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Research Article

Biochemical Clinical and Pathological Profile of Pancreatic Head Carcinoma in North Africa

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ABSTRACT

Objective: A statistical clinical assessment of the effects of bilirubin and others hem catalyze biochemical parameters over the main signaling pathways involved in pancreatic head cancer to determine their carcinogenic impact using a molecular approach.

Material and Methods: Patients' data were collected at surgery department Sidi bel Abbes University Hospital (North Africa) patients were diagnosed with pancreatic cancer between 2013 and 2016. The data inclusion criteria were: Age, gender, medical history, surgical history, the year of diagnosis, as well as biological records such as: bilirubin, fibrinogen, creatinine and urea rates.

Results: 44 patients with pancreatic cancer were included in our study (sex ratio=1.75). The mean age was 67.61 years. The most recorded medical history was diabetes with a rate of 43.2%, concerning surgical histories, 27.3% patients underwent a cholecystectomy. M1 was the most common diagnosis stage (27%). 81.81% of patients had hyperbilirubinemia, 6.81% had a normal bilirubinemia, 25% had high level of fibrinogen, 3.6% had a normal level. 77.3% had normal ureanemia, 18.2% had hyper-ureanemia and 15.9% had hypocreatinemia, 68.2% had normal level, 13.6% had hypercreatinemia. We matched patients' groups with bilirubin level using Spearman's correlation test and found a significant P value (P=0.015). We calculated the correlation between bilirubinemia and the stage of diagnosis, using the one-way ANOVA test and we found a significant P value (P=0.013).

Conclusion: Our results represent an interesting shortcut to synthesize specific biochemical antibodies for bio-marking and diagnosis use, or even to lower serum level to reduce cancer aggressiveness.

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Introduction

Pancreatic cancer is one of the leading causes of cancer mortality and one of the most lethal malignant neoplasms across the world [1]. It has been reported that patients with curative resection have longer median survival times (11.5 vs 3.6 months) and higher 5-year survival rates (10.1% vs 3.7%) than patients with inoperable pancreatic cancer [2]. Around 60-70% of pancreatic cancers are located in the pancreatic head, leading to hyperbilirubinaemia caused by obstruction of the central bile

duct in 70-80% of these patients [3, 4]. The prerequisite for the appropriate management of affected patients is to determine clearly the underlying cause of hyperbilirubinaemia. Therefore, a combination of laboratory parameters should be analysed since patterns of abnormalities are more meaningful than elevations or reductions of individual parameters [5].

However, we have noticed that both bilirubin (direct and indirect) had a high level which lead us to raise many questions and mainly about

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hyperbilirubinemia which was mainly present in patients diagnosed with advanced stage of cancer. For a better understanding of this biochemical unbalance, we underwent a retrospective analytical survey as well as a statistical clinical assessment of the effects of bilirubin and others hem catalyze biochemical parameters over the main signaling pathways involved in pancreatic head cancer to determine their carcinogenic impact using a molecular approach.

Material and Methods

I Patient’s Data

We collected patients’ raw data at the level of surgery department of Hassani Abdelkader University Hospital of Sidi bel Abbes region (Western Algeria, North Africa). 44 patients’ medical records diagnosed with pancreatic cancer between 2013 and 2016 were included in our study with a total of 28 men and 16 women (sex ratio=1.75). The mean age at the diagnosis was 67.61 years with a minimum age of 24 and maximum of 86 years. The data inclusion criteria were: Age, gender, medical history, surgical history, the year of diagnosis, as well as biological records such as: bilirubin, fibrinogen, creatinine and urea rates. An absolute confidentiality of the patients’ vital information was maintained for ethical purposes and an ethical approval was obtained from institutions in which the study was carried out.

II Statistical Study

We used SPSS 20.0 (statistical package for the social sciences, IBM Corporation; Chicago; IL; USA; August 2011). The raw data were analysed using rates and cross-tabulations. Pearson’s Chi square (X2) test and non-parametric test helped us to associate different categorical parameters. The P value was the referee to accept or to reject our hypotheses; its limit of significance was the rate of 5%.

