



Levels of Testosterone, Progesterone and Follicle Stimulating Hormone in Male Sickle Cell Subjects in Nnamdi Azikiwe University Teaching Hospital, Nnewi

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Abstract

Background of study: Sickle cell disease (SCD) is a genetic blood disorder affecting red blood cells accompanied with fertility challenges. Apart from distortions in sex hormone levels, accessory sex organs abnormalities may occur.

Objectives: The aim of this study was to evaluate the fertility status of male subjects with sickle cell disease using progesterone, testosterone and follicle stimulating hormone (FSH) levels as markers.

Materials and methods: A total of 90 male subjects (consisting of 30 HbSS subjects in steady state, 30 HbAS individuals and 30 normal subjects (HbAA) as the control subjects) aged 18 to 65 years were randomly recruited for this study. The genotypes of the subjects were determined using electrophoretic procedure while the serum testosterone, FSH and progesterone levels were assessed using ELISA technique. Full blood count was determined by the Sysmex automated procedure and the disease severity was evaluated using the severity scoring technique.

Result: There was a significant difference ($P < 0.05$) in the mean serum level of testosterone in the different blood genotype groups. Furthermore, a non-significant positive correlation existed between the serum levels of testosterone ($r = 0.287$), progesterone ($r = 0.198$) and FSH ($r = 0.078$) when compared with disease severity in HbSS subjects in steady state ($r = 0.287$) ($P > 0.05$) respectively.

Conclusion: The significantly decreased serum level of testosterone in HbSS subjects compared with the HbAS and HbAA individuals suggests that there is an increased risk of infertility in male individuals with sickle cell disease.

Keywords: Testosterone; Progesterone; Follicle Stimulating Hormone; Sickle Cell; Male Infertility

Introduction

Homozygous sickle cell disease is a genetic disorder caused by a point mutation in the beta globin gene, which results in the substitution of valine for glutamic acid [1]. The resultant hemoglobin variant, HbS, polymerizes at low oxygen tension, causing the

characteristic sickle deformity of the red cells, the main aetiopathogenic feature of this disease [1]. Infertility is a known complication in males with sickle cell disease. This has been attributed to relative primary gonadal failure, impotence, and priapism, delayed or impaired sexual development [2]. The ejaculate volume, sperm

motility, sperm density, and normal sperm morphology were significantly reduced in the patients when compared with the control subjects. Most importantly, primary testicular failure is characterized by low levels of testosterone in which infertility results mainly from diseases or conditions that primarily affect and destroy the testis [3]. The low levels of testosterone results in reduction of fertility, which is aggravated by impotence, secondary to earlier priapism [4].

Oligospermia due to local ischaemia caused by sickling phenomenon and tissue hypoxia have been reported in sickle cell disease patients [5]. Hypopituitarism reported in HbSS disease, results from intravascular thrombosis and pituitary infarction [6]. Sickle cell disease is associated with high folate demand. This with zinc deficiencies have been implicated in pituitary and primary gonadal dysfunction. It is noted that reduction in semen volume, sperm count and motility in sickle cell male patients are probably attributed to low level of testosterone [7].

Sex steroids, also known as gonadal steroids, are steroid hormones that interact with vertebrate androgen or estrogen receptors [8]. Their effects are mediated by slow genomic mechanisms through nuclear receptors as well as by fast non-genomic mechanisms through membrane-associated receptors and signaling cascades [9]. Natural sex steroids are made by the gonads (ovaries or testes), by adrenal glands, or by conversion from other sex steroids in other tissue such as liver or fat [10]. Sexual reproduction motivation is influenced by hormones such as testosterone, estrogen, progesterone, oxytocin, and vasopressin. In most mammalian species, sex hormones control the ability to engage in sexual behaviours.

Testosterone is the most important male sex hormone. It is responsible for genital development, beard growth, muscle development and general male characteristics [11]. The measurement of serum or plasma levels is an index of leydig cell function and high or low values correlate well with hypo- or hyper-gonadism. Testosterone appears to be a major contributing factor to sexual reproduction motivation in male primates, including humans. The elimination of testosterone in adulthood has been shown to reduce sexual reproduction motivation in both male humans and male primates [11]. Male humans who had their testicular function suppressed with a GnRH antagonist displayed decreases in sexual desire and masturbation two weeks following the procedure.

