Pretransfusion Hemoglobin F Level in Thalassemia Patients: Effect of Well-Balanced Versus Poor Transfusion

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Abstract:

Background: Thalassemia is a common condition in Iraq. More than ten thousand patients registered in Iraq. If well-balanced hypertransfusion regimen to maintain pretransfusion hemoglobin level above the internationally agreed 9.0 gm/ dL could suppress the patients' bone marrow and shutdown the hematopoiesis to the extent of not producing any hemoglobin F.

Patients and Methods: One hundred well-balanced transfusion-dependant thalassemia patients were evaluated for Hemoglobin F level prior to their scheduled transfusions. Hemoglobin level must have been more than 9.0 gm/ dL to qualify the patient to be entered into this group. All such patients must have showed minimal skeletal changes of thalassemia. Another hundred patients with frank features of thalassemia and poor history of blood transfusion were also enrolled in the study. We aimed at knowing whether HbF is significantly different in the two groups. It could indicate that patients' bone marrow could be totally turned off and no abnormal hemoglobin will be allowed to be produced.

Results: Seventy nine percent of our enrolled transfusion-dependent thalassemia patients who fulfilled the criteria and were well managed showed correction of their HbF level to near zero! Thirty five percent of the poorly transfused patients also corrected their abnormal HbF level.

Conclusions: This study showed that marrow micromilieu could be manipulated in patients with thalassemia in such a way so as to totally shutdown production of abnormal hemoglobin F as a result of provision of normal hemoglobin through blood transfusion. The fact that even one third of poorly transfused patients could show the same results indicates that any degree of transfusion support will have its impact on the marrow.

Keywords: Thalassemia, HbF, Blood Transfusion, Electrophoresis.

Introduction:

The thalassemias are a heterogeneous group of the hemoglobin disorders in which the production of normal hemoglobin is partly or completely suppressed as a result of the defective synthesis of one or more globin chains [(1)].

Several types of thalassemia have been described and named according to the affected globin-chain, the most common types of clinical importance being α and β thalassemia [(2)].

Thalassemia is more prevalent in the Mediterranean basin, the Middle East, Southern and Eastern Asia, the South Pacific and South China, with reported carrier rates ranging from (2%) to (25%) [(3)].

Definition:

The term "thalassemia" refers to a group of blood diseases characterized by decreased synthesis of one of the two types of polypeptide chains (α or β) that form the normal adult human hemoglobin molecule (HbA: α2β2),

resulting in decreased filling of the red cells with hemoglobin, and anemia [4].

Four major types of hemoglobin [4]**:**

a) "Embryonic" hemoglobins, which are detectable from the 3rd to the 10th week of gestation and represent **δ2ε2, α2ε2, ζ2γ2** tetramers.

b) "Fetal" hemoglobin (HbF **α2γ2**), which constitutes the predominant oxygen carrier during pregnancy.

c) "Adult" hemoglobin (HbA **α2β2**), which replaces HbF shortly after birth, and.

d) A minor adult component, (HbA_2 **α2δ2**).

Types:

Normal adult Hb contains (HbA 97%; HbA_2 2-3%; HbF<1%). A normal person globin chain is designated αα/αα per cell and β/β per cell as shown in table (1). Any defect, reduction or absent production of one or more of these globin chains lead to Hb disorders. This could be mild, moderate or sever, heterozygous or homozygous according to globin chain synthesis defect [5, 6].

Hemoglobin F:

Hemoglobin F is the major hemoglobin during intrauterine life. Its oxygen affinity is higher than that of hemoglobin A and this facilitates oxygen transfer from the mother to the fetus [7].

During the first year of life, the percentage of hemoglobin F falls progressively to values close to adult levels. A slower fall to final adult levels may continue for several years, even up. To puberty and beyond [7, 8].

Possibilities of β-Thalassemia (transfusion depended) [9]:

β°/ β°: thalassemia major**.**

β^{+}/ β^{+}: thalassemia major

β°/ β^{+}: thalassemia major/ thalassemia intermedia.

β^{+} / β^{+}: thalassemia major/ thalassemia intermedia.

β^{++}/ β^{++}: thalassemia intermedia.

Hemoglobin Electrophoresis

Hemoglobin electrophoresis is still the most common technique for the initial detection and characterization of variant hemoglobin, although high performance liquid chromatography **(HPLC)** is increasingly taking its place [10].

Aims of the Study:

This study was planned to:

- Figure out if well-balanced transfusion of thalassemia patients could completely suppress patients' own hematopoiesis.
- Evaluate if HbF is a good measure for proper patient's response to transfusion.

Patients and Methods:

Over a one year period in Sulaymaniyah Thalassemia Centre, two hundred patients with thalassemia major were selected for the purpose of this study.

