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Serum Pentraxin 3 as a Biomarker of Hepatocellular Carcinoma in Egyptian Liver Cirrhotic Patients

Omar Hasan Mohamed *, Mohamed Negm Eldin Salem, Mohamed Mahmoud Abdel-Halim

Department of Hepatology, Gastroenterology and Infectious Diseases, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

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*Corresponding author
Email: mrh77809@gmail.com

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ABSTRACT

Background: Hepatocellular carcinoma [HCC] is the most common primary hepatic cancer in adults, accounting for 70.48% of all liver malignancies in Egypt.

The aim of the work: To assess the potential diagnostic value of serum PTX3 level in Egyptian patients with various stages of liver disease including chronic hepatitis, cirrhosis, and HCC, to assess its potential in distinguishing HCC from cirrhosis.

Patients and Methods: This case control study included 100 patients attending the outpatient clinic of the Hepatology, Gastroenterology and Infectious Diseases Department at Al-Azhar University Hospitals [Al Hussien and Sayed Galal University Hospitals] with various stages of liver disease. Patients were divided into 4 groups: Group 1: 25 patients with chronic hepatitis. Group 2: 25 patients with cirrhosis. Group 3: 25 patients with HCC. Group 4: 25 healthy persons without chronic liver diseases or other comorbidities [e.g. CKD, DM].

Results: PTX3 showed a moderate positive correlation with AST, total bilirubin, and direct bilirubin, and a moderate negative correlation with albumin. PTX3 levels differed significantly between hepatitis B and C patients in the chronic hepatitis group, but not between the cirrhosis and HCC groups.

Conclusion: PTX3 is a good serum biomarker for diagnosing HCC, with 96% sensitivity and 72% specificity at a cutoff of 9 ng/ml.

Keywords: Serum Pentraxin 3; Biomarker; Hepatocellular carcinoma; Liver Cirrhotic Patients.

INTRODUCTION

Hepatocellular carcinoma [HCC] is the commonest primary hepatic cancer in adults. Globally, it is the sixth most common cancer and the third most common cause of cancer mortality. In Egypt, liver malignancy constitutes 11.75% of cancers of all gastrointestinal tract organs and 1.68% of total cancers. HCC represents 70.48% of all liver malignancies among Egyptians. HCC is the ultimate complication of cirrhosis [1].

There is a rise in the incidence of HCC in Egypt; this is attributed to the development of successful screening programs. In addition, there is a rising survival rate of cirrhosis which led to a rise in HCC incidence. Moreover, there is progression of complications of hepatitis C virus [HCV] [2].

Pentraxin 3 [PTX3] is a long pentraxin of the pentraxin superfamily, and it is a typical acute-phase protein. It is connected to innate immunity, inflammation, tissue repair, angiogenesis and tumors [3]. Recent studies linked PTX3 with HCC progression as it was found that PTX3 level is high in tumor tissues, which was related to poor prognosis in HCC [4].

Serum PTX3 is considered an accurate biomarker of fibrosis in chronic HCV infection [5]. Also, high levels of plasma PTX3 was found to be a risk factor for HCC chronic HCV infection [6]. This strong association between PTX3 overe-xpression and HCC proves the role of PTX3 in immunologic dysregulation and inflammation in the pathogenesis of HCC [7].

The aim of this study was to assess potential diagnostic value of serum PTX3 level in patients with various stages of liver disease in Egyptian patients including chronic hepatitis, cirrhosis and HCC to assess the potential diagnostic value in distinguishing HCC from cirrhosis.

PATIENTS AND METHODS

This study was a case control study included 100 patients who attend to outpatient clinic of Hepatology, Gastroenterology and infectious diseases department in Al-Azhar University Hospitals [Al Hussien and Sayed Galal University Hospitals] with various stages of liver diseases including chronic hepatitis, cirrhosis and HCC. Patients were divided into 4 groups as following: Group 1: 25 patients with chronic hepatitis. Group 2: 25 patients with cirrhosis. Group 3: 25 patients with HCC. Group 4: 25 healthy persons without chronic liver diseases or other comorbidities e.g. [CKD, DM].

Inclusion criteria: Age, all adult patients aged more than 18 years, chronic hepatitis, liver cirrhosis and hepatocellular carcinoma.

Exclusion criteria: Age less than 18 and patients with other comorbidities e.g. CKD and cardiac diseases and other chronic autoimmune diseases e.g. systemic lupus erythematous.

