Electrocardiographic changes among beta-thalassemia patients in Baquabah teaching hospital

A Research Submitted in Partial Fulfillment of the Requirements for the Degree of Bachelor in Medicine at University of Diyala

By

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Acknowledgement

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ABSTRACT

Thalassemia is group of genetic disorder ranging from mild sing and symptoms to severe type which required transfusion of blood continuously , mainly the disordered occur with in bone marrow production by defect on alpha or beta chain production and calcified to three major groups thalassemia Mainor appear with exhaustion or infection of the body to thalassemia intermediate or non-dependent transfusion type to most severe one which it is dependent transfusion or thalassemia major

Reasonably most severe one come with most complication and that type of disorder effecting in all tissue body including the heart which our subject searching around it .

Ferritin in serum concentration of thalassemia patients used to screen consequences of iron overload in thalassemia patients. The study is aimed to defined the best preferred point of ferritin to screen for cardiac hemosiderosis changes in EKG in these cases. The study divided into three groups of people thalassemia major , thalassemia Intermediate, and controlled people to show the difference between them. Study -based on patients living throughout Baqubah teaching hospital ,Diyala , Iraq . this is diagnostic research, index test was serum ferritin levels measured by chemiluminescent immunoassay , EKG electrode for monitoring cardiac hemosiderosis. A tip point of 9893 ng/dl for ferritin and thelowermost107ng/dl .

Introduction

β-thalassemia is an hereditary disease preferred by a lack of β-chain globin production , hemolysis of RBC , ineffective erythropoiesis occur due to imbalanced between beta globin chain producing accumulation of excessive beta chain in early erythroid precursor this lead to generation of fetal anemia usually associated with splenomegaly and extramedullary hemopoisis

B-thalassemia including 3 main types classified according to amount of reduction of beta chain ranging from beta thalassemia minor (have only mild anemia without any other feature) to thalassemia Intermediate non-transfusion-dependent thalassemia (NTDT) to (thalassemia major) transfusion-dependent thalassemia (TDT).
iron overload one of the most common complication seen in patient with beta thalassemia major that appear due to iron hypersensitivity for absorption from intestine to hemoglobin instability , lack of production , anemia and hypoxia drive erythropoietin and red-cell transfusion is well-documented as the most problematic issues, bringing severally ramifications to these patients, such as cardiac hemosiderosis

Sincerely cardiac hemosiderosis, especially the moderate-to-severe one, as the evident signs of iron overload, have been the most clinical concerns and also the primary causes of mortality in population, thalassemia must be screened for these severe adverse complications. Various indices and methods are utilized to assess iron levels in these patients, including serum markers of labile iron (ferritin and transferrin saturation) and EKG a trusted measurement estimating the levels of iron deposit in the heart.

Besides a rather unavailability, MRI have been expensive assay, rending introducing the ferritin test as an alternative test to screen organs involved by hemosiderosis in such an iron-overloaded condition . Although serum ferritin reflects iron stores, its values are unreliable in the case of some concomitant illnesses surging ferritin level, including malignancies, infectious diseases, hepatitis, and critical and inflammatory diseases.

Congestive heart failure is the leading cause of morbidity and mortality in these population and sudden cardiac death can also occur, even in the absence of known cardiac dysfunction

The ferritin test is a non-specific test providing different sensitivities and specificities at dissimilar cut off points for evaluating cardiac hemosiderosis in multiple studies. Clinical sequelae, such as heart failure, cardiac dysrhythmia, and pulmonary hypertension from transfusion iron accumulation, still prevail in thalassemia patients. In contrast, no consensus exists on the optimum cut off of ferritin for screen cardiac hemosiderosis. Moreover, maintaining serum ferritin levels below the best cut off may determine the incidence of cardiac hemosiderosis for these cases. A ferritin levels between 1500 and 2500 ng/mL have been proposed to early predict cardiac hemosiderosis amid thalassemia, therefore, we decided to determine the cutoff point and diagnostic test values of the serum ferritin test to evaluate cardiac and liver hemosiderosis in this population.

Monitoring cardiac function with echocardiography is the standard of care for TM patients, however, diastolic and systolic dysfunction are later signs of iron overload .
Monitoring for rhythm disturbances is done using electrocardiography (ECG)

Thus the goal of this study was to determine whether standard 12 lead electrocardiogram analysis could be used to “predict” cardiac iron deposition. Specifically, we hypothesized that many of the nonspecific changes observed in electrocardiograms from thalassemia major patients would be relatively more common in those with cardiac iron overload.

