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Role of Osteopontin as a Potential Marker of Hepatocellular Carcinoma

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Abstract

Background: Osteopontin is an important tumor marker, since it presents as an immobilized extracellular matrix molecule in addition to present as a secreted form in body fluids involving plasma. Osteopontin levels in the plasma were found to be significantly higher in Hepatocellular Carcinoma (HCC) patients than in healthy control individuals and also higher than in patients with chronic liver diseases.

Aim of Study: The aim of the present study is to evaluate the role of plasma OPN level as potential markers of HCC among HCV infected patients, compared to AFP. Also, its relationship with clinicopathological features of HCC patients.

Study Design: This is a retrospective case control study.

Subjects and Methods: The study included 100 adult subjects; they were classified in to 4 groups: Group 1: It included 30 apparently healthy individuals (control group). Group 2: It included 30 patients with HCV positive chronic hepatitis. Group 3: It included 20 patients with HCV positive liver cirrhosis without HCC. Group 4: It included 20 patients with HCV positive liver cirrhosis and HCC. Serum Osteopontin was measured by Enzyme-Linked Immunosorbent Assay ELISA.

Results: The mean OPN level was (33.1 ± 16.4) ng/ml, (27.8 ± 13.8) ng/ml, (92.87 ± 18.5) ng/ml and (232.13 ± 59.7) ng/ml for control, HCV, cirrhosis and HCC groups respectively, p-value=0.0010 and there were highly statistical significant differences between the four groups (p<0.001). The mean AFP level was (4.6±2.4) ng/ml, (8.01±2.76) ng/ml, (24.8±25.9) ng/ml and (639±2226.8) ng/ml for control, HCV, cirrhosis and HCC groups respectively, p-value=0.0014 and there were highly statistical significant differences between the four groups (p<0.001).

Conclusion: OPN can be used for diagnosis of HCC and differentiation between HCC and CLD, OPN has higher sensitivity and specificity than AFP and can be used for early diagnosis. Combination of OPN wih AFP has increased both sensitivity and specificity for detection of HCC.

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Key Words: *Hepatocellular carcinoma – Chronic liver disease – Osteopontin.*

Introduction

HEPATOCELLULAR Carcinoma (HCC) represents the major common cause of primary liver cancers and the fourth most frequent type of cancer all over the world following lung, breast and bowel cancers with a growing occurrence, causing one million deaths per year [1].

Owing to the lack of reliable clinical HCC markers, fewer than 20% of patients are diagnosed at a stage where curative treatment can be performed. The poor outcome of patients with HCC is related to the late detection with more than two-thirds of patients diagnosed at advanced stages of disease. Because the poor outcomes of HCC patients are often related to late detection, recent practice guidelines recommend continued surveillance for patients at high risk [2].

Osteopontin is a 314 amino acid phosphoglycoprotein that undergoes extensive post-translational modifications including phosphorylation, glycosylation and cleavage resulting in molecular mass variants ranging from 25 to 75kDa, it is a component of the non-collagenous bone matrix. It was firstly isolated from bone and a variety of calcified tissues [3].

Osteopontin is an important tumor marker, since it presents as an immobilized extracellular matrix molecule in addition to present as a secreted form in body fluids involving plasma. Osteopontin levels in the plasma were found to be significantly higher in HCC patients than in healthy control individuals and also higher than in patients with chronic liver diseases [4].

The levels of OPN increase in HCC tissues when the carcinomas show invasion of bile duct or vascular tissues and intra hepatic spread. In additions patients with high OPN expression have significantly poor overall survival and shorter time to tumor returning (TTR) than the patients with low OPN expression [5].

Subjects and Methods

This retrospective case-control study was carried out at the Clinical Pathology Department, Faculty of Medicine, Menoufia University in the period between January 2018 to April 2019. Patients were selected from outpatients' clinics and inpatients of Internal Medicine Department, Menoufia University Hospitals. Approval for the study was obtained from the Research Ethics Committee. Informed medical consent was obtained from all participants before the study. The study included 100 individuals, divided into 4 groups:

- *Group I:* Included 20 apparently healthy individuals (control group).
- *Group II:* Included 20 patients with HCV positive chronic hepatitis without cirrhosis.
- *Group III:* Included 30 patients with HCV positive liver cirrhosis without HCC.
- *Group IV:* Included 30 patients with HCV positive liver cirrhosis and HCC.

