. (Table 4)

This table showed Pearson's correlation coefficients (r) between pancreatic stone protein level and blood culture (Positive) were -0.098, with a weak negative relationship between the two variables. (Table 5)

Statistically significant variance is observed among four groups according to CRP and procalcitonin (p value < 0.05) as level of CRP was the highest among cases surgical group (mean value 238) compared to other groups and mean value was at the lowest level among control medical group. As regard procalcitonin mean value was at the highest level among cases surgical group (mean value 16.2) compared to other groups and mean value was at the lowest level among control surgical group (mean = 0.52). While statistically insignificant variance is observed among four groups according to pancreatic stone protein (p-value > 0.05) however the mean value was the highest among control surgical compared to other groups. (Table 6)

Statistically insignificant variance is observed among the four groups (case medical group, case surgical group, control medical group and control surgical group) regarding outcome (p value < 0.05), however the percentage of died cases was the highest among control surgical group (100% died) and the lowest among cases surgical group (45.5%). (Table 7)

Table (1): General characteristic among the examine groups.

	Cases group (number = fifty)	Control group (number = fifty)	Test of Sig.	p
Age				
Mean ± SD.	**54.74 ± 18.65**	**64.36 ± 15.7**	**t = -2.79**	**0.006**
Median (IQR)	**60 (40.25 - 70)**	**66.5 (55.5 - 76.5)**		
Range (Min-Max)	**74 (7 - 81)**	**67 (18 - 85)**		
Sex				
- **Male**	**32 (64%)**	**32 (64%)**	**X2 = 0**	**1**
- **Female**	**18 (36%)**	**18 (36%)**		

t: Independent T test **IQR:** interquartile range **SD:** standard deviation
χ2: Chi- Square test **p**: p value for comparing between the studied groups
P-value < 0.05: Significant; P-value < 0.001: Highly significant; P-value > 0.05: Non-significant;

Table (2): Cause of sepsis and hospital stay before sepsis among the study groups.

	Cases group (number = fifty)	Control group (number = fifty)	Test of Sig.	p
Cause of sepsis				
- **Medical**	**39 (78%)**	**47 (94%)**	**X2 = 5.316**	**0.021**
- **Surgical**	**11 (22%)**	**3 (6%)**		
Hospital stay before sepsis				
Mean ± SD.	**10.04 ± 8.04**	**8.42 ± 5.15**	**t = 1.2**	**0.233**
Median (IQR)	**9 (3 - 12.75)**	**7 (5 - 11)**		
Range (Min-Max)	**35 (3 - 38)**	**25 (3 - 28)**		

Table (3): Procalcitonin and pancreatic stone protein levels among the study groups.

	Cases group (number = fifty)	Control group (number = fifty)	Test of Sig.	p
Procalcitonin				
Mean ± SD.	**13.02 ± 27.64**	**4.29 ± 14.11**	**t = 1.988**	**0.051**
Median (IQR)	**1.65 (0.45 - 8.18)**	**0.5 (0.08 - 1.57)**		
Range (Min-Max)	**100.98 (0.02 - 101)**	**96.4 (0 - 96.4)**		
Pancreatic stone protein				
Mean ± SD.	**0.21 ± 0.17**	**0.25 ± 0.25**	**t = -0.971**	**0.334**
Median (IQR)	**0.15 (0.12 - 0.2)**	**0.17 (0.12 - 0.24)**		
Range (Min-Max)	**0.85 (0.07 - 0.92)**	**0.94 (0.04 - 0.98)**		

Table (4): Pearson's correlation coefficients (r) between Procalcitonin level and other variables.

	Procalcitonin level	
	Pearson's correlation coefficients (r)	P
CRP		
	0.348	**<0.001**
WBCs		
	0.085	**0.403**
Neutrophile (%)		
	0.128	**0.204**
Lymphocyte (%)		
	-0.095	**0.348**
Blood culture (Positive)		
	0.197	**0.050**
Mortality rate		
	-0.048	**0.637**

Table (5): The correlation coefficients (r)of Pearson among pancreatic stone protein level and other variables.