The Hemoglobin F of one hundred well-balanced transfusion-dependant thalassemia patients was evaluated. Hemoglobin levels prior to each transfusion in the medical chart of the patient were more than 9.0 gm/dl. All patients showed minimal skeletal changes of thalassemia. Another hundred patients with frank features of thalassemia and poor history of blood transfusion with hemoglobin level less than 7.0gm/dl also enrolled. HbF at the first diagnosis was also included in the study for the purpose of comparison with the HbF level at time of data collection.

Comparison between the two groups, as far as the HbF is concerned, should address any significant difference between the two groups. Significant

number of patients with thalassemia major and normal HbF level should indicate that marrow could be totally turned off and no abnormal HbF will be allowed to be produced.

Results:

The total number of the thalassemic patients in this study 200, one hundred well control blood transfusion and one hundred poor control. (46%) of them are male and (56%) are female patients.

Table (1) shows 200 patients with thalassemia major, 114 of them normalized their HbF level (< 2%) and out of this number (79) well control and (35) poor control. While non-normalized HbF level (> 2%) are 86 patients out of this number (21) well control and (65) poor control.

Table (2) shows significant correlation of HbF at the time of diagnosis between well and poor control patients, while highly significant correlation of HbF after repeated blood transfusions between well and poor control patients.

Figure (1) shows the age in this study is in the region of 10 years old with mean of age is 12 years.

Figure (2) shows the most frequent HbF level at the time of diagnosis of thalassemia major is between (81-91%) with the mean of HbF level is (82%) for all 200 patients (well and poor control).

Figure (3) shows (79%) of thalassemic patients have their HbF level returned to normal with the mean of HbF level in well control group is (1.4%). While only (21%) of the thalassemic patients their HbF level significantly reduced but not normalized.

Figure (4) shows about (50%) of thalassemic patients HbF level less than (2.5%) and (35%) of patients returned to normal (< 2%), with the mean of HbF level in poor control group is (12%). While (65%) of the thalassemic patients HbF level reduced but less than in well control patients.

Table (1): Frequency of normalized and non-normalized HbF.

	Frequency	Total %	Well control %	Poor control %
Normalized HbF	114	57	79	35
Non-normalized HbF	86	43	21	65
Total	200	100	100	100
P value			0.000	

Table (2): Relationship of HbF at time of diagnosis and after repeated transfusions in the well and poorly control groups.

Control status	HbF at time of diagnosis Mean ±Std. Deviation	P value	HBF after repeated transfusion Mean ±Std. Deviation	P value
Well	80.7 ± 11.0	0.018	1.3 ± 3.1	0.000
Poor	83.9 ± 7.5		11.7 ± 17.3	

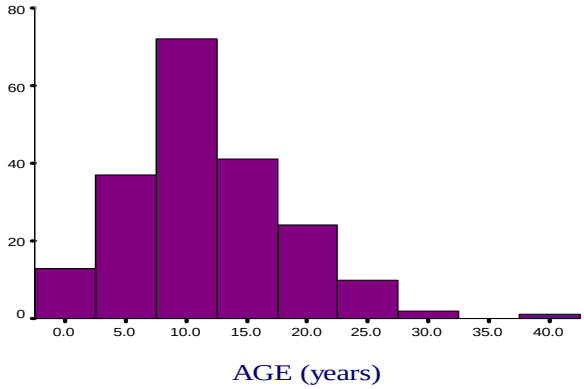

Figure (1): Age distribution.

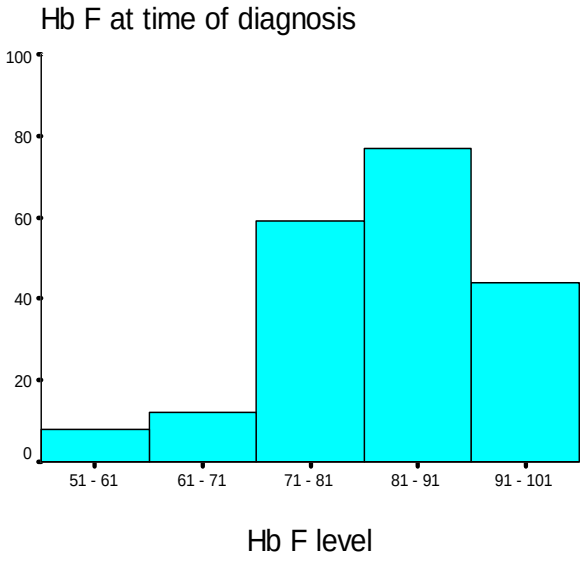

Figure (2): Frequency of HbF level in thalassemia patients.