Results

Of 44 patients, 28 were men (63.6%) and 16 women (36.4%) with a sex ratio (men/women) of 1.75. It means that pancreatic head cancer is more common in men than women. Our patients belonged to different age groups that is why we have chosen to organize these ranges by 20 years subclasses. As mentioned above, the mean age of diagnosis was 67.61 years with a minimum of 24 and maximum of 86 years. The majority of our patients were aged between 61 and 80 years (Table 1).

As shown in (Table 1), our studied group suffered from several kind of symptoms, the most frequent ones were jaundice, dark urine, discoloured stools, epigastric and hypochondria pain, pruritus, vomiting, fever and chronic diarrhea. The most recorded medical history was diabetes with a rate of 43.2% (19 patients) followed by high blood pressure 27.3% (12 patients) and also some particular cases of rheumatism and hypothyroidism. Concerning surgical histories; 12 patients (27.3%) underwent a cholecystectomy; 13% had hernia surgery while 2.3% had appendectomy.

We found that most of our patients were diagnosed in metastatic stage (M1) (27%) followed by node and tumors stages (N1, T4, T3, T2, T1 and Tis) as illustrated in (Table 1). We reported as well that some

biological rates were above the normal level, i.e. 81.81% of our population had hyperbilirubinemia while 6.81% had a normal bilirubinemia, in the other hand, 25% had high level of fibrinogen while 3.6%) had a normal level. 77.3% of per patients had normal ureanemia while 18.2% had hyper-ureanemia and 15.9% had hypocreatininemia, 30 or 68.2% had normal level while 6 or 13.6% had hypercreatininemia. We matched patients’ groups with bilirubin level using Spearman’s correlation test and found a significant P value (P=0.015). We noticed that most patients with an advanced age expressed a hyperbilirubinemia.

Table 1: Patient’s medical features.

Characteristics	Number of cases	Percentage(%)
Sex (n= 44)		
Male	28	63.6
Female	16	36.4
Sex ratio	-	1.75
Age		
(< 20)	00	00
(21-40)	02	6.5
(41-60)	07	18.2
(61-80)	29	68.7
(80<)	06	16.3
Symptoms and signs		
Jaundice	24	54.5
Epigastric pain	15	34
Right hypocondrium pain	12	27.3
Vomiting and nausea	11	25
Dark Urine	18	50
Pruritus	11	25
Discolored saddle	16	36.3
Chronic diahrea	02	4.5
Fever	02	4.5
Medical histories		
Diabetes	19	43.2
High blood pressure	12	27.3
Rheumatism	01	2.3
Hypothyroidism	01	2.3
Stress	01	2.3
Surgical histories		
Cholecystectomy	12	27.3
Hernia	06	13.6
Appendicectomy	01	2.3
Stage of diagnosis		
Tis	01	2.3
T1	02	0.5
T2	06	13.6
T3	08	18.2
T4	10	22.7
N1	05	11.4
M1	12	27.3

We calculated the correlation between bilirubinemia and the stage of diagnosis, using the one-way ANOVA test and we found a significant P value (P=0.013). Figure 1 shows that most of our patients diagnosed at an early stage had a normal bilirubinemia while those diagnosed at an advanced stage had a hyperbilirubinemia. We tested the quantity of bilirubinemia and hemoglobinemia (Figures 2 & 3). Our null hypothesis

concluded that the distribution of hyperbilirubinemia was the same across categories of hypohemoglobinemia (Figure 3). According to SPSS test, P value was over than 0.5 (P=0.865) which confirms the null hypothesis. The relationship between hem and bilirubin concludes that the enzymes responsible of hem catabolism are over-secreted as well.

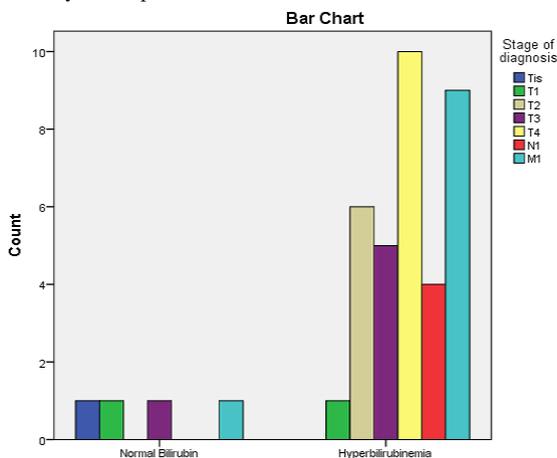


Figure 1: Bilirubinemia distribution according to the stage of diagnosis.