The following patients were excluded from the study:

1- Patients having extra hepatic malignancy.

2- Patients having any bony lesions or inflammatory diseases.

3- Patients with any chronic liver disease other than HCV.

All participants in this study were subjected to complete history taking (previous hepatic disorders, predisposing factors preceding liver disease, age, sex, alcohol intake and blood transfusion), Thorough clinical examination (abdominal examination, jaundice, edema and ascites), imaging studies including abdominal ultrasonography for all patients (liver, spleen, portal vein, ascites) and Triphasic computed tomography for HCC group (HCC size, number, site, portal vein thrombosis).

The subjects were also subjected to the following laboratory investigations:

- Complete Blood Picture (CBC).
- Liver function tests including AST, ALT, albumin, total protein, total bilirubin, direct bilirubin and Prothrombin Time (PT).
- Kidney function tests including blood urea and serum creatinine.
- Viral markers including HBsAg and HCV antibodies.
- PCR for HCV.
- Serum AFP.
- Serum Osteopontin by ELISA.

Sample preparation:

Samples were collected by sterile venipuncture each sample was 8ml from each subject and each sample was distributed as follows:

- 1.8ml blood was collected into tube containing 0.2ml of tri sodium citrate solution to perform PT.
- 2ml blood were collected in tube containing k3-EDTA as an anticoagulant for CBC.

The remaining of the blood was allowed to clot in a plain vacutainer tube at room temperature and the sera were separated by centrifugation. The separated sera were divided and kept in 2 separate sterile plastic tubes. One tube was directly used for performing liver, kidney function tests and viral markers and the second tube was kept frozen at –20ºC to –80ºC and was used for determination of AFP and OPN.

Analytical methods:

- Complete blood count was performed on Sysmex XS-500I from sysmex corporation, Japan.
- Liver and kidney function tests were done on Au-680 autoanalyzer provided by Beckman Coulter/Olympus, Japan.
- Prothrombin time was done on Sysmex CA-1500. autoanalyzer using reagents supplied by Siemens.
- *HBsAg:* The analysis of serum HBsAg was done by electrochemiluminescence immunoassay "ECLIA' on the cobas e 411 immunoassay analyzer from Roche diagnostics.
- *Anti HCV antibody:* The analysis of serum anti HCV antibody was done by "ECLIA' on the cobas e 411 immunoassay analyzer.
- *Serum AFP:* Serum AFP level was measured by ELISA technique supplied by SUNRED ELISA KIT, China.

Serum Osteopontin level was measured by ELISA technique:

The Human OPN ELISA is an in enzyme-linked immunosorbent assay, supplied by SUNRED ELISA KIT, China, for the measurement of human OPN quantitatively. OPN was measured in serum. This assay utilized an antibody particular for human OPN coated on a 96-well plate. We pipetted Standards and samples into the wells and OPN present in a sample was attached to the wells by the immobilized antibody and added biotinylated anti-human OPN antibody. After washing unbound biotinylated antibody away. We pipetted HRP-conjugated streptavidin to the wells. We washed the wells then we added a TMB substrate solution to the wells and the developing color was proportional to the amount of OPN bound, then color was changed from blue to yellow by stop Solution, and we measured the intensity of the color at 450nm.

Serum osteopontin levels were determined and measured by (ELISA) using BIORAD ELISA reader diagnostics (Germany).

Calculation of results:

Standard density was taken as the horizontal, the optical density value for the vertical, the standard curve was drawn on graph paper, corresponding density was founded according to the sample optical density value by the Sample curve.

Statistical analysis:

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data. Quantitative data were represented as number and percentage, mean ± SD, the following tests were used in parametric quantitative independent groups which were student *t*-test in non-parametric normally distributed data while skewed data by Mann Whitney. Differences and association of qualitative variables between two groups by Chi square test (χ^2). While between multiple groups by one way ANOVA for normally distributed data and Kruskal Wallis for skewed data, correlation by Pearson's or Spearman's correlation. *p*-value was set at <0.05 for significant results and <0.001 for high significant result.

Results

Table (1): Statistical comparison between studied groups regarding OPN and AFP.