Sample size: The sample size was calculated using the formula of **Charan *et al.*** [8], assuming a standard deviation of the outcome = 11, as reported by **Deng *et al.*** [9], a type I error value of 5%, a type II error value of 10%, and an effect size of 10.42 as reported by **Deng *et al.*** [9]. Using this formula, the required sample size per group was calculated to be 23. Adding 10% for potential dropouts, the sample size required per group was 25. Therefore, the total sample size required for the two groups was 100 [25 subjects in each group].

Methods

All patients were subjected to full medical history [sociodemographic characters, history of present illness, Past history and family history]. Examination included general examination [vital signs, appearance, built, decubitus] and local examination [inspection, palpation, percussion, auscultation].

Laboratory tests included complete Blood count, liver functions, random blood sugar, prothrombin [time, concentration and INR], kidney functions tests [urea, creatinine and uric acid, HCV Ab [Enzyme-Linked Immunosorbent Assay - ELISA], serum AFP [Automated Eleceyes], HBV Surface Antigen [ELISA], HBV Core IgG [ELISA] Or Immunoassay], HIV Ab [ELISA] and Serum PTX3 Concentration [Quantikine Human Pentraxin 3 Immunoassay]: [Load patient serum into the immunoassay system, the assay likely used specific antibodies to capture and detect PTX3 and Calibration with known standards ensured accurate concentration measurement].

Imaging: Pelviabdominal ultrasound [US] to assess liver size, Characteristics findings of liver cirrhosis in ultrasound: altered parenchymal echogenicity with coarsened echotexture and surface nodularity, Tri phasic abdominal CT with

contrast [if indicated] and abdominal MRI [if indicated].

Statistical analysis: All statistical analyses were performed using the SPSS statistical package for social science version 25. Descriptive statistics were applied in numerical form [mean, SD or percentages] to describe the quantitative variables. Diagrammatic and tabular forms were used to describe the qualitative variables. Associations between variables were tested for significance by using Chi-square test for categorical variables and the Student [t] test/ ANOVA for continuous variables with normally distributed data. Mean difference was tested by Tukey post hoc test. Non-normally distributed data were tested using Chi-square test for categorical variables and Mann-Whitney U/ Kruskal Wallis tests for continuous variables. Correlations between quantitative variables were assessed using the Pearson's coefficient. Diagnostic accuracy was assessed through estimation of sensitivity, specificity, Positive Predictive Value [PPV] and Negative Predictive Value [NPV], positive likelihood ratio [LR], negative likelihood ratio [LR] and area under the ROC curve. Results were considered statistically significant at a p-value of less than or equal 0.05.

RESULTS

Results of the current work revealed that, patients were diverse [significant differences] regarding patient age, gender, marital status, and chronic medical diseases. However, no significant differences were found regarding residence and smoking. Patients with liver cirrhosis and hepatic cell carcinoma were older than patients with chronic hepatitis and normal group and males were significantly higher among hepatic cell carcinoma than chronic hepatitis or liver cirrhosis. Finally, chronic medical diseases were significantly higher among liver cirrhosis and hepatic cell carcinoma than chronic hepatitis or normal group [Table 1].

In addition, clinical manifestations [pallor, ascites and jaundice] showed statistically significant variances [data not tabulated].

There were statistically significant differences among study groups regarding AFP and PTX3. Alpha-fetoprotein showed the highest concentrations in patients with HCC. In addition, values are higher in chronic hepatitis and liver cirrhosis than the normal group. Similarly, PTX3 showed significantly higher concentrations in HCC and liver cirrhosis than chronic hepatitis and normal group. Interestingly, the chronic hepatitis group had lower values of PTX3 than normal group [Table 2].

Table [3] showed that there is only statistically significant difference of ALT among [Chronic hepatitis group and HCC group, Liver cirrhosis group and HCC group, normal group and HCC group]., P = 0.04, 0.003, 0.002 respectively. There is statistically significant difference of T. Bilirubin between each pair of groups except between hepatic cell carcinoma and liver cirrhosis group [p =0.82]. There is statistically significant difference of AST between each pair of groups. Regarding D. Bilirubin, there is statistically significant difference between each pair of groups except between [Liver cirrhosis group and HCC group, normal group and Liver cirrhosis group] p= 0.56, 0.86 respectively. Finally, there is statistically significant difference of Albumin between each pair of groups except between normal and Chronic hepatitis groups, P =0.13.