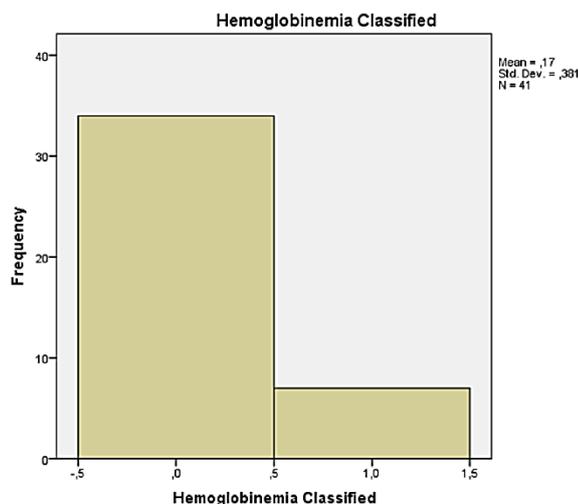


Figure 2: Hemoglobinemia distribution.

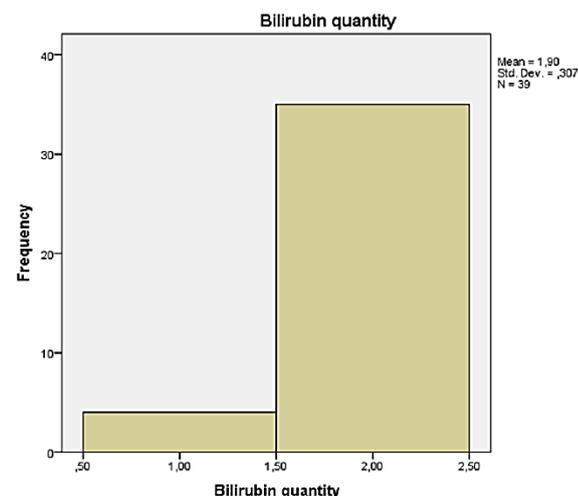


Figure 3: Comparison between Bilirubin and hemoglobin frequencies.

Discussion

28 men and 16 women were involved in our investigation, which confirms that pancreatic cancer affects more men than women. This could be due the fact that men are more likely to have a tobacco and alcohol addictions in North Africa, which represents a major risk factor for pancreatic cancer, several results concords with our findings [6-8]. We noticed that the mean age of our patients was 67.61 years, this advanced age of diagnosis could be explained by the accumulation of many medical histories like diabetes and high blood pressure associated to the specific followed diet, all these are recognized as risk factors for pancreatic cancer which was confirmed other authors [6, 9, 10].

We confirmed the hypothesis that diabetes is associated with the increased risk factor for pancreatic head cancer since it was the most recorded medical history with the rate of 43.18%. Non-insulin dependent diabetes can lead to chronic pancreatitis, which represent also a risk factor for pancreatic cancer [9, 11-13]. Surgical histories were also significant as 27.3% patients underwent a cholecystectomy which is a non-negligible rate; this result matched with those of many authors [14, 15]. This was explained by the fact that cholecystokinin (CCK) plays an important role in pancreatic carcinogenesis as it plays a role of a growth factor for malignant cells. The other important finding was that cholecystokinin A and B receptors are differentially expressed in normal pancreas and pancreatic adenocarcinoma. It was demonstrated that the human CCK-A receptor is selectively expressed by pancreatic adenocarcinoma, but not by normal pancreas [15-17].