	Control (n=20)	HCV (n=20)	Cirrhosis (n=30)	HCC (n=30)	F/Kruskal Wallis	*p*-value	Post hoc
OPN (ng/ml):							
Mean ± SD	33.1±16.4	27.8±13.8	92.87±18.5	232.13±59.7	86.9	0.0010	p_1=0.795
Range	15-80	15-65	70-140	150-350			p_2=0.0013
							p_3=0.0012
							p_4=0.0014
							p_5=0.0011
							p_6=0.0013
AFP (ng/ml):							
Mean ± SD	4.6±2.4	8.01±2.76	24.8±25.9	639±2226.8	50	0.0014	p_1=0.06
Range	1.1-9.1	2.5-14.1	6.1-112	4-10945			p_2=0.039
							p_3=0.0014
							p_4=0.037
							p_5=0.0012
							p_6=0.015

OPN : Osteopontin.
AFP : Alfa Fetoprotein.
HCV : Hepatitis C Virus.
HCC : Hepatocellular Carcinoma.
p>0.05 : Non-significant.
p<0.05 : Significant.
p<0.001 : Highly significant.
p_1 : Control & HCV.
p_2 : Control & cirrhosis.
p3: Control & HCC.
p4: HCV & cirrhosis.
p5: HCV & HCC.
p6: Cirrhosis & HCC.

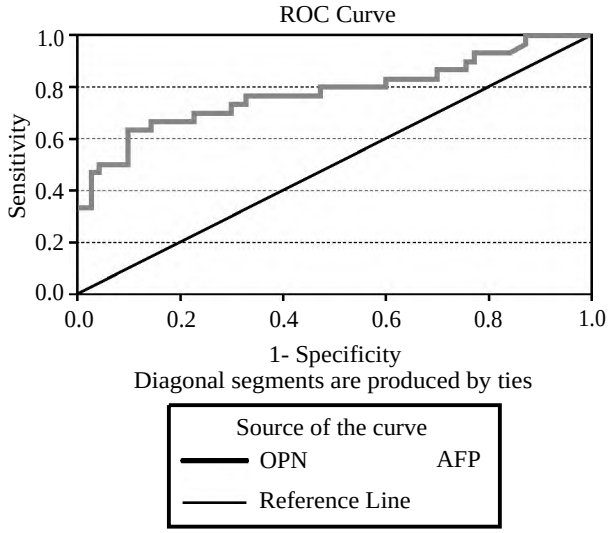

Fig. (1): ROC curve for detection of HCC cutoff.

Table (2): Area under the curve and cut off value of OPN and AFP.

Area under the curve					
Test result Variables	Area	Cutoff	*p*	95% confidence interval	
				Lower Bound	Upper Bound
OPN	1.00	<164.5	0.00**	1.00	1.000
AFP	0.780	<6.5	0.00**	0.669	0.892

This table showed that area under the curve for OPN and AFP was 1.00, 0.776 and cut off values were >164.5 and >6.5 respectively.

Rough AUC guidelines:

0.50-0.60 - Not so good.
0.60-0.75 - Fair.
0.75-0.90 - Good.
0.90-0.97 - Verygood.
0.97-1.00 - Excellent.

Table (3): Sensitivity and specificity of OPN and AFP.

	Sensitivity	Specificity	PPV	NPV	Accuracy
• OPN	92.7%	98.1%	96.7%	98.5%	98.0%
• AFP	80.0%	96.0%	97.0%	92.1%	94.0%
• AFP & OPN	93.4%	98.6%	98.6%	96.7%	96.7%

PPV: Positive Predictive Value.
NPV: Negative Predictive Value.

This table showed sensitivity, specificity of OPN and AFP alone and combined in screening of HCC:

1- For AFP sensitivity and specificity were 80.0% and 96.0% respectively with 97.0% positive predictive value and 92.1 % negative predictive value.
2- For OPN sensitivity and specificity were 92.7% and 98.1% respectively with 96.7% positive predictive value and 98.5% negative predictive value.
3- For combination of AFP and OPN sensitivity and specificity were 93.4% and 98.6% respectively with 98.6% positive predictive value and 96.7% negative predictive value.

The combination of AFP and OPN has increased sensitivity and specificity of AFP for detection of HCC.

Discussion

An increased serum level of OPN was frequented in cases of HCC with a higher expression in the HCC tumor tissues, and beside that, the expression of OPN in the HCC tissue is increased and this suggesting the correlation between the increased level of OPN and the poor prognosis **[6]**.

