ISSN 2320 7159

INERNATIONAL JOURNAL OF MEDICAL RESEARCH

ORIGINAL ARTICLE

Association of Foetal Haemoglobin with Pancreatic Enzymes in Sickle Cell Disease Patients in Benin City, Nigeria

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A R T I C L E I N F O

doi: 10.5455/ijmr.20160724120220

Keywords:
Sickle cell disease,
Pancreatitis,
Serum Lipase,
Amylase,
Urine Amylase

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A B S T R A C T

Background & Objective: There are conflicting reports on the potential protective effects of foetal haemoglobin (HbF) in the elimination of symptoms of Sickle cell disease in the patients and reports which correlate the levels of HbF with pancreatic enzymes in SCD are scare in the literature. This study correlates the levels of HbF on pancreatic enzymes activities in SCD patients on steady clinical state.

Materials and Methods: Serum amylase and lipase as well as urine amylase were determined using commercially available reagents kits. Control sera were included in all assays to ensure accuracy and precision of the analytes. Student's t-test was used to compared data at 95% confidence intervals ($p<0.05$) and Pearson correlation coefficient was used to calculate the association of HbF with measured variables.

Results: Urine amylase ($p=0.01$), serum amylase ($p<0.001$) and lipase ($p=0.002$) were significantly decrease in sickle cell patients with high (>5%) HbF when compared to those with low (<4.9%) HbF. Foetal haemoglobin levels correlated negatively with serum lipase ($r = -0.468,\ p < 0.001$) and amylase ($r = -0.381, p < 0.01$) but the correlation with urine amylase ($r = -0.154,\ p = 0.314$) was not however significant.

Conclusion: SCD patients with lower HbF were characterized with higher levels of pancreatic enzymes than those higher HbF levels; hence SCD patients subjects with lower HbF are more predisposed to chronic pancreatitis. It would be interesting to repeat the study in SCD patients with abdominal pain in other to reveal the overall involvement of the pancreas in the disease process.

INTRODUCTION

Sickle cell disease (SCD) is the most common haemoglobinopathies in Nigeria and has constituted one of the public health problems. The disorder is characterized by chronic haemolyticanaemia and vaso-occlusive painful crisis[1]. In Africa, SCD is estimated to contribute to an equivalent of 5% of under –five deaths with up to 16% in Nigeria and only half of the affected children live beyond their 5 years[2]. The prevalence of the hemoglobin S gene in Nigeria was observed to be between 20 and 25%[3].

Though SCD is present from birth, symptoms are rare before the age of 3to 6 months because of a high percentage of foetal haemoglobin (HbF) levels in the circulation. The degree of haemoglobin S (HbS) polymerization in the circulation determines how likely the individual is to have a vaso-occlusive crisis or other adverse events. It is of interest to note that cells are less prone to sickling in individuals who retain a high level of HbF[4]. As more sickle cell haemoglobin (Hb-S) replace Hb-F in the individual, episode of profound anaemia and multiple organ involvement (such as cerebrovascular events, acute vaso-occlusive episodes, retinopathy, acute chest syndrome, hepatobiliary system[5] and renal damage) occur[6]. The clinical manifestations of sickle cell anaemia result from the increase in blood viscosity, red cell adherence to vascular walls, and vascular occlusions. The sickled erythrocytes impede blood flow to target tissues and organs causing infarctions and ischemic necrosis[7]. Damage can occur to any organ in the body.

Increased levels of HbF have been reported to almost completely eliminate symptoms of sickle cell disease[8,9]. However, other studies did not find significant difference in painful episodes or acute chest syndrome between different levels of HbF in sickle cell patients[10]. Even though we have previously reported on increased levels of pancreatic enzymes in SCD patients with proteinuria (in press) no study on serum amylase and lipase in SCD patients with low or high HbF levels has been reported in the literature to the best of our knowledge. This study therefore seeks to evaluate the impact of HbF on pancreatic enzymes levels in SCD patients on steady clinical state.

METHODOLOGY

Subjects: The study was conducted at the Department of Medical Laboratory Science, College of Medical Sciences, University of Benin, Benin City. The SCD patients were recruited from among patients on routine visit to the Sickle cell centre, Benin City. Those subjects with edema, severe jaundice, abnormal chest and abdominal findings and those with other haemoglobinopathies were excluded from the study. The study protocol was approved by the Edo state ethical clearance committee before the commencement of the study. While control subjects were apparently healthy haemoglobin AA selected from among students of the University. Informed consent was given by all participants.

Sample preparation: Five milliliters of blood was collected ascetically and dispensed into a plain container. Urine sample was also collected into sterile universal container and was used for amylase and protein. The blood sample was allowed to clot at room temperature and was centrifuged at 1500rpm for 10 minutes, the serum was separated into a separate tube. The serum was stored at -20^{o}C for 2 weeks prior to analysis for serum amylase and lipase. Serum amylase and lipase as well as urine amylase were determined using reagents supplied by AGAPE diagnostics. The changes in absorbance were monitored spectrophotometrically every minute for 3 minutes at 405nm. Control sera were included in all assays to ensure accuracy and precision of the analytes.

Statistical Analysis: The data obtained were statistically evaluated using Statistical Package for social science (SPSS) version 16.0. Values are presented as mean± standard error of mean (SEM) for both tests and controls. Student's t-test was used to compared data at 95% confidence intervals ($p<0.05$).Pearson correlation coefficient was used to calculate the association of HbF with measured variables.