Table [4] showed that there was statistically significant difference of INR between each pair of groups except between [Liver cirrhosis group and HCC group – normal group and Chronic hepatitis group], P =0.54, 0.05 respectively. Regarding PT, there was statistically significant difference between each pair of groups except between normal group and Chronic hepatitis group, p= 0.62.

PTX3 was proportionately and significantly correlated with each of AST, total bilirubin, direct bilirubin, INR, PT, RBS, AFP, jaundice, pallor, ascites and hepatic encephalopathy. However, it was inversely and significantly correlated with albumin [Table 5].

The area under the curve [AUC] for PTX3 and AFP showed that, both substances had a good diagnostic power for HCC. However, AFP seems to have a better diagnostic power than PTX3. However, at the cut off value of 9, PTX3 had a better sensitivity but lower specificity. On the other hand, AFP at a cut-off value of 21.65 had lower but good sensitivity with the best specificity [Table 6, figures 1 and 2].

Table [1]: Patient characteristics and risk factors among study groups

	Item	Chronic hepatitis	Liver cirrhosis	Hepatic cell carcinoma	Normal group	Test	p
Age group	20 -30	2 [8%]	0 [0.0%]	0 [0.0%]	14 [56%]	92.52	**<0.001***
	31- 40	6 [24%]	0 [0.0%]	0 [0.0%]	7 [28%]		
	41 -50	9 [36%]	3 [21%]	1 [4%]	1 [4%]		
	51-60	7 [28%]	7 [28%]	11 [44%]	1 [4%]		
	61 -70	1 [4%]	13 [52%]	8 [32%]	2 [8%]		
	71-80	0 [0.0%]	2 [8%]	5 [20%]	0 [0.0%]		
Gender	Male	11 [44%]	9 [36%]	17 [68%]	18 [72%]	9.49	**0.023***
	Female	14 [56%]	16 [64%]	8 [32%]	7 [28%]		
Marital status	Single	3 [12%]	1 [4%]	0 [0%]	9 [36%]	17.24	**<0.001***
	Married	22 [88%]	24 [96%]	25 [100%]	16 [64%]		
Residence	Rural	20 [80%]	18 [72%]	16 [64%]	8 [32%]	1.70	0.63
	Urban	5 [20%]	7 [28%]	9 [36%]	17 [68%]		
Smoking	Yes	6 [24%]	4 [16%]	6 [24%]	5 [20%]	0.66	0.88
	No	19 [76%]	21 [84%]	19 [76%]	20 [80%]		
Chronic medical diseases	Diabetes	2 [8%]	10 [40%]	6 [24%]	2 [8%]	11.00	**0.012***
	Hypertension	5 [20%]	5 [20%]	7 [28%]	4 [16%]		
	None	18 [72%]	10 [40%]	12 [48%]	22 [88%]		

Table [2]: Difference of AFP and PTX3 among study groups

Item	Chronic hepatitis	Liver cirrhosis	Hepatic cell carcinoma	Normal group	test	p
AFP	4.91±3.54	4.72±3.44	187.42±89.34	2.16±1.09	53.34	**<0.001***
PTX3	0.94±0.35	12.25±4.44	17.15±9.17	2.05±0.29	83.13	**<0.001***

Table [3]: Post hoc difference of liver functions among study groups

Study group	ALT			AST			T. Bilirubin			D. Bilirubin			Albumin	
	Mean rank	Z	P value	Mean rank	Z	P value	Mean rank	Z	P value	Mean rank	Z	P value	Mean difference	P value
Chronic hepatitis	27.9	-1.17	0.22	17.28	3.99	0.001*	16.2	4.57	0.001*	16.18	-3.57	0.001*	1.93	0.001*
Liver cirrhosis	23.1			33.72			34.8			34.82				
Chronic hepatitis	21.26	2.05	0.04*	15.76	4.72	0.001*	15.86	4.74	0.001*	18.02	3.75	0.001*	1.57	0.001*
Hepatic cell carcinoma	29.74			35.24			35.14			32.98				
Liver cirrhosis	19.46	2.93	0.003*	20.26	2.54	0.01*	25.02	0.23	0.82	24.3	0.59	0.56	0.36	0.01*
Hepatic cell carcinoma	31.54			30.74			25.98			26.7				
Normal group	21.6	1.9	0.06	20.18	-2.5	0.01*	29.67	-2.13	0.03*	29.86	-2.27	0.02*	0.25	0.13
Chronic hepatitis	29.4			30.82			21.24			21.14				
Normal group	25.02	-0.23	0.82	14.82	-5.19	0.001*	17.6	-3.85	0.001*	22.02	-1.72	0.86	2.18	0.001*
Liver cirrhosis	25.98			36.18			33.4			28.98				
Normal	19.08	-3.12	0.002*	14.3	-5.44	0.001*	16.4	-4.43	0.001*	21.06	-2.16	0.03*	1.82	0.001*
Hepatic cell carcinoma	31.92			36.7			34.6			29.94				