Studies on OPN tissue expression have shown that OPN is elevated in a number of tumors compared with normal specimens. Moreover, intensity of OPN expression appears to correlate with patients' survival and clinicopathological data **[7]**.

As OPN is a secreted molecule that is found in the circulation and in body fluids, it has been explored as a potential noninvasive biomarker for the diagnosis or progression of cancer **[8]**.

The aim of the present study is to evaluate the role of plasma OPN level as a potential marker of HCC among HCV infected patients, compared to AFP.

This study was carried on 100 subjects classified into 4 groups: Group 1 (control group), included 30 apparently healthy subjects, Group 2 included 30 patients with HCV positive chronic hepatitis (chronic hepatitis C without cirrhosis), Group 3 included 20 patients with HCV positive liver cirrhosis without HCC and Group 4 included 30 patients with HCC.

In the current study the mean age was significantly higher in HCC (59±8.6) and cirrhotic (62.03 ± 11.6) groups than in control (39.8 ± 6.5) and HCV (42.4±6.3) groups with no significant difference between HCC and cirrhotic groups.

The age of HCC patients ranged from 38 to 77 years with a mean ± (SD) was 59.2±8.6 years and this is probably attributed to the duration of the underlying liver disease. These results were in agreement with Salem et al., in which the age of

HCC patients ranged from 39 to 70 years with a mean of 56.7±8.9 years **[9]**. In Keddeas and Aboshady, the age of the patients with HCC ranged from 40 to 72 years **[10]**. also Di Bisceglie stated that HCC is reported to develop in the fifth decade **[11]**. The same results were reported by Johnson, who found that the average age of patients ranged from fifth to sixth decades of life **[12]**.

In contrary to our results, Baghdady et al. reported that the mean age was significantly higher in HCC group (58.7±5.) than in non HCC group (46.72±9) **[13]**.

Our results showed that there were highly significant differences among groups as regard OPN and AFP markers highest in HCC followed by CLD followed by normal levels in control group and HCV group.

The mean of OPN in control, HCV, CLD and HCC groups was (33.1 ± 16.4) ng/ml (27.8± 13.8) ng/ml, (92.87± 18.5) ng/ml and (232.13±59.7) ng/ml respectively, (p-value=0.001).

There was no significant difference between control group and HCV group regarding OPN level (p_1-value=0.795). The mean of OPN in cirrhosis group was highly significantly higher than control group (p_2-value=0.0013). The mean of OPN in HCC group was highly significant higher than control group (p_3-value=0.0012). The mean of OPN in cirrhosis group was highly significant higher than HCV group (p_4-value=0.0014). The mean of OPN in HCC group was highly significant higher than HCV group (p_5-value=0.0011). The mean of OPN in HCC group was highly significant higher than cirrhosis group (p_6-value=0.0013).

The mean of AFP in control, HCV, CLD and HCC groups was (4.6±2.4) ng/ml, (8.01 ±2.76) ng/ml, (24.8±25.90) ng/ml and (639±2226.8) ng/ml respectively, (p-value=0.001).

There was no significant difference between control group and HCV group regarding AFP level (p_1-value=0.06). The mean of AFP in cirrhosis group was significantly higher than control group (p_2-value=0.039). The mean of AFP in HCC group was highly significant higher than control group (p_3-value=0.0014). The mean of AFP in cirrhosis group was significantly higher than HCV group (p_4-value=0.037). The mean of AFP in in HCC group was highly significant higher than HCV group (p_5-value=0.0012). The mean of AFP in HCC group was significantly higher than cirrhosis group (p_6-value=0.015).

These results were similar with those of Fouad et al., who reported that there was statistically significant increase in the serum OPN levels in the HCC group compared to the benign chronic liver disease groups (HCV without cirrhosis, HCV with cirrhosis, fatty liver disease), healthy subjects, OPN was superior to AFP in the selective detection, diagnosis of HCC and in predicting liver cirrhosis [14].

Salem et al., found that: Significant elevation of plasma osteopontin levels and AFP levels in HCC patients than HCV patients' levels and lower levels in normal control group **[9]**. Also Lee et al., reported that elevated osteopontin (OPN) levels in tumor tissues may be indicative of greater malignancy in human Hepatocellular Carcinoma (HCC) [15].

