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Assessment of some serum tumor and physiological markers in Beta-Thalassemia major patients in Baghdad province

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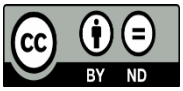
ABSTRACT

Thalassemia major is caused by a mutation in the beta globin gene that impair the production of beta globin chain. There is increased survival of patients with beta thalassemia major due to effective chelating treatment also safe blood transfusion system. This leads to increase to have hepatocellular possibility. In this study 47 patients with beta thalassemia major were randomly selected and Hemoglobin (Hb), White blood cell (WBC), platelets, ferritin level and tumor markers alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA) were investigated. The results indicated there is a positive correlation of serum ferritin with age of patients and only 4 of them have high AFP while for CEA 5 patients have high level. Inconclusion, patients with beta thalassemia with duration time more than 10 years should check these tumor markers to avoid any consequences in the future.



1. Introduction

Thalassemia are heterogeneous groups of inherited disorder in synthesis of Hemoglobin [1]. Generally, the defect of beta chain is the most common genetic disease in Mediterranean region. Decreased or absent beta chain synthesis in patients with beta thalassemia, consequently anemia due to erythroblast desolation in bone marrow and red cells hemolysis in circumferential blood. Beta Thalassemia Major is most severe form of the long-life transfusion dependent anemia that led to several organs' dysfunction mainly due to iron overload [2]. However, the survival of patients with Thalassemia major had been increased mainly due to efficient chelating agents and safer blood transfusions services. In the past, hepatocellular carcinoma was not as widespread, in thalassemia patients as it is today as those patients die younger from heart failure due to iron over load [3]. Cancers of the liver are the seventh most prevalent cancer globally and second causes of cancer mortality [4], [5]. Its incidence increases with advancing age showed higher prevalence in males. The most important risk factors for hepatocellular carcinoma HBV, HCV, obesity, chronic alcohol intake and type 11 diabetes. Data about etiology and treatment outcomes of hepatocellular carcinoma appeared to be very few in patients with Thalassemia dependent transfusion [6], [7]. Moreover, the data about

hepatocellular carcinoma are minimal in the population. In this study, we aim to estimate patients with transfusion dependent Thalassemia patients with alpha fetoprotein and carcinoma embryonic antigen. These two tumor markers were concerned with hepatocellular carcinoma.

2. Material and methods

Patients attending Al-karma center for Thalassemia (47) patients were randomly selected, (27) male and(20) females History was taken from each patient about age, gender, frequency of blood transfusions, family history of Thalassemia, consanguinity, splenectomy and. Other complications. Blood sample were obtained from each patients putting in EDTA tubes for measurement of Hemoglobin WBC, and platelets using hematological autoanalyzer (Mindray c30), after calibration of the instrument. Another tube was gel tubes for serum to do serum ferritin level and the two tumor markers alpha fetoprotein and carcinoembryonic antigens. The estimated tumor markers and ferritin using E411 Roche. Using Roche kits for ferritin and alpha fetoprotein and carcinoembryonic antigens.

3. Results

The total number of Thalassemia patients including in this study 47 patients, 27 males with average age of 14.6 ± 7.3 years and 20 patients were female with average age of 14.1± 5.75. The results indicated that there is a positive correlation (r= +0.336, p-value 0.04) between serum ferritin and the patients participate in this study. however, there is no correlation between WBC, Hemoglobin and platelets count with serum ferritin. As shown in table (1) number of patients with high level of tumor marker AFP, represent four patients out of 47 patients representing 8.5%.

Table 1. Studied tumor marker (AFP) with ferritin, HBV, plat., WBc, and Hb parameters among some thalassemia patients

Age (years)	Gender	Marital status	Hb	WBC	Platelets	Ferritin	HBV	AFP (IU/ml)
11	Female	single	50	10.2	340	1200	-ve	6.38
11	Male	Single	8.8	6.10	313	978	-ve	80.89
11	Male	Single	8.4	4.2	148	11320	-ve	6.61
12	Male	Single	8.0	3.6	225	7294	-ve	7.90

While table (2) identified number of patients with high level of tumor marker CEA five patients out of 47 patients examined in this study that is equal to 10.6%of all patients.

Table 2. Studied tumor marker (CEA) with ferritin, HBV, plat., WBc, and Hb parameters among some thalassemia patients

Age (years)	Gender	Marital status	Hb	WBC	Platelets	Ferritin	HBV	CEA (ng/ml)
16	Female	Married	9.4	5.4	282	7812	-ve	50.40
9	Female	Single	6.2	-	-	3912	-ve	10.50
11	Male	Single	9.6	7.10	253	1650	-ve	7.10
8	Male	Single	6.6	3.3	122	4984	-ve	10.54
7	Male	Single	8.0	6.8	274	3226	-ve	6.68

4. Discussion

In spite of the development of the field's knowledge, there is no published guideline on liver cancers in beta Thalassemia patients had been published [8]. Consequently, for patients the possibility of not getting the finest cares possible because of its rarity. Several in-vitro studies, animals, and human reported excess iron a role in the development of liver cancer [9], [10]. This may occur directly through an impact on cellular proliferation, DNA interaction with the inactivation of tumor suppressor gene, or indirectly by the creation

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of a free radical and reactivated oxygen species that increases the hepatic inflammatory process and fibrogenic processes in the liver. Also, there is proof suggesting the iron overload's immunological effect on lowered immune surveillance for cancer [11]. Regarding AFP the high level which is mildly elevated as reported by the present Study. Approximately patients with AFP more than 400 ng/ml had bigger tumors and about 65% of patients have vascular invasions and 5 years survival was significantly less than those with AFP 20 -400 ng / ml and those with lower than 20 ng/ml [12]. Therefore, higher levels is recognized as an aggressive behavior of hepatocellular carcinoma and associated with a micro vascular invasions, poor cellular differentiation and poor prognosis.

AFP is regarded as tumor marker for hepatocellular carcinoma for a several years however it is elevated in only two thirds of hepatocellular carcinoma patients [13], [14]. AFP is now considered as risk factor of tumor recurrence for liver resection and hepatic transplantation. Considering the tumor marker CEA about 10% of examined patients had mild elevation of the level of CEA. It is well known that it could be elevated in non-malignant conditions like hepatitis liver cirrhosis, smoking, infections, pancreatitis, and hypothyroidism, and inflammatory bowel diseases [15], [16]. Also, this marker is elevated in malignant diseases like hepatobiliary carcinoma, hepatoma colorectal cancer, lung, ovarian, cervical, lung, lymphoma,. CEA level more than 10ng/ml or trending upwards are commonly associated with a malignant condition while level more than 20ng/ml are suspected as metastasis. It is well known that CEA is metabolized by liver. Therefore, biliary obstructions and liver dysfunction were associated with rising level of CEA. If clinical doesn't suspect any particular disease and CEA below 10 ng/ml no further study is recommended. The patients should advise to stop smoking and to repeat the test after 3 months.

5. Conclusion

Patients with beta-thalassemia with duration more than 10 years should undergo investigation for tumor markers especially with liver sources. If the level of CEA are more than 10ng/ml at any stage further investigation like CT scan and PET CT or organ specific investigation are indicated.

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