	Pancreatic stone protein level	
	Pearson's correlation coefficients (r)	P
CRP		
	0.128	0.204
WBCs		
	0.003	0.974
Neutrophile (%)		
	0.119	0.236
Lymphocyte (%)		
	-0.125	0.214
Blood culture (Positive)		
	-0.098	0.334
Mortality rate		
	0.011	0.910

Table (6): Procalcitonin, pancreatic stone protein and CRP levels among the study groups.

	Cases group (number = fifty)		Control group (number = fifty)		P value
	Medical (n=39)	Surgical (n=11)	Medical (n=47)	Surgical (n=3)	
Procalcitonin					
Mean ± SD.	12.8±27.1	16.2±30.3	4.1±14.4	0.52±0.55	0.009*
Median (IQR)	1.5(0.29:8.3)	3.4(1.3:12.7)	0.43(0.07:1.5)	0.37(0.06:0.37)	
Range (Min-Max)	0.2:101	0.56:101	0:96	0.06:1.15	

Post hoc analysis	P1=0.12 P2=0.004* P3=0.17	P4=0.001* P5=0.04*	P6=0.73		
Pancreatic stone protein					
Mean ± SD.	**0.19±0.14**	**0.21±0.23**	**0.24±0.20**	**0.43±0.31**	**0.08**
Median (IQR)	**0.14(0.12:0.19)**	**0.13(0.10:0.19)**	**0.17(0.13:0.25)**	**0.27(0.23:0.27)**	
Range (Min-Max)	**0.04:0.86**	**0.09:0.92**	**0.04:0.98**	**0.24:0.80**	
CRP					
Mean ± SD.	**138.7±97**	**238.4±36.5**	**129±100**	**189±29,8**	**0.006***
Median (IQR)	**110(72.2:248)**	**267(136:315)**	**100(49:223)**	**172(172:172)**	
Range (Min-Max)	**4.2:354**	**127:334**	**0.2:327**	**172:222**	
Post hoc analysis	P1=0.003* P2=0.63 P3=0.26	P4=0.001* P5=0.59	P6=0.19		

_* significant at p value <0.05,
P 1 = p value among cases medical group and case surgical group
P 2 = p value among cases medical group and control medical group
P 3 = p value among cases medical group and control surgical group
P 4 = p value among cases surgical group and control medical group
P 5 = p value among cases surgical group and control surgical group
P 6 = p value among control medical group and control surgical group,
test used is Kruskal Wallis followed by post hoc analysis to differentiate between subgroups.

Table (7): Comparison between different study groups regarding outcome.

	Cases group (number = fifty)		**Control group (number = fifty)**		**P value**
	Medical (n=39)	**Surgical (n=11)**	**Medical (n=47)**	**Surgical (n=3)**	
Outcome					
Died	**27(69.2%)**	**5(45.5%)**	**26(55.3%)**	**3(100%)**	**0.18**
Survived	**12(30.8%)**	**6(54.5%)**	**21(44.7%)**	**0**	

DISCUSSION

Our study shows that in the Cases group, the age varied between 7 to 81. with mean ± standard deviations = 54.74 ± 18.65 whereas in control group the age varied between 18 to 85 with mean ± standard deviations = 64.36 ± 15.7 with statistically significant difference (p = 0.006) among both groups. According to Sex, statistically insignificant variance was observed among both studied groups (p= 1).

Our results were consistent with **García de Guadiana-Romualdo et al.** [8] that stated that mean age in cases group was 66 ± 36 while in control group the mean age was 73 ± 27 with statistically significant variance (p-value = 0·028) among cases with sepsis from other noninfectious causes of SIRS (systemic inflammatory response syndrome). Regarding Sex, statistically insignificant variance was observed among both studied groups (p-value = 0·798).

Our study demonstrated that cause of sepsis and hospital stay before sepsis among the study groups. Regarding cause of sepsis, a significant variance was observed among both studied groups (p-value = 0.021). Hospital stays before sepsis in Cases group varied between 3 and 38 with mean ± standard deviations = 10.04 ± 8.04 while in Control group the Hospital stay before sepsis ranged from 3 to 28 with mean ± SD = 8.42 ± 5.15 with statistically insignificant variance (p-value = 0.233) among both groups.