Serum OPN levels were significantly higher in patients with HCC on top of HCV cirrhosis compared to healthy controls ($p \leq 0.009$) with an AUC of 0.853, (95% confidence interval with 85.55% sensitivity and 72.98% specificity) at cut-off level >19.55 (ng/ml) showing significance as a diagnostic marker for the tumor **[16]**.

El-Din Bessa et al., also found that: Plasma levels of OPN and AFP in HCC cirrhotic patients being significantly higher than in cirrhotic patients without HCC and healthy controls **[17]**.

The same was demonstrated in a study by Kim et al., who determined plasma levels of OPN, AFP, in a group of 62 HCC patients, in 60 patients with chronic liver diseases, and in 60 healthy control individuals showing that plasma OPN levels in the HCC patients were significantly higher than those patients with CLD or of a healthy control group **[8]**. The same was demonstrated in a study by Abohalima and Salem who determined plasma levels of OPN, AFP, in 150 subjects. Subjects were divided into three groups: (Group I) include 50 HCV cirrhotic patients with HCC, (group II) include 50 HCV cirrhotic patients without HCC and (Group III) include 50 healthy subjects as control group. The three groups included in the study differed Significantly as regard AFP and OPN levels, with group I (cirrhotic patients with HCC) had significantly higher levels than group II and III (cirrhotic patients without HCC and healthy controls respectively). Also group 2 patients had significantly higher OPN and AFP levels than group 3 (healthy controls) **[18]**. Similar results were also reported by Nabih et al., similarly Zhang et al., **[19,20]**. Abu El-Makarem et al., found that the median plasma OPN level was significantly higher in the HCC

group than in the cirrhotic patients group or in the normal control group [21].

This high increase of plasma OPN level in HCC patients is mainly attributed to the nature of osteopontin as a secreted phosphorylated glycoprotein that is implicated in proliferation and migration of several malignancies including HCC (Xiaobo et al., 2006) [22].

In our study, there was a statistical significant positive correlation between the levels of AFP and OPN (r=0.569 & p=<0.001) and this was in agreement with that of Salem et al., who found that there was significant positive correlation between OPN and AFP and similarly Zhang et al., found that the plasma OPN level positively correlated with the serum AFP concentration [9,20]. Also Abdel-Hafiz et al.,) reported that there was a significant correlation between serum OPN and AFP [16]. However, Kim et al., and Sun et al., found that the correlation between plasma OPN and serum AFP was insignificant and therefore, they had stated that plasma OPN levels might be helpful for the diagnosis of HCC in the patients with non-diagnostic AFP level [8,23].

In our study, there was a statistical significant positive correlation between the age and the levels of AFP and OPN. So the diagnostic performance will be affected by the patients' age. This was similar with Salem et al., who found OPN and AFP showed direct significant correlation with the age of the patients [9]. However most studies disagreed with this fact, as those of Kim et al., and Sun et al.,) [8,23]. This discrepancy may be attributed to the difference in sample size.

The present study showed a positive non-significant correlation between OPN and biochemical liver profiles including AST, ALT while showed significant positive correlation with total bilirubin in HCC group. Kim et al., found that, among HCC patients, median plasma OPN levels were significantly increased in correlation with the degree of liver function deterioration [8]. Salem et al., found that OPN showed direct significant correlation with AST and ALT levels [9]. While it showed inverse significant correlation with total bilirubin. It was explained by as the functional liver status in HCC patients deteriorated, plasma OPN level increased in reverse. Fouad et al., found that OPN showed positive non-significant correlation between OPN and biochemical liver profiles including AST and bilirubin while showed positive significant correlation between OPN and ALT [14].

In our study there was negative non-significant correlation between the levels of OPN and size of focal lesions in HCC group (p-value=0.84). The relation between OPN and tumor size was also studied by Salem et al., and they found that tumors <3cm, present in 40% of patients, showed median plasma OPN level 140 with a range of (100-336 ng/mL), and tumors ›_3cm, present in 60% of patients, showed median plasma OPN level 229 with a range of (131-438ng/mL) (p-value: 0.28) [9]. Zhang et al., also found that tumors ‹5cm showed median plasma OPN level 176.90ng/mL and tumors >5cm showed median plasma OPN level 172.92ng/mL [20]. Also Mohamed et al., (2016), reported that there was no significant correlation between plasma OPN and the size of the tumor [24]. In contrary to our results Abu El Makarem et al., reported that the median plasma OPN level in tumors <5cm was 510ng/mL and in and tumors ›_5cm was 1230 and this was statistically significant (p-value: 0.001) [21].