We noticed most of our studied group had some common symptoms such as jaundice, dark urine, discoloured saddle, epigastric and hypochondria pain, pruritus and vomiting. The combination of those symptoms associate with radiography and the rate of blood components could be the way to avoid surgery to some patients in the diagnosis of pancreatic cancer. Nonetheless; these symptoms are not specific only to pancreatic cancer; hence, further surveys are required to confirm the diagnosis without surgery [18]. The majority of patients were diagnosed at M1 stage; this could be explained by the very poor means of diagnosis and the lack of health professional during the 90's; the misinterpreted symptoms of that cancer as well as the anatomic deeper site of the pancreas also play a major role [11, 19, 20]. The American Cancer Society stated that more than half of pancreatic cancer patients are diagnosed at an advanced metastatic disease stage, once cancer has spread to other organs due to its deep location [9].

We made a comparative study between the level of hyperbilirubinemia and hypohemoglobinemia and we found that they have similar rates. This study was the first of its kind in our area. We reported that the level of hem oxygenase-1 (HO-1) and carbon monoxide (CO) are also highly expressed by patients with hyperbilirubinemia. The abnormal expression of both HO-1 and CO plays a resistant role into the cells. The ROSs (reactive oxidant species) are present in the body to help the regulation of homeostasis (reduction of oxygen) through the NADPH oxygenase (Nox) and their final product is H2O2 (Hydrogen peroxide), which activates HIF-1 into the cytoplasm in the stress condition to lead cell to hypoxia (Figure 4).

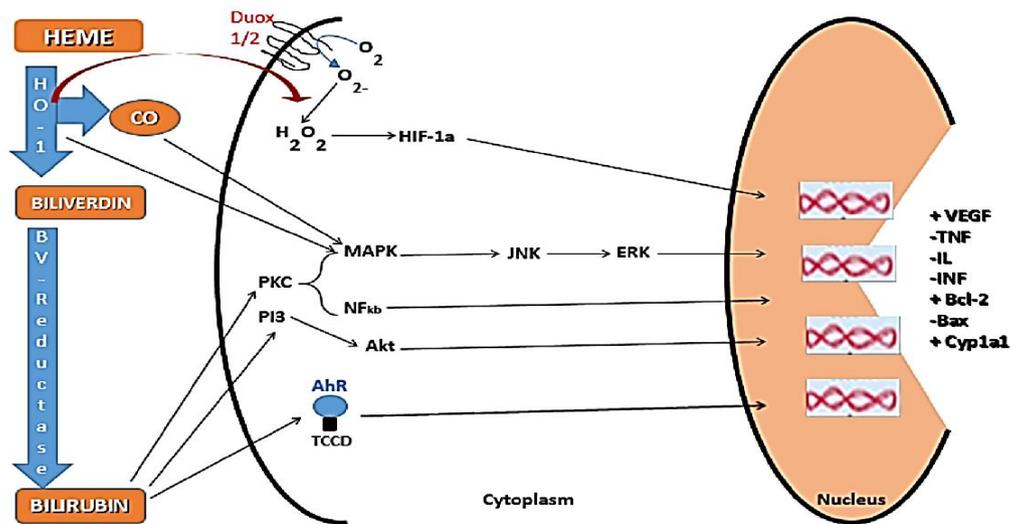


Figure 4: Effects of Hem catabolism products in intracellular signal transduction.

It is undeniable that cancer plays the role of a troublemaker for homeostasis, thus we found that some biochemical compounds were in excess such as bilirubin that was noticeably high in more than 80% of the studied population. This result caught our interest as it could represent an interesting shortcut for researchers to synthesize their specific antibodies for bio-marking and diagnosis use, or even to lower their serum level to reduce cancer aggressiveness [21].

Conclusion

According to the place of pancreatic head cancer among human diseases, researchers continue to focus on the wellbeing of patients. Our study has found an evidence for an association between hyperbilirubinemia and pancreatic head cancer progression by activating the survival and proliferation pathways and inhibiting apoptosis signaling pathway. This result was the first of its kind in our research area and concurs with those of other authors for other types of cancer such as brain and liver.

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Ethical Statement

An absolute confidentiality of the patients' vital information was maintained for ethical purposes and an ethical approval was obtained from institutions in which the study was carried out.

Conflicts of Interest

None.

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