Z by Mann-Whitney Test Mean difference by Tukey post hoc test P<0.05

Table [4]: Post hoc difference of coagulation profile among study groups

Study group	PT			INR		
	Mean rank	Z	P value	Mean rank	Z	P value
Chronic hepatitis group	14.44	- 5.41	0.001*	16.18	- 4.53	**0.001***
Liver cirrhosis group	36.56			34.82		
Chronic hepatitis group	20.1	- 2.66	0.008*	16.44	- 4.41	**0.001***
Hepatic cell carcinoma group	30.9			34.56		
Liver cirrhosis group	30.64	- 2.51	0.01*	26.76	- 0.61	0.54
Hepatic cell carcinoma group	20.36			24.24		
Normal group	26.48	- 0.49	0.62	21.44	- 1.99	0.05
Chronic hepatitis group	24.52			29.56		
Normal group	14.56	- 5.36	0.001*	14.84	- 5.19	**0.001***
Liver cirrhosis group	36.44			36.16		
Normal group	20.8	- 2.33	0.002*	14.94	- 5.14	**0.001***
Hepatic cell carcinoma group	30.2			36.06		

Table [5]: Correlation between PTX3 and other variables among study groups

	PTX3	
	r	P
AST	0.542	**0.001***
ALT	0.073	0.470
Total bilirubin	0.619	**0.001***
Direct bilirubin	0.378	**0.001***
Albumin	- 0.687	**0.001***
INR	0.550	**0.001***
PT	0.443	**0.001***
RBS	0.207	**0.038***
AFP	0.504	**0.038***
Jaundice	0.396	**0.001***
Pallor	0.262	**0.009***
Ascites	0.626	**0.001***
Hepatic encephalopathy	0.866	**0.001***

Table [6]: Diagnostic value of PTX3 and AFP in diagnosis HCC

	[AUC]	P value	Cut off value	Sensitivity	Specificity	LR+	LR-
PTX3	0.887	0.001	9	0.960	0.720	3.43	0.05
AFP	0.976	0.001	21.65	.880	0.987	8.8	0.1