In our study there was negative non-significant correlation between the levels of OPN and number of focal lesions in HCC group (p-value=0.587).

In contrary to our results Salem et al., Abu El Makarem et al., and Mohamed et al., reported that there was a significant correlation between plasma OPN and number of nodules [9,21,24].

In our study, the sensitivity, specificity, PPV and NPV of plasma OPN levels in HCC patients were 92.7%, 98.1%, 96.7%, and 98.5% respectively at a cut-off value > 164.5. AUC for OPN was 1.00 with CI (1.00-1.000).

For AFP at a cut-off value >6.5ng/ml; the value of sensitivity, specificity, PPV and NPV of plasma AFP levels in HCC patients were 80.0%, 96.0%, 97% and 92.1%. 1respectively. AUC for AFP was 0.780 with CI (0.669-0.892).

Results of our study were in agreement with the study done by El-Din Bessa et al., who reported that the sensitivity and specificity of OPN for HCC diagnosis were 88.3% and 85.6%, respectively, at a cut-off value of 9.3ng/mL with OPN having a greater AUC value (0.918) than AFP (0.712) [17]. Also Kim et al., found that the diagnostic sensitivity and specificity of OPN for HCC was 87% and 82%, respectively (cut-off value: 617.6ng/mL) with OPN had a greater AUC value (0.898) than AFP (0.745) [8].

The meta analysis of seven studies by Wan et al., estimated OPN and AFP sensitivity and specif-

icity as follows: Sensitivity, 0.86 (0.79-0.91) vs. 0.66 (0.53-0.76), specificity, 0.86 (0.69-0.94) vs. 0.95 (0.87-0.98), and the AUC, 0.92 vs. 0.87 **[18,25]**. Also, Nabih et al., ROCs showed that the Area Under the Curve (AUR) for OPN and AFP was 0.824 and 0.730, respectively **[19]**.

A meta-analysis of 8 studies (4 for prognosis and 4 for diagnosis, 1399 patients) was done by Cheng et al., the summary estimates for plasma OPN and AFP in diagnosing HCC in the studies included were as follows for OPN sensitivity, 88% (95% CI: 84%-91%), specificity, 87% (95% CI, 83%-90%) and AUR 0.91 (95% CI, 0.85-0.97) while for AFP, sensitivity was 68% (95% CI: 63%-73%), specificity 97% (95% CI, 94%-99%); and AUR 0.68 (95% CI, 0.45-1.03) **[26]**.

Many studies reported better diagnostic accuracy of OPN over AFP in HCC diagnosis. Abohalima and Salem found that OPN AUR for HCC diagnosis was 0.991 (95% CI: 0.948 to 1.000) and it differed significantly (p=0.01) from AFP AUR (0.889, 95% CI: 0.810 to 0.943). At a cutoff value of OPN > 178ng/ml, the test had sensitivity of 98% and specificity of 96% while AFP at a cutoff value of >185ng/ml had sensitivity and specificity of 86% and 94% respectively in HCC diagnosis **[18]**.

Abu ElMakarem et al., reported AUR for OPN was (0.998; 95% CI: 0.952-1) which was significantly (p=0.0001) higher than that yielded by AFP (0.91; with 95% CI: 0.826-0.961). The sensitivity, specificity, of plasma OPN were 97.67% and 100%, at a cut-off value of 300ng/ml. For AFP at a cut-off value >43ng/mL; the values of sensitivity, specificity, were 74.4% and 100% respectively **[21]**.

In contrary to our results, the plasma levels of OPN show low diagnostic accuracy for HCC compared to AFP. However, OPN may have a complementary role in diagnosing HCC in patients with non-diagnostic levels of AFP **[27]**. Also Zekri et al., reported that OPN levels in HCC patients were not significantly higher than that in those with chronic liver disease **[28]**. Also in another study it was proved that the mean OPN level was not significantly different from HCV patients while both were significantly higher than control group **[29]**. Moreover it was reported that OPN is not a suitable marker for HCC diagnosis in patients with liver cirrhosis of alcoholic etiology because OPN levels increase with disease severity regardless the presence of HCC. These results confirm the lack of useless ness of tumor markers in HCC early diagnosis and reinforce the importance of radiological methods in the surveillance of risky groups **[30]**.

