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# Serum cancer antigen 15.3 concentrations in patients with beta-thalassemia minor compared to those with cancer and healthy individuals

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## Abstract

**Background**: High serum level of cancer antigen 15.3 (CA15.3) has been reported in some malignant and nonmalignant conditions including thalassemia major which could have been resulted from ineffective erythropoiesis. We aimed to evaluate the serum level of CA15.3 in carriers of beta-thalassemia by comparing them with cancer patients and healthy individuals.

**Methods**: This cross-sectional study was done from February to December 2011 in Southern Iran. Participants consisted of 32 subjects with beta-thalassemia minor, 49 with cancer and 25 healthy individuals. The serum levels of CA15.3 were measured and compared in different groups.

**Results**: The serum levels of CA 15.3 in all participants were in the normal range (<35 U/mL). Also it did not significantly differ among various groups of the participants (p=0.723). Age was not significantly correlated with the serum level of CA 15.3 (r= 0.039, p=0.702). The most frequent cancer in the group of patients with malignancies was hematologic malignancies (96%) with the highest frequency for acute lymphoblastic leukemia (37 patients). Frequency of thalassemia minor in patients with cancer was 11 (22.4%).

**Conclusion:** No correlation was found between CA 15.3 serum level with beta-thalssemia minor or with childhood malignancies. Compared to general population, a high proportion of beta-thalssemia minor was observed in patients with cancer in our study. Future prospective studies are needed to evaluate the relationship between cancer and beta-thalassemia minor accurately.

**Keywords**: Beta-thalassemia minor, Cancer, Cancer antigen 15.3.

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## Introduction

Thalassemia minor is the most frequent genetic cause of anemia in the world. Iran is in the thalassemic belt with a frequency of about 6 -10% in the Northern and Southern provinces (1). Cancer antigen 15.3 (CA15.3), a product of MUC1 gene; is an epithelial mucin and its high level is associated with breast cancer. In patients with breast cancer, evaluation of CA15.3 has not been recommended by National Comprehensive Cancer Network guidelines for surveillance purposes, but its monitoring suggested to detect recurrences of cancer evaluating therapeutic response of advanced disease and the assessment of prognosis in patients with early breast cancer (2, 3). Also it may be high in nonmalignant

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conditions such as inflammatory processes and some hematologic disorders like sickle cell anemia and thalassemia major (4). Improving management of thalassemia major has led to increased life expectancy and subsequently increased frequency of age related conditions such as malignancies (5-7). As a result, some investigators have opted to check serum tumor markers in these patients. However, they showed an increased frequency of serum CA15.3 independent from the presence of malignancy in these patients. The suggestive mechanism is erythroid hyperplasia which could result in high level of MUC1 expression on bone marrow-appoptosing progenitor cells (5, 8). Up to our knowledge, evaluation of serum CA15.3 in patients with thalassemia minor has not been conducted. Our hypothesis was that patients with beta-thalassemia minor has a higher serum level of CA15.3 compared to healthy individuals and patients with thalassemia major but with a milder degree. Present study was designed to measure the serum level of CA15.3 in patients with beta-thalassemia minor compared to healthy individuals and to patients with cancer. Also we aimed to determine the frequency of beta-thalassemia minor in a population of young patients with malignancies.

## Methods

In this cross-sectional study, 32 carriers of beta-thalassemia, 25 healthy individuals, and 49 patients with cancer were recruited from February to December 2011. Carriers of beta-thalassemia were non-randomly selected from the volunteers referred for premarital screening in an outpatient clinic affiliated to Shiraz University of Medical Sciences, Southern Iran. All patients with cancer who referred to pediatric hematology-oncology clinic of Shiraz University of Medical Sciences in the study period were recruited. Healthy controls were randomly selected from healthy individuals who referred to pediatric hematology-oncology clinic for checkup examination. Cancer was diagnosed by bone marrow aspiration and tissue pathology examination. Patients with cancer were subdivided to 2 groups of with and without beta-thalassemia minor. In all participants, complete blood count (CBC) and hemoglobin electrophoresis were conducted. The CA 15.3 was checked by CanAg CA 15-3 EIA Kit, Sweden in all participants. The protocol for this study was approved by the Ethics Committee of Shiraz University of Medical Sciences. Written informed consent was obtained from all participants or their parents.

Test of normality was done by Kolmogorov-Smirnov test (CA15.3, $p=0.2$ and age, $p=0.156$). Comparison of serum level of CA15.3 level and age among various groups were done by ANOVA Test. To find the statistically significant difference among different groups, post hoc Tukey HSD Test was performed. Sex distribution was compared among the studied groups using Chi-square test, and p value less than 0.05 was considered statistically significant.

## Results

Participants were divided to 4 groups including: Group 1, beta-thalassemia minor; group 2: patients with cancer and without beta-thalassemia minor; group 3: patients with cancer and beta-thalassemia minor, and group4: healthy individuals. Comparisons of the mean age and sex ratio as well as mean serum CA 15.3 level among the four groups of participants are shown in Table 1.