Material and methods

Ethical consideration

The study was approved by the Ethics Committee and Institutional Review Board (IRB) of Diayla University of Medical college , Iraq . The university based on the study protocol, and all methods was performed in accordance with the relevant guidelines and regulations. After taking informed consent from the patients , their parents and guardians, patients' medical files was registered in the online database. The cases kept sure their information would be confidential and their identity will not reveal under any circumstances.

Study design and patients

The current study were diagnostic accuracy performed cross-sectionally through data recording (from October 2022 to February 2023) in the Baqubah blood center in which 50 users have registered information concerning β-thalassemia cases in different cities across Baqubah province. The study population included patients who had been entered with the definitive diagnosis of thalassemia in the registry located Baqubah Hospital, Diyala, Iraq . The data comprised patients' demographic , laboratory, which are available on your kind .

Inclusion criteria

The inclusion criterion were documented β-thalassemia from both type NTDT (thalassemia Intermediate) and TDT (thalassemia major) and normal hemoglobin people as control . A long side clinical manifestations, genetic tests and first hemoglobin electrophoresis contribute to confirming the diagnosis. The lack of ferritin test results and EKG data on the heart was considered the criteria.

Data collection

Variables included demographic data, such as age, sex,ferritin levels (ng/mL) , hemoglobin level (g/dL) , history of splenectomy, hepatomegaly, dependency on red-cell transfusion, use of hydroxyurea, deferiprone (DFP), deferoxamine (DFO), deferasirox (DFX), vitamin D3 supplementation, folic acid, the severity of cardiac hemosiderosis.

Statistical analysis

Our goal of the research is identifying the ECG change than preclude the iron position and my sample divided into two group based on T2* more than 20 (cardiac iron deposition) or T2* below than 20 (no cardiac iron)

Bases on age and gender and duration of treatment for anti-iron drugs , change on ECG reading

75 cases enrolled in study aging from 2-40 years , all cases from the same ethnic group and the geno-type were not present for all

Mean ± standard deviation or number (percentage) was used to present the results. The independent student's t- and chi-square tests were applied to compare the variables between two groups, cardiac hemosiderosis and non-cardiac hemosiderosis. A receiver operating characteristic (ROC) analysis was run using serum ferritin levels as an index test alongside any grade of cardiac hemosiderosis and moderate-to-severe cardiac hemosiderosis as the adverse events. The optimum cutoff points, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) . After finding the best cutoff

points of serum ferritin levels, the values were categorized and turned into dichotomous variables. Then, logistic regression was utilized to reckon the odds ratio (OR)

Next, the impact of multiple potential confounders, including age, red-cell transfusion dependency, DFP, DFO, DFX were controlled to estimate an adjusted OR. Ultimately, sub-group analyses were implemented based on splenectomized and non-splenectomized cases and iron chelators to define the best cutoff point for each sub-category.