RESULTS

Table 1showsserum lipase, amylase and urine amylase levels in SCD patients with high HbF compared with those with low HbF levels. Urine amylase ($p=0.01$), serum amylase ($p<0.001$) and lipase ($p=0.002$) were significantly decrease in sickle cell patients with high HbF when compared to those with low HbF.

Table 1: Comparison of measured variables in SCD patients with high and low foetal haemoglobin

Measured Variables	SCD patients with high HbF(≥5%)	SCD patients with low HbF(≤4.9%)	P value
No of Subjects	25	75	
Age (years)	21±1.02	23±0.91	
Urine Amylase (U/L)	244±12.00	318.52±24.00	0.01
Serum Amylase (U/L)	53.38±5.20	74±2.73	0.001
Serum Lipase (U/L)	53.38± 5.20	74 ± 2.73	0.002

Foetal haemoglobin level correlated negatively with serum lipase ($r = -0.468,\ p < 0.001$) and amylase ($r = -0.381, p < 0.01$) but the association with age ($r=-0.138,\ p = 0.367$), and urine amylase ($r = -0.154,\ p = 0.314$) were not statistically significant.

Table 2: Correlation of HbF with age, serum amylase, lipase and urine amylase in SCD patients with low (<4.9%) HbF levels

Correlation studies	r- value	p- value
Age	-0.138	0.367
Serum amylase	-0.381	0.001
Urine amylase	-0.154	0.314
Lipase	-0.468	0.001

Table 3: Correlation of HbF with age, serum amylase, lipase and urine amylase in SCD patients with high (>5%) HbF levels

Correlation studies	r- value	p- value
Age	0.395	0.85
Serum amylase	0.287	0.220
Urine amylase	0.314	0.70
Lipase	-0.347	0.133

No statistically significant association was observed between HbF and age (r = -0.395, p = 0.850), serum amylase (r =0.287, p = 0.220), urine amylase (r = 0.414, p = 0.70), and lipase (r = -0.347, p = 0.133) in SCD patients with high HbF levels.

Table 4 indicates that statistically significant increases were observed for urine amylase (p=0.029), serum amylase (p< 0.001), lipase (p< 0.008) and HbF (p< 0.001) in SCD patients compared with controls.

Table 4: Comparison of Urine and serum amylase, lipase and foetal haemoglobin levels in SCD patients and normal haemoglobin AA (controls)

Measured Variables	SCD patients	Controls	P value
No of subjects	N = 100	N = 50	-
Age (Years)	21.0± 1.02	23.0±0.91	>0.05
Urine amylase (U/L)	294.07±16.28	215±10.25	=0.029
Serum amylase (U/L)	64. 82 ± 3.35	33.60±3.02	<0.001
Serum lipase (U/L)	54.10±3.34	33.3±3.23	=0.008
Fetal haemoglobin (%)	2.85±0.25	0.97±0.17	<0.001

DISCUSSION

The study evaluates the levels of urine amylase, serum amylase, lipase and HbF in SCD patients, and also determines the association of HbF with the measured pancreatic enzymes in SCD patients with high (>5%) HbF and those with low (<4.9%) in order to show the impact of HbFon the measured pancreatic enzymes. The data indicate that urine amylase (p= 0.029), serum amylase (p = 0.005), lipase (p = 0.008) and HbF (p<0.001) were significantly higher in SCD patients than controls. SCD with high HbF had significantly lower urine amylase (p < 0.01), serum amylase (p < 0.001) and lipase (p < 0.002) than SCD patients with low HbF.

HbF was negatively associated with serum amylase (r=-0.381;p<0.001) and lipase (r=-0.468;pp<0.001) while age (r=-0.138;p=0.367) and urine amylase (r=-0.154;p=0.314) were not significant in those subjects with low HbF levels. On the other hand, no significant association was observed between HbF and age (r=0.395; p=0.85), serum amylase (r=0.287; p=0.220), lipase (r=-0.347; p=0.133) and urine amylase (r=0.314; p=0.70) in subjects with high HbF levels.

This study revealed that SCD patients with high HbF levels had relatively lower levels of pancreatic enzymes than those with low HbF levels. This finding is consistent with previous reports[11,12] where it was observed that HbF has some protective roles against the development of proteinuria and renal insufficiency in SCD patients. High proportions of HbF are even better than high proportions of HbA in preventing the formation of haemoglobin polymers in sickle red blood cells. The symptoms of SCD are almost completely eliminated with HbF levels above 25%; however, any increase in HbF level was observed to improve the overall survival[13,14]. Most of the SCD patients with high HbF were reported to be free from most of the severe clinical manifestations associated with SCD[15] .On the contrary, Atweh and Schechter[10] did not find any significant difference in painful episodes or acute chest syndrome in subjects with different levels of HbF.SCD patients may sometimes be at risk of acute pancreatitis both from biliary obstruction and potentially from micro-vessel occlusion with resultant ischemia, activation of pancreatic enzyme and injury to pancreatic tissue[16]. Gallstone may also block the flow of pancreatic enzymes leading to inflammation of pancreas. In conclusion, SCD is associated with increase amylase and lipase levels. HbF was observed to have impacted relatively on the enzymes activities in SCD patients and subjects with lower HbF were characterized with higher levels of pancreatic enzymes than those higher HbF levels, hence SCD patients subjects with lower HbF are more predisposed to chronic pancreatitis. It would be interesting to repeat the study in SCD patients with abdominal pain in other to reveal the overall involvement of the pancreas in the disease process.

No Conflict declared

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