Carriers of beta-thalassemia were significantly older than the other groups ($p<0.0001$ for comparison of this group with each of the other three groups based on post hoc Tukey HSD Test). Male to female ratio was not significantly different among the studied groups ($p=0.804$). The serum levels of CA 15.3 in all participants were in the normal range (<35 U/mL) and its concentrations shown no significant difference among various groups of the participants ($p=0.723$). Age was not significantly correlated with the serum level of CA 15.3 ($r= 0.039$, $p=0.702$).

Table 1. Comparison of age, sex, and cancer antigen 15.3 concentration among different groups of patients with beta-thalassemia minor, malignancies and healthy controls.

| Groups | Age (year) mean±Sd (range) | Sex m/f | Ca Ag 15-3 (U/mL) mean±Sd (range) |
|---|---|---|---|
| Beta-thalassemia minor (n= 32) | 24.3 ± 7.2 (6-45) | 21/11 | 12.8 ± 4.4 (4.9-21.4) |
| Cancer (n=38) | 12.6 ± 5.4 (1-24) | 29/9 | 12.6 ± 4.6 (3.8-20.8) |
| Cancer and beta-thalassemia minor (n= 11) | 13.6 ± 4.3 (6-20) | 8/3 | 11.1 ± 2.7 (5.2-15.1) |
| Healthy individuals (n=25) | 13.7 ± 5.8 (5-24) | 18/7 | 12.3 ± 4.8 (5-24.5) |
| p value | <0.0001* | 0.804 | 0.723 |

* Statistically significant, Ca Ag 15-3, Cancer antigen 15.3

As shown in Table 2, of 49 patients with cancer, 96% had hematologic malignancies with the highest frequency for acute lymphoblastic leukemia (37 patients). Only three were diagnosed for Wilms tumor, meduloblastoma and neuroblastoma.

Of 49 patients with malignancies 11 (22.4%) diagnosed as thalssemia minor by their CBC and hemoglobin electrophoresis results.

Table2. Distribution of the types of cancers in patients

| Type | Number | % |
|---|---|---|
| ALL | 37 | 76 |
| AML | 3 | 6 |
| Burkittlymphoma | 1 | 2 |
| HL | 1 | 2 |
| NHL | 4 | 8 |
| Wilms tumor | 1 | 2 |
| Meduloblastoma | 1 | 2 |
| Neuroblastoma | 1 | 2 |

Acute lymphoblastic leukemia: (ALL), acute myeloblastic leukemia: (AML), Hodgkin lymphoma: (HL), non Hodgkin lymphoma: (NHL)

## Discussion

We evaluated serum level of CA 15.3 in carriers of beta-thalassemia by comparing them to the three other groups including patients with cancer and those with or without beta-thalassemia minor as well as healthy individuals. We did not find any significant difference with regard to the CA 15.3 concentrations among the groups. These results were against our hypotheses. Moreover, we expected that the higher serum level of CA 15.3 in patients with cancer compared to the reference range. This is in contrast with the results of other reports which showed increased levels of CA 15.3 among patients with solid tumors (9). We could not find any publication that has investigated the serum levels of CA 15.3 in patients with hematologic malignancies. As we mentioned most of our patients had hematologic malignancies and mostly acute lymphoblastic leukemia. This result suggests that the CA 15.3 may not be associated with hematologic malignancies and thus it cannot be used as a tumor marker.

We found a frequency of 22.4% (11 out of 49) of beta-thalassemia minor in the group of patients with malignancies. Compared to the prevalence rate of about 10% in the general population, our results suggest the possible association between beta-thalassemia minor and cancer. Also we observed that most patients with cancer (96%) had hematologic malignancies. Therefore the suggestive mechanism could be shorter life span of red blood cells, and theoretically erythroid hyperplasia secondary to ineffective erythropoiesis which could cause errors in cell division leading to hematologic malignancies. These findings did not support the results of the previous study in our center which showed protective effect of minor thalassemia against childhood malignancies (1).

Our study was limited due to lack of matched matched of carriers for beta-thalassemia with other groups because most of participants in this group selected from persons who were screened for marriage. But other groups were selected from younger children and persons referred to pediatric hematology-oncology clinic. However, we did not find a significant correlation between age and serum CA 15.3

concentration in our participant. Moreover our research was a cross-sectional study and we cannot conclude strongly about the relationship between cancer and beta-thalassemia minor. To document the accurate correlation we need a cohort study for this matter. Moreover, during the course of our study, most of our patients in the cancer group had hematologic malignancies.

## Conclusion

The values of CA 15.3 serum levels were in the normal range for both in carriers of beta-thalassemia and in patients with malignancies. No correlation was found between CA 15.3 serum level with thalssemia minor or with childhood malignancies. Compared to normal population, a high proportion (22.4%) of thalssemia minor was observed in patients with cancer in our study. Future prospective studies are needed to evaluate the relationship between cancer and beta-thalassemia minor accurately.

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All authors declare that they have no conflict of interest.

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