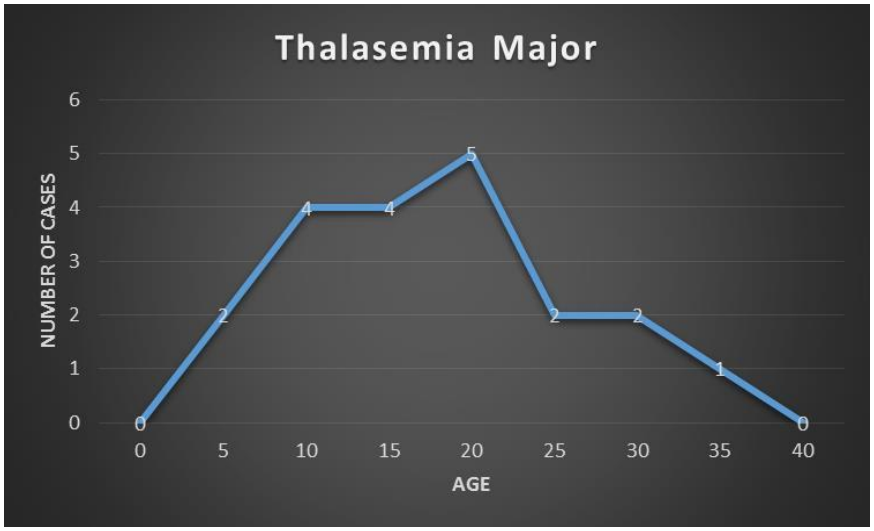

Figure 1-1

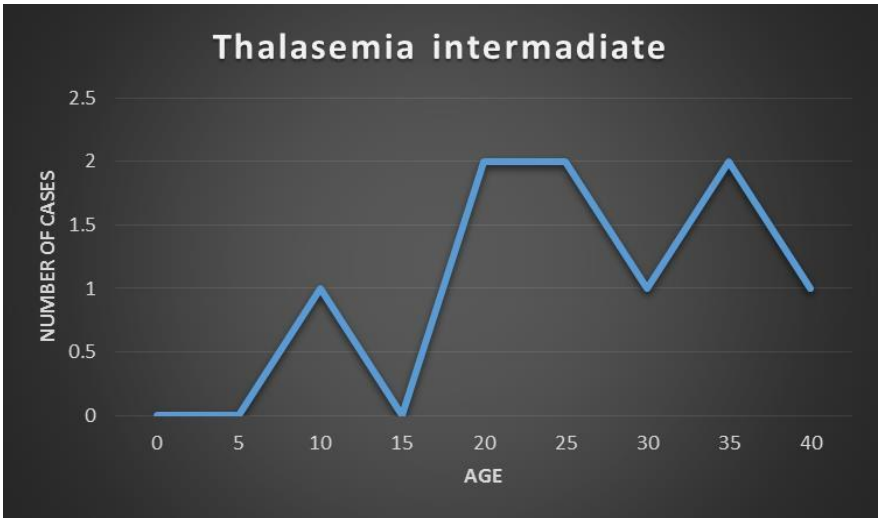

Figure 1-2

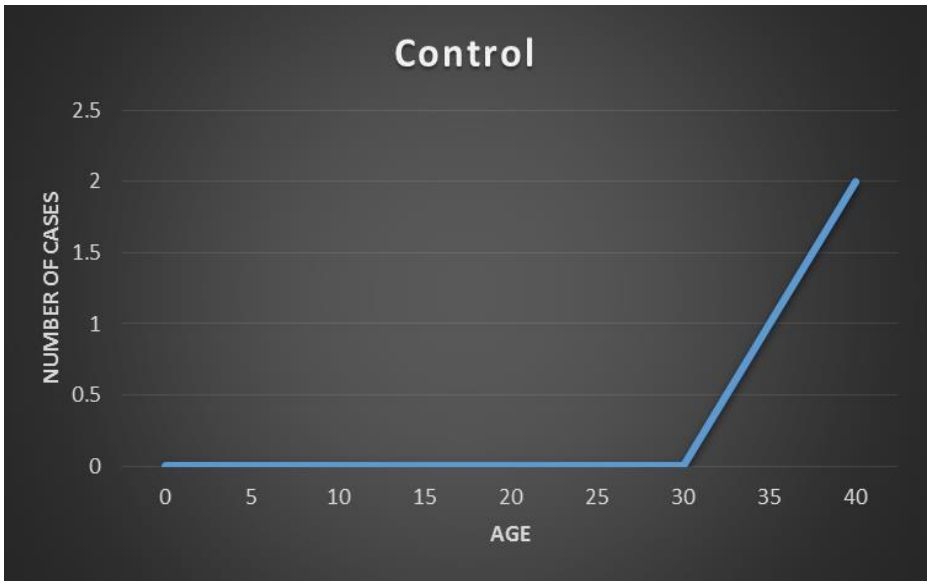

Figure1-3

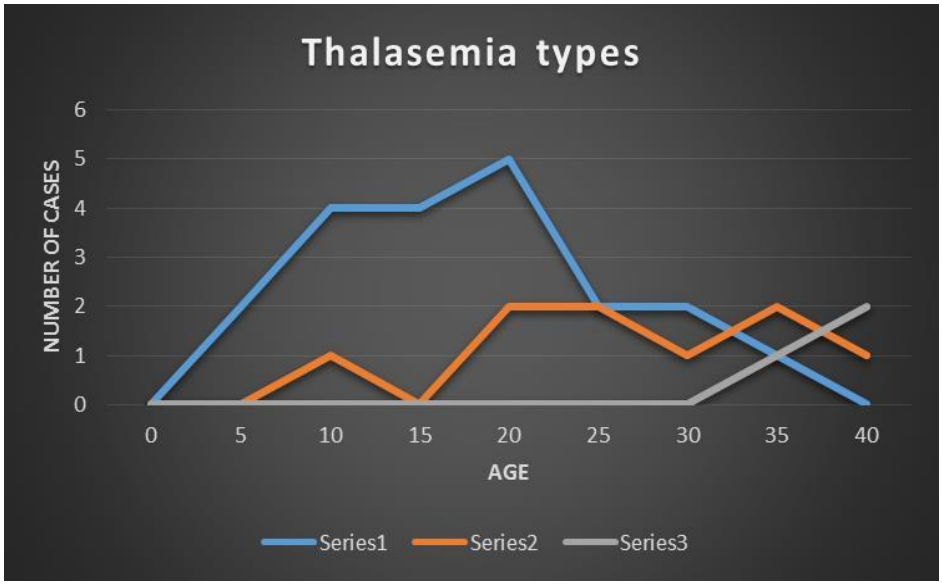

Figure1-4

The Result

The study present, 75 case of patient were divided into three groups: group 1 (25) thalassemia major, group 2 (25) thalassemia intermediate and group 3 (25) normal people (control) , in group 1 mean for the age of onset of affected cases , was ranging from (20-40)
Years, and percent of female to male was 64% and mean of age for patients Included in this study was 25-year. Percentage for Patient taken chelating Therapy was 98% compared to patients not taking the chelating therapy, And mean for the duration of chelating therapy was 14.6 years ranging (6 - 34) Year, and for frequency of transfusion per year was 24 with transfusion Performed every 2 weeks. The mean for Hemoglobin Concentration was 7, 3 mg/di ranging (from 5.1-10) and serum ferritin was 2441 ng/dl ranging (From 202-14688 number of patients with splenectomy was 23(96%) and Those with bone marrow failure was 2(4%)

23**/**75 of cases have cardiac iron and most of the are the older and with tendency to female gender , increasing in the rate of heart and QT interval are the most finding in these patients and we can follow up these patient according to QT interval because it appear the most significant sign in ECG reading

Discussion

Cardiac hemosiderosis are the main causes of morbidity and mortality in beta thalassemia major . results of study indicated cardiac hemosiderosis in 38.3%. Different rates of cardiac hemosiderosis was reported in previous studies. Mean age differences of the studied populations, variations in sample size, and of chelation regimes may considerably affect the incidence of cardiac hemosiderosis in different studies. it is known that deferiprone results in

cardiac chelating agent was deferoxamine , our results was in accordance with some previously published studies that demonstrated a statistically significant inverse correlation between plasma ferritin levels and cardiac hemosiderosis .