Progesterone (C21steroid, pregn-4-ene-3, 20 dione) is a steroid hormone that is synthesized from both tissue and circulating cholesterol. The adrenals, ovaries and placenta during pregnancy are the major production sites of progesterone [12]. Majority of this steroid is metabolized in the liver to pregnanediol and conjugated as a glucuronide prior to excretion by kidneys. The primary role is played in reproductive organs such as the synthesis of corticosteroids and androgens in males [12]. Progesterone is the precursor to many hormones including testosterone, the sex hormone that emphasizes male characteristics and oestrogen the sex hormone that emphasizes female characteristics. Progesterone plays an important role in regulating blood sugar, building bone mass, regulating brain activity, developing intelligence and body functions. It also contributes to the process that converts fat into energy, regulates thyroid hormone production and can help reboot libido. As men age, progesterone levels drop sharply as oestrogen levels increases, causing symptoms such as; low libido, hair loss, weight gain, fatigue, depression, erectile dysfunction and impotence [12].

Follicle stimulating hormone (FSH) is a glycoprotein hormone. There are three other glycoprotein hormones, namely thyroid stimulating hormone, luteinizing hormone (both produced by anterior pituitary gland) and human chorionic gonadotropin (produced by the placenta) which are structurally similar [13]. Follicle-stimulating hormone (FSH) is a gonadotropin, a glycoprotein polypeptide hormone. FSH is synthesized and secreted by the gonadotropic cells of the anterior pituitary gland and regulates the development, growth, pubertal maturation, and reproductive processes of the body [13]. FSH and luteinizing hormone (LH) work together in the reproductive system. FSH regulates the development, growth, pubertal maturation and reproductive processes of the human body. In both males and females, FSH stimulates the maturation of germ cells. In males, FSH induces Sertoli cells to secrete androgen-binding proteins (ABPs), regulated by inhibin's negative feedback mechanism on the anterior pituitary. FSH stimulates primary spermatocytes to undergo the first division of meiosis, to form secondary spermatocytes. FSH enhances the production of androgen-binding protein by the Sertoli cells of the testes by binding to FSH receptors on their basolateral membranes and is critical for the initiation of spermatogenesis [13].

Justification of study

Infertility is a major problem in sickle cell disease patients, especially in males [14]. Abnormalities may involve the accessory sex

organs, seminal vesicles and the prostate gland, as well as marked decrease in ejaculate volume [15]. Sickle hemoglobin (HbS) polymerizes in low oxygen tension environment which may lead to impairment in the production, function and quality of male sex hormones [1]. Sickle cell disease may result to several negative effects on sexual development and function in men such as delayed sexual maturation, sex hormone disturbances, priapism (persistent painful erection usually requiring medical attention), erection problems and reduced fertility [1]. Information gathered from this study may be valuable in assessing the fertility status of male subjects with sickle cell disease. This may ultimately contribute to effective and efficient management of this condition.

Materials and Methods

Materials

- ELISA Machine (Mindray MR-96A)
- Zip Zone electrophoresis chamber and EV 243 power supply (Helena Biosciences, UK).

Methods

Study site

Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Anambra State, Nigeria.

Study design

This is a case-control study designed to assess the levels of testosterone, progesterone and Follicle-stimulating hormone in subjects with sickle cell diseases in Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Anambra State, Nigeria. A total of 90 male subjects within the age range of 18 to 65 were randomly recruited for the study. These comprised 30 homozygous sickle cell (HbSS) subjects in steady state, 30 heterozygous sickle cell (HbAS) individuals and 30 normal individuals (HbAA) (control). The selection of the steady state group depended on subjects not experiencing crisis for at least two weeks and not receiving blood transfusion for at least three months prior to the study.

Inclusion and exclusion criteria

Homozygous sickle cell disease (HbSS) individuals in steady state, heterozygous sickle cell disease (HbAS) individuals and normal control subjects (HbAA) within the age range of 18 to 65. However, individuals outside the age range of 18 to 65, subjects with other sickle cell syndromes such as HbS β -thalassemia, HbSE, HbSC, HbSD-Punjab and others, individuals with less than two weeks history of blood transfusion, males who are a part of special

program that may have affected their clinical, biochemical, hematological status and other variables, chronic alcohol consumers, subjects with chronic diseases such as diabetes mellitus, hypertension or rheumatoid arthritis.

Ethical approval

The ethical approval for this research (NAUTH/CS/66/VOL.10/62/2017/023) was obtained from the Ethics Committee of Nnamdi Azikiwe University Teaching Hospital (NAUTH) and in accordance with the Helsinki Declaration by the World Medical Association (WMA) on the ethical principles for medical research involving human subjects; informed consent was obtained from the participants prior to study.

Sample collection

Five [5] ml of venous blood was collected aseptically from each subject through venipuncture and 2ml dispensed into an EDTA bottle for the determination of genotype and full blood count. The remaining 3ml was dispensed into a plain container and centrifuged at 5000rpm for 5 minutes. The serum was extracted and used for the estimation of testosterone, FSH and progesterone.

Determination of hemoglobin genotype

The method of Daniel [16] as modified by Manafa, *et al.* [17] was used for cellulose acetate paper hemoglobin electrophoresis.