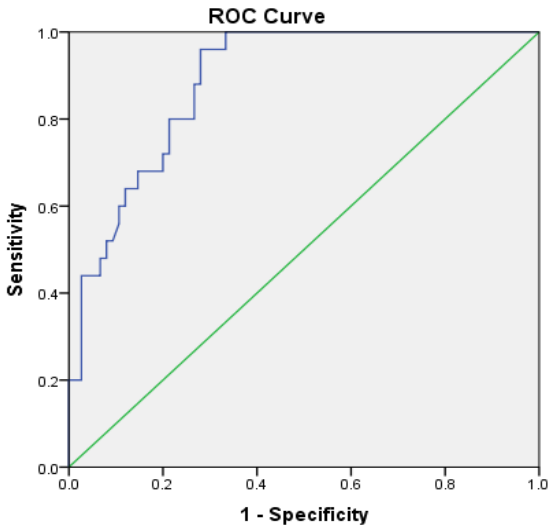

Figure [1]: ROC curve analysis for PTX3 in diagnosis of HCC

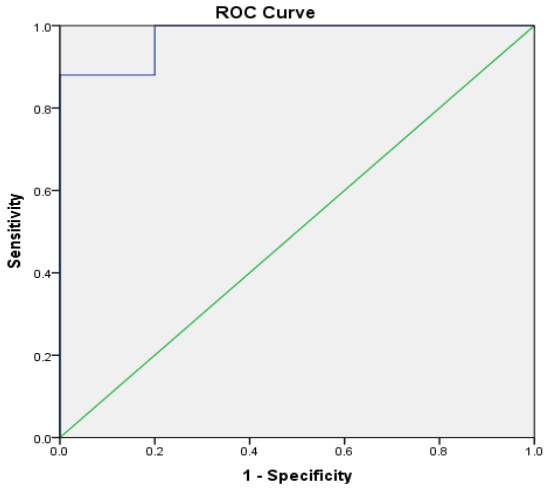

Figure [2]: ROC curve analysis for AFP in diagnosis of HCC

DISCUSSION

Our study revealed that more than half [56%] of normal study group were between 20 -30 years old, while more than half of liver cirrhosis group [52%] were between 60-70 years old, about one third [36%] of Chronic hepatitis group are between 40-50 years old and about half of HCC group [44%] were between 50-60 years old. Regarding the gender of study group, the majority of normal and HCC groups [72%, 68%] respectively are males, while the majority of Hepatitis C and liver cirrhosis group were females [56%, 64%] respectively. Regarding the marital status, more than half of the four study groups were married [64% for normal group, 88% for Chronic hepatitis group, 96% for liver cirrhosis group and 100% for HCC group]. Finally, regarding the resident place the majority of Chronic hepatitis group, liver cirrhosis group and HCC group [80%, 72%, 64%] respectively live in rural areas while the majority of normal group [68%] live in urban area.

Our results are consistent with **Deng *et al.*** [9] who aimed to evaluated whether measurement of serum pentraxin 3 [PTX3] could improve diagnosis of HCC in chronic HBV infection. Their study included HBV-related chronic hepatitis [n = 159], cirrhosis [n = 99] and HCC [n = 107], and healthy controls [n = 151] were analyzed. They reported that there were [male/female, 249/116; age, 41.31 ± 13.69 [18–78] years] and 151 healthy controls [male/female, 97/54; age, 42.28 ± 14.13 [18–76] years]. The male/female ratio and age between patients with chronic HBV infection and healthy controls were comparable [P > 0.05]. Of the 365 patients, 159 [43.6%] were diagnosed with chronic hepatitis, 99 [27.1%] with cirrhosis and 107 [29.3%] with HCC. They reported that there were significance differences between the studied groups regarding age, and gender.

Our findings revealed that the majority of study group are non-smokers [80% for normal group, 76% for chronic hepatitis group, 84% for liver cirrhosis group and 76% for HCC group. The highest percentage [28%] of hypertension is in HCC group while the highest percentage [40%] of diabetes is in liver cirrhosis group. **Wong *et al.*** [10] reported that HCC incidence was greatest among more rural regions.

As well, **Le *et al.*** [11] who reported that hepatocellular carcinoma patients living in the rural area more likely died at home than those living in the urban area, [P = 0.007]. In addition, **Bhattarai *et al.*** [12] reported that a total of 338 [56.4 %] of patients with liver cirrhosis were from rural areas.

Our results agreed with **Carmo *et al.*** [6] reported that diabetes was more prevalent in the HCC group [36.0% P<0.0001]. Moreover, **Gao *et al.*** [13] who reported that there was no significance between patients with liver cirrhosis group and patients without liver cirrhosis group regarding smoking, hypertension and diabetes.

Our findings showed that there is a major increase in the mean of AFP in HCC group [187.42]. The mean of AFP in Chronic hepatitis group [4.91] is more than the mean of AFP mean in liver cirrhosis group [4.72]. Regarding PTX3, HCC group scored the highest mean [12.39] while Chronic hepatitis group scored the lowest mean [0.94]. These results supported

with **Deng *et al.*** [9] who reported that there were significant differences between the studied groups regarding AFP and PTX3, which significantly higher in HCC group. Furthermore, **Carmo *et al.*** [6] demonstrated that there were significant differences between the studied groups regarding AFP, which significantly higher in HCC group.

PTX3 has been revealed to be an extrinsic oncosuppressor in preclinical models and certain tumors through regulating complement-driven macrophage-mediated tumor progression and tuning cancer-related inflammation [3, 13]. **Carmo *et al.*** [6] demonstrated that elevated PTX3 expression has been shown to be associated with poor prognosis in certain cancers, such as Elevated PTX3 plasma level was a risk factor for HCC occurrence in chronic HCV infection.