The result may be importance in unequipped centers where present of T2*MRI is available.
Other studies have reported different correlation strengths ranging from no correlation to moderate correlation.
Our study indicated a strong correlation between plasma ferritin levels and cardiac ECG reading that was in accordance with previous studies.
in a recently published study reported a statistically significant strong correlation between serum ferritin levels and cardiac values. This may be explained by the fact that the vast majority of patients (97.5%) included in their study received poor chelation therapy or be matter of time and methods of treatment .
These finding emphasizes why importance of using cardiac ECG as a non-invasive and non-cost procedure for estimating of cardiac iron overload T2*MRI values.
Another important aspect of our study was that a statistically significant moderate correlation was seen between age and cardiac ECG while the correlation of age with ECG reading were strong and isignificant.
Similar results have been reported previously.
However, cardiac iron overload develops slowly in a time-dependent manner so that it progresses as the patient ages. Therefore, age of patients have more pronounced impact on the development of cardiac hemosiderosis

This research present to us the effect on the accumulation of iron on body tissue and specially the heart that complication accursing with the grade of

accumoulion of iron the vast majority of these cases coming with thalassemia major and the effect decrease with the decrease of the numberless of blood transfusion

Conclusions

Millions of individuals throughout the world suffer from thalassemia . Families, physicians, researchers, and, of course, the government must all work together to combat the disorder. A combination of research methodologies could result in a better knowledge of therapy effects and more realistic thalassemia management.

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