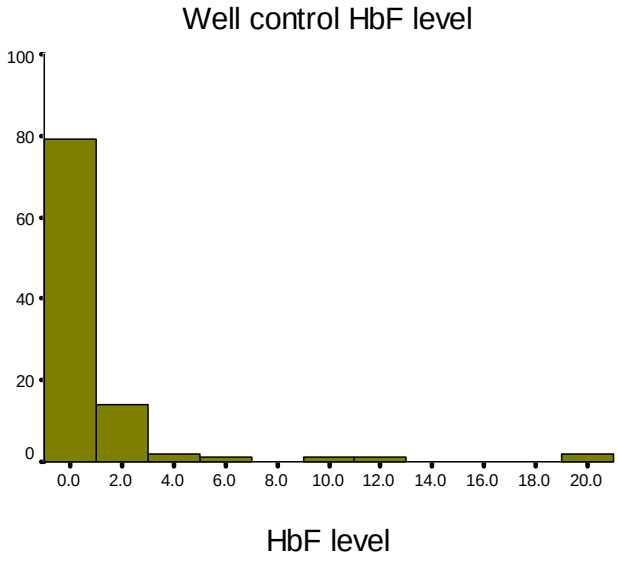

Figure (3): Frequency of well control group.

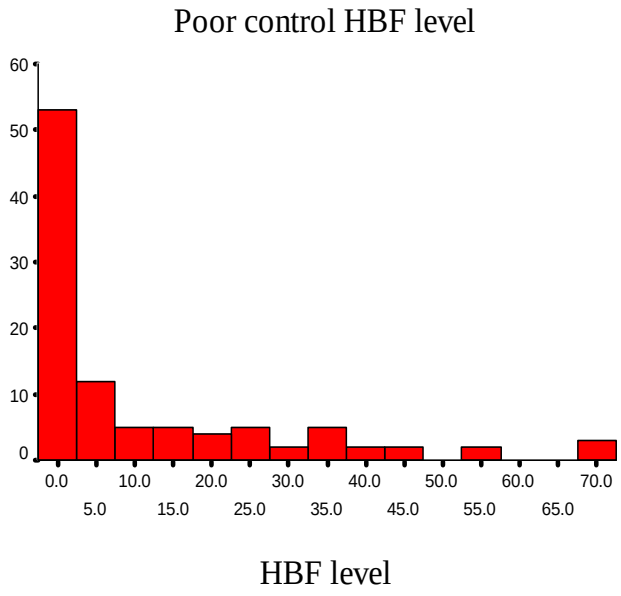

Figure (4): Frequency of poor control.

Discussion:

Thalassemia is a major health problem, placing an immeasurable emotional, psychology and economic burden on millions of people around the world.

Thalassemia is a major health problem and it's a heterogeneous group of the hemoglobinopathies in which the production of normal hemoglobin is partly or completely suppressed as a result of the defective synthesis of one or more globin chains.

In this study we took 200 patients selectively, comprising 100 well control transfusion depended patients versus 100 poor control patients. Out of this 200 thalassemia patients at Hiwa Hospital-Thalassemia Department we found that 108 female (54%) and 92 male (46%) patients.

HbF level is a standard test to diagnose the thalassemic patients, which show high level at the time of diagnosis of thalassemia major patients. In this study the HbF level occurs between (81-91%) with the mean of HbF level is (82%) for all 200 patients (well and poor control) at the time of diagnosis.

Normalized HbF level appear after repeated transfusion in (57%) of patients (114) (out of this number (79) good control and (35) poor control patients), while non-normalized HbF level appear in (43%) of patients (86) (out of this number (21) good control and (65) poor controls patients). High significant number of patients with thalassemia major and normal hemoglobin F indicates that marrow suppression with overzealous transfusion support is proved in these patients and bone marrow totally turned off and no abnormal hemoglobin will be allowed to be produced.

In the well control patients the mean of HbF level was (1.4%), with minimum level was (0.0%) and maximum level (19.90%) while in poor control patients the mean of HbF level was (12%), with minimum level was (0.0%) and maximum level was (71.90%).

While the mean of Hb level at the time of collection data were compared with the mean of Hb level after repeated transfusions showed the level increased

in about 1 gm in the well control group with well response to blood transfusions, while only about 0.5 gm in the poor control group.

There is a significant correlation of HbF at the time of diagnosis between well and poor control patients, while there is highly significant correlation of HbF after repeated blood transfusions between well and poor control patients.

Conclusions:

This study showed that marrow micromilieu could be manipulated in patients with thalassemia in such a way so as to totally shutdown production of abnormal hemoglobin F as a result of provision of normal hemoglobin through blood transfusion. The fact that even one third of poorly transfused patients could show the same results indicates that any degree of transfusion support will have its impact on the marrow. Regular blood transfusion is a good opportunity for the thalassemia patients to correct their HbF level to nearly normal level.

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