In HCV-related HCC patients, PTX3 was high compared to non-cancer patients with mild or severe liver fibrosis. Higher PTX3 expression in tumor tissues was also related to poor prognosis in HCC patients [4]. **Narciso-Schiavon *et al.*** [14] who concluded that circulating levels of PTX3 are increased in patients with liver cirrhosis, particularly those with acute decompensation. Serum PTX3 is related to the severity of the disease, the presence of ACLF and 90-day mortality. These results are promising and indicate a potential use for PTX3 as an inflammatory and prognostic biomarker for patients with liver cirrhosis

In the present study revealed that the highest mean of ALT, AST, T. bilirubin, D. bilirubin are in HCC group [47.22, 57.26, 3.95, 2.87] respectively and the lowest mean for ALT and AST is in normal group [23.6, 21.52] respectively. The mean of ALT in liver cirrhosis group [26.28] is less than the mean of ALT in Chronic hepatitis group [32]. The highest mean of Albumin is [4.78] for the normal study group while the lowest mean of Albumin is in liver cirrhosis group [2.59]. Our results are consistent with **Carmo *et al.*** [6] who demonstrated that there were significant differences between the studied groups regarding AST which significantly higher in HCC group. Also, **Deng *et al.*** [9] who reported that there were significant differences between the studied groups regarding ALT, and albumin, which significantly higher in Chronic hepatitis group. Otherwise, they reported that there was no significance between the studied groups regarding AST, and total bilirubin.

Our findings observed that the highest mean [15.36] for PT is in liver cirrhosis group and the lowest mean of PT [10.76] is for Chronic hepatitis group while the highest mean for INR [1.29] is in liver cirrhosis group and HCC group equally and the lowest INR mean [0.96] is in normal group. Our results agreed with **Makram *et al.*** [15] who reported that INR significantly higher in patients with HCC and liver cirrhosis compared to the normal control.

In the present study showed that there was a moderate positive correlation between PTX3 and AST, total bilirubin and direct bilirubin [r = 0.542, 0.619, 0.378 respectively, P value = 0.001], while there is a moderate negative correlation between PTX3 and Albumin [r = -0.687, P = 0.001]. Also revealed that there isn't any correlation between PTX3 and ALT [P value = 0.470]. In contrast with our results **Narciso-Schiavon *et al.*** [14] who demonstrated that there was no correlation between PTX3 and total bilirubin, and albumin.

We found that there is moderate positive correlation between PTX3 and INR, PT [r = 0.550, 0.443 respectively. P value = 0.001] while there is weak positive correlation between PTX3 and RBS [r = 0207, P=0.038]. In contrast with our results **Narciso-Schiavon *et al.*** [14] who demonstrated that there was no correlation between PTX3 and INR. Also, **Napoleone *et al.*** [16] demonstrated that negative correlations of PTX3 with prothrombin time were in accordance with a function of PTX3 in the extrinsic pathway of coagulation.

In the present study showed that there is weak positive correlation between PTX3 and pallor [r=0.262], moderate positive correlation between PTX3 and jaundice, ascites [r = 0.396, 0.626] respectively and there is strong positive correlation between hepatic encephalopathy and PTX3 [r=0.866]. There is moderate positive correlation between jaundice and ascites [r=0.49], jaundice and hepatic encephalopathy [r=0.42] and pallor and hepatic encephalopathy [r= 0.403]. There is a strong positive correlation between ascites and hepatic encephalopathy [r=0.766]. When comparing PTX3 levels in terms of the presence of complications of cirrhosis, similar levels of PTX3 were observed in subjects presenting decompensation in infection [4.5 vs. 3.5 ng/mL; p = 0.197], ascites [4.0 vs. 3.6 ng/mL; p = 0.384] and grades III or IV encephalopathy [4.2 vs. 3.0 ng/mL; p = 0.247] [14].

While **Gurel *et al.*** [17] who reported that PTX3 was neither associated with ascites nor with variceal size.

