

Increased levels of pancreatic enzymes in sickle cell anemia and the effect of proteinuria

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Abstract

Background/Objective: Sickle cell disease (SCD) is the most common hemoglobinopathy in Nigeria, and the condition can affect any part of the body including the pancreas. The study seeks to evaluate the levels of pancreatic enzymes in blood and urine of SCD patients in steady clinical state, and the effect of proteinuria on the enzyme levels as proteinuria was previously reported in SCD subjects. **Materials and Methods:** Urine and plasma amylase, serum lipase, and proteinuria were determined in 150 subjects comprising 100 SCD patients and 50 age/sex matched apparently healthy subjects with normal hemoglobin using commercially available reagent test kits. **Results:** Urine amylase ($P = 0.029$), serum amylase ($P < 0.001$), lipase ($P = 0.008$), and proteinuria ($P < 0.001$) were significantly higher in steady state SCD patients compared with controls. Significant decreases were observed in urine amylase ($P = 0.022$), serum amylase ($P < 0.001$), lipase ($P < 0.001$), and proteinuria ($P < 0.001$) in SCD patients without proteinuria compared with SCD patients with proteinuria. **Conclusion:** Pancreatic enzymes levels were increased in SCD patients which indicate that these patients may be predisposed to pancreatitis and the levels of these enzymes were further increased in those with proteinuria.

Key words: Lipase and proteinuria, serum amylase, sickle cell disease

INTRODUCTION

Sickle cell disease (SCD) also known as drepanocytosis is an autosomal recessive genetic disorder characterized by chronic anemia and vaso-occlusive painful crisis. SCD is caused by a single nucleotide substitution of thymidine for adenine (GAG→GTG) of the β -chain that results in the amino acid valine instead of glutamic acid.^[1] This basically is responsible for all the changes in the properties of the hemoglobin (Hb) molecule, with tendencies to polymerize in the deoxygenated state,^[2] in which the red cells assumed an

abnormal rigid, elongated, and crescent cell shaped which obstruct normal blood flow through microvessels. This impedes blood flow to organs and tissues causing infarctions and ischemic necrosis.^[3,4] Most organs of the body are affected thus leading to acute or chronic multisystem dysfunction.

In our previous studies,^[4,5] we reported the involvement of kidney pathology in SCD. Functional changes occur in the kidney with increasing age, proteinuria, severe anemia, and hematuria were observed to be reliable markers and predictors of chronic renal disease in SCD disease. Oral glucose intolerance was also reported in a group of patients, indicating that insulin secretion from the pancreas may be compromised in a steady state SCD.^[6] Abdominal pain was observed to be common in SCD and may present a diagnostic challenge since pancreatitis is uncommon in SCD patients.^[7,8]

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Some cases of acute pancreatitis were, however, reported in African-Americans who had no evidence of drug- or toxin-induced injury or obstruction etiology.^[3] This study was therefore designed to evaluate pancreatic enzymes and the effect of proteinuria in steady state SCD patients.

MATERIALS AND METHODS

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 a routine visit to the Sickle Cell Centre, Benin City. Those subjects with edema, severe jaundice, abnormal chest and abdominal findings, and those with other hemoglobinopathies 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 Hb AA selected from among students of the University. Informed consent was given by all participants.

Sample preparation

Five milliliters of blood were collected aseptically and dispensed into a plain container. A urine sample was also collected into a sterile universal container and was used for amylase and protein. The blood sample was allowed to clot at room temperature and was centrifuged at 1500 rpm for 10 min; the serum was separated into a separate tube. The serum was stored at -20°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 min at 405 nm. The urine protein was initially evaluated using urinalysis test strip and the urine samples showing positive were re-assayed by the quantitative sulfosalicylic acid colorimetric method. 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 (Chicago IL, USA). The values are presented as mean \pm standard error of the mean for both tests and controls. Student's *t*-test was used to compare data at 95% confidence intervals ($P < 0.05$). One-way analysis of variance was used to compare mean values between SCD patients with and without proteinuria as well as the controls.

RESULTS

A total of 150 subjects (100 SCD patients and 50 apparently healthy Hb AA subjects) were evaluated in the study. The age ranged from 15 to 24 years with the mean of 23.1 ± 1.0 years for the SCD patients while the controls range from 17 to 25 years with the mean of 24.3 ± 0.9 years. Urine amylase ($P = 0.029$), serum amylase ($P < 0.001$), lipase ($P = 0.008$), and proteinuria ($P < 0.001$) were

significantly higher in steady state SCD patients compared with controls [Table 1].

Table 2 shows the measured variables in SCD patients with and without proteinuria. Significant decreases were observed in urine amylase ($P = 0.022$), serum amylase ($P < 0.001$), lipase ($P < 0.001$), and proteinuria ($P < 0.001$) in SCD patients without proteinuria compared with SCD patients with proteinuria. However, SCD patients with or without proteinuria had higher levels of measured parameters compared with control subjects.