In contrast with our results, **Pugin et al.** [9] who found that regarding hospital stays, statistically significant rise was observed in hospital stay days in septic ICU patients comparing with non-septic ICU patients. P < 0.0012.

Also, in contrast with our results, **Parlato et al.** [10] found that the ICU hospital stay for sepsis patients were longer than non-septic patients

Our study showed Procalcitonin and pancreatic stone protein levels among the study groups. Procalcitonin in Cases group varied between 0.02 and 101 with mean ± standard deviations = 13.02 ± 27.64 whereas within Control group the Procalcitonin varied between 0 to 96.4 with mean ± standard deviations = 4.29 ± 14.11 with statistically insignificant variance (p-value = 0.051) among both groups. Pancreatic stone protein in Cases group varied between 0.07 to 0.92 with mean ± standard deviations = 0.21 ± 0.17 whereas within Control group the Pancreatic stone protein varied between 0.04 to 0.98 with mean ± standard deviations = 0.25 ± 0.25 with statistically insignificant variance (p= 0.334) among both groups.

In contrast with our results, **García de Guadiana-Romualdo et al.** [8] who observed which concenterations of PCT, and PSP were significantly greater in cases with sepsis compared to within no infected patients.

As well, **Michailides et al.** [11] who stated which a significant variance was observed in the median pancreatic stone protein on admission for cases with sepsis and patients without sepsis (p = 0.037).

Our research showed correlation coefficients (r) of Pearson among Procalcitonin level and other variables. correlation coefficients (r) of Pearson among Procalcitonin level and CRP were 0.348, with a strong positive relationship between the two variables. correlation coefficients (r) of Pearson among Procalcitonin level and Blood culture (Positive) were 0.197, with a strong positive relationship between the two variables.

Our results were consistent with **Bakhshiani et al.** [12] who reported which a significant positive association among the serum Procalcitonin concentrations and CRP within the septic patients (r = 0.515, P = 0.049). Nevertheless, no correlation detected among Procalcitonin level and Leukocytic count (P > 0.05).

Our study showed correlation coefficients (r) of Pearson among pancreatic stone protein concentrations and other variables. correlation coefficients (r) of Pearson among Pancreatic stone

protein concentrations and Blood culture (Positive) were -0.098, with a weak negative relationship between the two variables.

Also, our outcomes were line with **Michailides et al.** [11] who reported which they didn't find a significant association among pancreatic stone protein and any other of the frequently utilized well-known indicators of inflammation (CRP, Ferritin, LDH, Fibrinogen).

In contrast with our outcomes, **Scherr et al.** [13] who found which PSP level showed weak correlation with CRP (r 5 0.15, P 5 .04), and PCT (r 5 0.34, P, .01).

Our study shows that there is statistically significant difference between four groups regarding CRP and procalcitonin (p value < 0.05) as level of CRP was the highest among cases surgical group (mean value 238) compared to other groups and mean value was at the lowest level among control medical group. As regard procalcitonin mean value was at the highest level among cases surgical group (mean value 16.2) compared to other groups and mean value was at the lowest level among control surgical group (mean = 0.52). While there is statistically insignificant variance among four groups according to pancreatic stone protein (p value > 0.05) however the mean value was the highest among control surgical compared to other groups.

Our results were consistent with **Clec'h et al.** [14] who reported that as regard procalcitonin mean value was at the highest level among cases surgical group (mean value 16.2) compared to cases medical group.

Our research shows which statistically insignificant variance among the four groups (case medical group, case surgical group, control medical group and control surgical group) regarding outcome (p value < 0.05), however the percentage of died cases was the highest among control surgical group (100% died) and the lowest among cases surgical group (45.5%).

Our results were consistent with **Clec'h et al.** [14] who stated which statistically insignificant variance was observed among case medical group, and case surgical group regarding outcome (p value < 0.05).

CONCLUSION

Procalcitonin is a good predictor of mortality, Procalcitonin and CRP is a good marker for sepsis.

Pancreatic stone protein is possibly inadequate in critically ill patients for diagnosing of sepsis. PSP performance in the diagnosis of sepsis is, at least, comparable to other indicators (CRP, and PCT)

RECOMMENDATION

Additional research with larger scales is required to verify our findings.

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