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Haemoglobin F and clinical severity of sickle cell anaemia among Nigerian adults

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Summary
Haemoglobin F (HbF) has been a useful criterion in predicting the clinical severity of sickle cell disease (SCD). Thus different treatment modalities are geared towards raising its level. This study estimated HbF levels in sickle cell anaemia patients. HbF levels were then compared with clinical parameters such as the average number of bone pain crisis per year, transfusion requirement, enlargement of both the spleen and liver and the haematocrit level. The mean HbF value was 7.4 ± 3.6%. Males recorded a higher mean level than females 7.6 ± 3.9%, and 6.7 ±3.6% respectively, ($P > 0.05$). HbF of 7.4% was used to divide the patients into two broad groups. Patients with HbF of more than 7.4% were older compared to those with less than 7.4% ($P > 0.5$), the former group was also less transfusion dependent ($P > 0.05$) even though their haematocrit was not significantly different ($P > 0.05$) from those with HbF of < 7.4%. The patients with higher HbF levels are also more likely to retain their spleen longer than their counterpart with lower values. It appears that clinical severity has a relationship with HbF values even though most were not statistically significant. There is a need for larger studies to study this relationship more closely.

Keywords: *Clinical severity, sickle cell anaemia, HbF*

Résumé
L'hémoglobine F (HbF) a été un criteré utile dans la prédiction de la sévérité clinicale des maladies aurx hématies falciformes. Alors, les différentes moldalités de traitement sont dirigées á augmenter son nivean. Cette étude a estimé la quantité de HbF chez les patients sonffrant de l'amémie falciforme. Le taux de HbF a été comparé avec les paramétres chniques tels que le nombre moyen des crises du mal ddes os par an, la demande de transfusion, l'élargement á la fois de la rate et du faie et le taux d'haemotocrite. Le taux moyen de HbF était de 7,4±3.6%. Les hommes avaient un taux moyem plus élevé que les femmes 7.6 ±3.9% et 6.7 ±3.6% respectivement ($P>0.05$). 7,4% de taux de HbF a été utilise pour divider les patients en daux en daux grand groupes. Les malades ayant in taux supériur á 7,4% ($P > 0,5$), le dermier group ne dependant pas beanconp de la transfusion ($P > 0,05$) bien que leur haematocrite n'était pas trés différent ($P > 0,05$) de ceux avec HbF inférienre á 7,4%. Les patients ayant un taux élevé de HbF ont plus de chance de retemir leur ... Longtemps que leur partemaire avec un taux faible. It aparait que la sévérité clinique a une relation avec la quantité de HbF, bien que la plupart n'était pas statisticallement significative. Il en découle un grand besoin d'étude, pour pouwoir établir cette relation plus chairement.

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Introduction

The treatment for sickle cell disease (SCD) is largely supportive since treatment like bone marrow transplantation is a procedure for a selected few, and cure by gene therapy is a thing for the future. Other treatment modalities for SCD are known to work by increasing fetal haemoglobin (HbF) synthesis, the agents used in such treatment could be cytotoxic drugs, growth factors or agents inducing differentiation.

The level of HbF is known to vary in SCD patients from different localities and even among those within the same locality [1,2]. HbF has been used to predict the clinical severity of this disorder, the prediction of severity based on HbF is however not absolute since there is an interplay between HbF and other genetic factors. This might be responsible for the difficulty in determining characteristics which favour survival. Numerous factors known to influence the level of HbF include the age and sex of the patients and the number of active α- globin genes [3]. This study assessed the effect of HbF on the clinical features of the disease in our environment and possibly predicts severity of the disease and survival. This has the advantage of reducing patient disability, morbidity and in fact mortality. It will also reduce some of the physical, financial and emotional burdens experienced by the patients' caregivers and family.

Patients and methods

Fifty sickle cell anaemia patients in steady state were selected by the systematic sampling method from the adult haematology clinic of the University College Hospital, Ibadan, Nigeria. Information was collected using an interviewer-administered semi-structured questionnaire, information obtained were demographic details such as age and sex of the patients. Also, history of blood transfusion and average of number of crisis per year were obtained. In addition, a physical examination was done to determine enlargement of the liver and spleen. laboratory investigations done included the following:

1. Haematocrit was determined by computing the average results of four haematocrit readings obtained in the steady state.
2. HbF was determined by the alkaline denaturation method of Betke [4] using an analogue spectrophotometer (Pye Unicam SP-600).

The mean HbF level of 7.4% was used as a denominator to classify the patients into two groups. Twenty-six and 24

There were more long survivors (those who were at least 30 years old) among patients who have HbF level of greater than 7.4%. Even though this group was less transfusion dependent, their haematocrit was not significantly different from those with HbF of less than 7.4%. Also, the rarity of vaso-occlusive crisis (bone pain crisis) was noted more among those with HbF of < 7.4% compared with those with higher HbF values.

In all but the mildest cases of sickle cell anaemia patients the spleen is eventually destroyed by multiple infarctions. Persistence of splenomegaly has been attributed to high levels of HbF and homozygous alpha thalassaemia, irreversibly sickled cell (ISC) count has also been found to be low in cases with splenomegaly. It is therefore not surprising that a palpable spleen was noted more in the group with a higher HbF level. The expected low ISC in this group cannot fully explain the fact that this group is less transfusion dependent since the steady state haematocrit remains the same in both groups.

The inability to categorically define the effect of HbF on clinical severity may explain why some patients have shown good response to drugs like hydroxyurea which increases the synthesis of HbF in sickle cell disease patients and others have not. The reason why there were more females among patients who have HbF < 7.4% is not immediately obvious. It appeared that HbF is related to patients' clinical severity. However, there is a need for more studies with a larger number of patients to study this phenomenon more closely.

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