- The sensitivity of OPN and AFP was 92.7% and 80.0% respectively. When AFP was combined with OPN sensitivity was 93.4%.
- The specificity of OPN and AFP was 98.1% and 96.0% respectively. When AFP combined with OPN specificity was 98.6%.

In our study the combination of AFP and OPN has increased sensitivity and specificity for detection of HCC. These results were in agreement with those obtained by Shang et al., who reported that the combination of both markers enhanced the sensitivity and specificity in detecting HCC indicating that these 2 markers are complementary **[31]**.

Collectively, our results indicated that plasma OPN could be used in the selective detection and diagnosis of HCC In conclusion, the results of the current study revealed that the plasma OPN level was elevated in the HCV-related HCC patients by comparison to the benign cirrhotic and non-cirrhotic HCV patients. Also, OPN is relatively comparable to AFP in the detection of HCC among high-risk groups. Although AFP has been considered the golden standard serum marker for HCC for years, in light of our data, the usefulness of AFP testing as the only biomarker for the population at risk should be questioned.

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دور الأستيوبونتين كعلامة محتملة لتشخيص مرض سرطان الكبد

يعتبر الإلتهاب الكبدى (سى) مشكلة طبية خطيرة فى مصر، وهناك علاقة قوية بين الإلتهاب الكبدى الوبائى (سى) وسرطان الكبد، وفى مصر ترتفع معدلات الإصابة بسرطان الكبد لتصل إلى حوالى ٤.٧٪ من إجمالى المصابين بأمراض الكبد المزمنة وبالرغم من أن قياس الألفا فيتو بروتين يعتبر بمثابة دلالة مهمة فى فحص مرضى سرطان الكبد، فقد أشارت بعض التقارير أنه ذات فائدة محدودة فى التفريق بين الأورام الكبدية وبالتالى فقد أقترحت دلالات أخرى لفحص سرطان الكبد. الأوستيوبونتين هو عبارة عن جليكوفسفوبروتين مرتبط بالأنتجرين.

الهدف من هذه الدراسة هو التحقق من إمكانية إستخدام مستوى الأستيوبونتين بوصفة علامة بيولوجية وأهميته الإكلينيكية كدلالة قوية لتشخيص مرضى سرطان الكبد. وقد أجريت هذه الدراسة بقسمى الباثولوجيا الإكلينيكية والباطنة العامة كلية الطب – جامعة المنوفية. إشتملت هذه الدراسة على مائة شخص تم تقسيمهم إلى أربع مجموعات:

- المجموعة الأولى: وتشمل عشرون شخصاً من الأصحاء ليكونوا المجموعة الضابطة.
- المجموعة الثانية: وتشمل عشرون شخصاً مصابون بالإلتهاب الكبدى (سى) إلا أنه لم يحدث التشمع الكبدى.
- المجموعة الثالثة: وتشمل ثلاثون مريضاً مصابون بالتشمع الكبدى.
- المجموعة الرابعة: ثلاثون مريضاً وتشمل المرضى المصابين بسرطان الكبد الناتج بالإلتهاب الكبدى الفيروسى سى.

وقد أسفرت الدراسة الحالية عن الآتى: كان هناك زيادة فى مستوى الأستيوبونيتن فى مرضى ورم الكبد ومرضى التشمع الكبدى بمقارنه بالنسبة الطبيعة فى الأصحاء والمصابون بالإلتهاب الكبدى (سى) غير المصاحب بالتشمع الكبدى ووجد أيضاً أن أعلى نسبة زيادة فى حالات سرطان الكبد ويليها مرضى التشمع الكبدى.

توصيات البحث: الدمج بين الألفافيتوبروتين والأستيوبونتين كمكمل أحدهما للآخر فى تشخيص حالات سرطان الكبد لكى نصل إلى أفضل قيمة حساسية لهما معاً ولكى يزيد دقة التشخيص إلى أفضل قيمة مقارنة بإستخدام كلا منهما على حده.