Our results showed that there is a significant statistical difference in PTX3 levels between hepatitis B and hepatitis C patients in Chronic hepatitis disease group [P=0.033] while there is not any significant statistical difference in PTX3 levels between hepatitis B and hepatitis C patients in liver cirrhosis and hepatic cell carcinoma groups. **Balin *et al.* [18]** who concluded that the chronic hepatitis B CHB patients were found to have lower serum PTX-3 levels compared to the control group, and these levels decreased even further as the stage of fibrosis progressed. In addition, the significant decrease in PTX-3 levels in patients with stage 1 fibrosis compared to the control group shows that PTX-3 can be used as a non-invasive marker for the early detection of fibrosis [P <0.001]. **Chen *et al.*** [19] who reported with PTX3 exhibited good diagnostic performance for the detection of early HCC from HBV chronically infected populations. Whether addition of PTX3 to ultrasound can improve the sensitivity of HCC detection deserves further investigation. Moreover, their study showed that the addition of PTX3 to AFP may allow further identification of HCC in the HBV-related liver diseases. Whether addition of both PTX3 and AFP to ultrasound can further improve the ability and accuracy of HCC detection also deserves investigation.

The present study reported that PTX3 was a good diagnostic test for HCC with cut-off vale 9 ng/ ml, sensitivity 96%, specificity 72% and Area under curve [AUC] was 0.887. AFP was an excellent diagnostic test for HCC with sensitivity 88%, specificity 98.7% and AUC [0.976]. In agreement with our finding **Balin *et al.*** [18] revealed that the AUC of PTX-3 was 0.863, the cut-off value was found to be 9.7 ng/mL, sensitivity was 62.1% and specificity was 91%.PTX-3 has been linked with metastatic risk as it induces EMT in hepatocytes, promotes fibrocyte differentiation and supports cellular invasion [20].

On the opposite, **Feder *et al.*** [21] who found no association between PTX-3 circulating levels and disease severity in individuals diagnosed with hepatocellular carcinoma, but they included a limited cohort in their study as they analyzed the serum of 31 patients.

Conclusion: Patients with chronic hepatitis and HCC had significantly higher PTX3 levels than patients with chronic hepatitis without HCC. Patients with cirrhosis and HCC also had significantly higher PTX3 levels than patients with cirrhosis without HCC. PTX3 is good serum biomarker for HCC with sensitivity 96%, specificity 72% at cut off value 9 ng/ml.

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REFERENCES

1. Holah NS, Al-Azhar D, Aiad AH, Sweed DM. Hepatocellular carcinoma in Egypt: epidemiological and histopathological properties. Menoufia Med J. 2015;28[3]:718-724. doi: 10.4103/1110-2098.167895.
2. Rashed WM, Kandeil MAM, Mahmoud MO, Ezzat S. Hepatocellular Carcinoma [HCC] in Egypt: A comprehensive overview. J Egypt Natl Canc Inst. 2020 Jan 16;32[1]:5. doi: 10.1186/ s43046-020-0016-x.
3. Doni A, Stravalaci M, Inforzato A, Magrini E, Mantovani A, Garlanda C, Bottazzi B. The Long Pentraxin PTX3 as a Link Between Innate Immunity, Tissue Remodeling, and Cancer. Front Immunol. 2019 Apr 4;10:712. doi: 10.3389/ fimmu.2019.00712.
4. Song T, Wang C, Guo C, Liu Q, Zheng X. Pentraxin 3 overexpression accelerated tumor metastasis and indicated poor prognosis in hepatocellular carcinoma via driving epithelial-mesenchymal transition. J Cancer. 2018 Jun 23;9[15]:2650-2658. doi: 10.7150/jca.25188.
5. Górka-Dynysiewicz J, Pazgan-Simon M, Zuwała-Jagiełło J. Accurate prediction of significant liver fibrosis using the Pentra score model in patients with chronic hepatitis C. Pol Arch Intern Med. 2020 Feb;130[2]:112-120. doi: 10.20452/pamw. 15134.
6. Carmo RF, Aroucha D, Vasconcelos LR, Pereira LM, Moura P, Cavalcanti MS. Genetic variation in PTX3 and plasma levels associated with hepatocellular carcinoma in patients with HCV. J Viral Hepat. 2016 Feb;23[2]:116-22. doi: 10. 1111/jvh.12472.
7. Chidambaranathan-Reghupaty S, Fisher PB, Sarkar D. Hepatocellular carcinoma [HCC]: Epidemiology, etiology and molecular classification. Adv Cancer Res. 2021;149:1-61. doi: 10.1016/bs.acr.2020.10.001.
8. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? Indian J Psychol Med. 2013 Apr;35[2]:121-6. doi: 10.4103/0253-7176.116232.