DISCUSSION

The data presented indicate that SCD patients on steady clinical state had significantly higher levels of urine amylase ($P = 0.029$), serum amylase ($P < 0.001$), lipase ($P = 0.008$), and proteinuria ($P < 0.001$) than subjects with normal Hb. The SCD Patients with proteinuria had higher levels of urine amylase, serum amylase and lipase, and proteinuria compared with those SCD patients without proteinuria. The finding of increased serum amylase in SCD patients compared with controls is consistent with that reported by Adekile and Akinseye-Akintujoye.^[6] Urine amylase and serum lipase were observed to be higher in SCD patients than controls. This may indicate a predisposition of SCD patients to chronic pancreatitis. The study by Adekile and Akinseye-Akintujoye^[6] was conducted on 26 SCD patients, and we have revisited the issue with a larger population size and assayed serum lipase and urine amylase as well as the effect of proteinuria on pancreatic enzymes in SCD patients. Even though acute pancreatitis was reported to be uncommon in SCD patients, some cases have been reported,^[7,8] and ischemic bowel secondary to SCD has been reported with increasing frequency.^[1,3] The etiology of abdominal pain in SCD was ascribed to mesenteric and retroperitoneal adenopathy, infarction in vertebral bodies, hepatobiliary disease, and splenic infarction.^[9] The conditions mentioned above are the natural history of SCD which are contributing factors to abdominal pain. It may be that chronic intermittent ischemia that occurred due to occasional obstruction of normal blood flow as a result of sickle red blood cell polymerization in reduced oxygen tension may have led to increased levels of pancreatic enzymes. Abadin *et al.*^[10] observed that the bowel injury seen in SCD patients with bowel ischemia may be due to an extreme manifestation of a spectrum of pathology that ranges from minor abdominal pain secondary to SCD, transient ischemia to transmural bowel infarction.^[10]

Table 1: Comparison of urine and serum amylase, serum lipase levels in SCD patients and normal hemoglobin AA controls

Measured variable	Reference range	SCD patients	Controls	P
Number of subjects		100	50	
Urine amylase (U/L)	24-470	294.07 \pm 16.3	215 \pm 10.3	0.029
Serum amylase (U/L)	30-86	64.82 \pm 3.3	33.60 \pm 3.0	0.001
Serum lipase (U/L)	20-86	54.10 \pm 3.3	33.30 \pm 3.2	0.008
Proteinuria (g/L)	None	0.18 \pm 0.10	0.00 \pm 0.00	0.001
	detectable			

SCD=Sickle cell disease

Table 2: One-way ANOVA of urine and serum amylase, serum lipase in SCD patients with and without proteinuria

Measured variables	SCD with proteinuria	SCD without proteinuria	Controls	P
Number of subjects	27	73	50	-
Urine amylase (U/L)	316.88±24.07 ^a	265.55±19.71 ^b	215.3±14.03 ^c	0.022
Serum amylase (U/L)	74.36±2.73 ^a	52.90±5.75 ^b	33.60±3.02 ^c	0.001
Serum lipase (U/L)	62.68±4.31 ^a	43.35±4.59 ^b	32.20±5.43 ^c	0.001
Proteinuria (g/L)	0.24±0.10 ^a	0.00±0.0 ^b	0.00±0.0 ^b	0.001

SCD=Sickle cell disease, ANOVA=Analysis of variance, ^a=P<0.001; ^b= P<0.005; ^c=P<0.05

In a report of hepatobiliary manifestations of SCD, it was observed that pancreas may be affected directly from red cell sickling process or as a result of chronic hemolysis and multiple transfusions.^[11]

Pancreatic enzymes in SCD patients with proteinuria were higher than those without proteinuria. With improved medical care, the life expectancy of SCD patients has increased, and chronic complications such as renal insufficiency also occur with increasing frequency.^[12] It was reported that 18% of all SCD patients with proteinuria may develop glomerular pathology with time.^[13] The increased levels of pancreatic enzymes observed in SCD patients with proteinuria compared to those without proteinuria may be as a result of glomerular involvement. It is suggested that the increased levels of the pancreatic enzyme may be due to increased hepatic secretions due to loss of protein. The altered glomerular permselectivity causing proteinuria may have caused increased secretion of the enzymes. The proposed mechanisms that established a relationship between proteinuria and increased pancreatic enzymes may be similar to that involved between proteinuria and lipid metabolism. The reduced plasma oncotic pressure occasioned by the loss of protein in urine may directly stimulate the synthesis of pancreatic enzymes by the liver.^[14,15]

CONCLUSION

Pancreatic enzyme levels are increased in SCD patients in steady clinical state and thus indicate that these patients may be predisposed to pancreatitis. The levels of these enzymes were further increased in those with proteinuria. In SCD patients with abdominal pain, clinicians should maintain high levels of suspicion of pancreatitis.

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Conflicts of interest

There are no conflicts of interest.

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