9. Deng H, Fan X, Wang X, Zeng L, Zhang K, Zhang X, *et al.* Serum pentraxin 3 as a biomarker of hepatocellular carcinoma in chronic hepatitis B virus infection. Sci Rep. 2020 Nov 20;10[1]: 20276. doi: 10.1038/s41598-020-77332-3.

10. Wong RJ, Kim D, Ahmed A, Singal AK. Patients with hepatocellular carcinoma from more rural and lower-income households have more advanced tumor stage at diagnosis and significantly higher mortality. Cancer. 2021 Jan 1;127[1]:45-55. doi: 10.1002/cncr.33211.

11. Le DC, Nguyen TM, Nguyen DH, Nguyen DT, Nguyen LTM. Survival Outcome and Prognostic Factors Among Patients With Hepatocellular Carcinoma: A Hospital-Based Study. Clin Med Insights Oncol. 2023 Jun 14;17:11795549231178171. doi: 10.1177/11795549231178171.

12. Bhattarai S, Gyawali M, Dewan KR, Shrestha G. Demographic and Clinical Profile in Patients with Liver Cirrhosis in a Tertiary Care Hospital in Central Nepal. JNMA J Nepal Med Assoc. 2017 Oct-Dec;56[208]:401-6. PMID: 29453469.

13. Gao C, Zhao HC, Li JT, Yao SK. Diabetes mellitus and hepatocellular carcinoma: comparison of Chinese patients with and without HBV-related cirrhosis. World J Gastroenterol. 2010 Sep 21; 16[35]:4467-75. doi: 10.3748/wjg.v16.i35.4467.

14. Narciso-Schiavon JL, Pereira JG, Silva TE, Bansho ETO, Morato EF, Pinheiro JT, *et al.* Circulating levels of pentraxin-3 [PTX3] in patients with liver cirrhosis. Ann Hepatol. 2017; 16[5]:780-787. doi: 10.5604/01.3001.0010.2789.

15. Makram MM, Eskander FG, Khalil FA, Salem NE. Assessment of Serum Aldo-Keto Reductase Family 1 Member B10 for Early Diagnosis of Hepatocellular Carcinoma Patients in Suez Canal University Hospital, Egypt. Afro-Egypt J Infect Endemic Dis. 2023;13[2]:90-100. doi: 10.21608/aeji.2023.193103.1281

16. Napoleone E, Di Santo A, Bastone A, Peri G, Mantovani A, de Gaetano G, Donati MB, Lorenzet R. Long pentraxin PTX3 upregulates tissue factor expression in human endothelial cells: a novel link between vascular inflammation and clotting activation. Arterioscler Thromb Vasc Biol. 2002 May 1;22[5]: 782-7. doi: 10.1161/01.atv.0000012282.39306.64.

17. Gurel H, Genc H, Celebi G, Sertoglu E, Cicek AF, Kayadibi H, Ercin CN, Dogru T. Plasma pentraxin-3 is associated with endothelial dysfunction in non-alcoholic fatty liver disease. Eur Rev Med Pharmacol Sci. 2016 Oct;20[20]:4305-12. PMID: 27831642.

18. Baran A, Stepaniuk A, Kiluk P, Kaminski TW, Maciaszek M, Flisiak I. Potential Predictive Value of Serum Pentraxin 3 and Paraoxonase 1 for Cardiometabolic Disorders Development in Patients with Psoriasis-Preliminary Data. Metabolites. 2022;12[7]:580. doi: 10.3390/metabo12070580.

19. Chen KW, Ou TM, Hsu CW, Horng CT, Lee CC, Tsai YY, *et al.* Current systemic treatment of hepatocellular carcinoma: A review of the literature. World J Hepatol. 2015 Jun 8;7[10]:1412-20. doi: 10.4254/wjh.v7.i10.1412.

20. Cabiati M, Gaggini M, De Simone P, Del Ry S. Data mining of key genes expression in hepato-cellular carcinoma: novel potential biomarkers of diagnosis prognosis or progression. Clin Exp Metastasis. 2022 Aug;39[4]:589-602. doi: 10. 1007/s10585-022-10164-9.

21. Feder S, Haberl EM, Spirk M, Weiss TS, Wiest R, Buechler C. Pentraxin-3 is not related to disease severity in cirrhosis and hepatocellular carcinoma patients. Clin Exp Med. 2020 May;20 [2]:289-297. doi: 10.1007/s10238-020-00617-4.

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