Principle

Charged particles when in an electric field migrate to their counter electrodes. In an alkaline pH (8.2 - 8.6), hemoglobin (Hb) is a negatively charged molecule and will migrate towards the anode. The various Hemoglobin move at different rates depending on their net negative charge, which in turn is controlled by the composition (amino acids) of the Hb molecule (globin chain). These appear as bands on cellulose acetate membrane. The samples are run with known controls.

Estimation of serum testosterone

Serum testosterone was estimated using the method as described by Singer [18]. This is basically an enzyme-linked immunosorbent assay technique.

Principle of the test

The principle of the following enzyme immunoassay test follows the typical competitive binding schematic. Competition occurs between an unlabeled antigen (present in standards, control and patient samples) and an enzyme-labeled antigen (conjugate) for a limited number of antibody binding sites on the micro-plate.

The washing and decanting procedures remove unbound materials. After the washing step, the enzyme substrate is added. The enzymatic reaction is terminated by addition of the stop solution. The absorbance is measured on a micro-titer plate reader. The intensity of the color formed is inversely proportional to the concentration of testosterone in the sample. A set of standards is used to plot a standard curve from which the amount of testosterone in patient samples and controls can be directly read.

Estimation of serum progesterone

Serum progesterone was estimated using the method as described by Wu and Lundy [19]. This is basically an enzyme-linked immunosorbent assay (ELISA) technique.

Principle of the assay

The Progesterone (Pig) ELISA Kit is based on a solid-phase enzyme immunoassay based on competitive binding method. The serum sample containing progesterone will compete with enzyme-conjugated progesterone for high affinity binding sites on a limited number of antibodies coated on to the plate. The amount of labeled antigen in the sample is reversibly proportional to the concentration of the unlabeled antigen. The actual concentrations in the samples are obtained by means of a standard curve based on known concentrations of unlabeled antigen analyzed in parallel with the unknowns. After washing, an enzyme substrate is added and allowed to react for a fixed time before the reaction is terminated. Absorbencies are measured at 450nm using ELISA plate reader.

Estimation of serum follicle-stimulating hormone

Serum FSH was estimated using the method as described by Midgley, [13]. This is essentially an enzyme-linked immunosorbent assay technique.

Principle of the test

The principle of this test follows is based on the use of two highly specific monoclonal antibodies: A monoclonal antibody specific for FSH is immobilized onto the microwell plate and another monoclonal antibody specific for a different region of FSH is conjugated to horse radish peroxidase (HRP). The complex formed on the plate are washed, and subsequently incubated with the HRP conjugate. After a second washing, the enzyme substrate is added. The enzymatic reaction is terminated by addition of the stop solution. The absorbance is measured on a microtiter plate reader at 450nm. The intensity of the colour formed is directly proportional to the concentration of FSH in the sample.

Estimation of full blood count (Fbc)

Full blood count was estimated by the method as described by Buttarello and Plebani [20]. This is principally a Sysmex procedure.

Principle

The aspirated blood sample will be measured to a predetermined volume, diluted at the specified ratio and then fed into each transducer chamber which has a minute aperture and also contain electrodes in which direct current flows. Blood cells suspended in the diluents pass through the aperture causing electrical resistance between the electrodes and the blood cell size will be detected as electric pulses. Blood cells count will be calculated by counting the pulses and the histogram determined by the pulse sizes.

Severity scoring system in sickle cell disease

The determination of disease severity score was performed according to the method described by Manafa, *et al* [17].

Anaemia score

- Hb \geq 10g/dl \rightarrow 0
- Hb \geq 8g/d < 10g/dl \rightarrow 1
- Hb \geq 6 < 8g/dl \rightarrow 2
- Hb \geq 4 < 6g/dl \rightarrow 3
- Hb < 4g/dl \rightarrow 4

Complications score

The complications included stroke, retinopathy, acute chest syndrome, nephropathy, priapism, leg ulcer, pulmonary hypertension, liver failure, and anemic heart failure.

Each complication was scored 1 except

- Nephropathy – 2
- Stroke – 2

WBC score

- Count < 9×10^9 cells/ μ l \rightarrow 0
- Count \geq 9 < 11×10^9 cells/ μ l \rightarrow 1
- Count \geq 11 < 15×10^9 cells/ μ l \rightarrow 2
- Count \geq 15×10^9 cells/ μ l \rightarrow 3

Transfusion score

$$\text{Life Transfusion Rate} = \frac{\text{Total Number of Blood Pint}}{\text{Age}}$$

Approximate to the nearest whole number.

Hospital admission

No of hospital admission per year =
 No of hospital admission in the last 3 years

 3

Approximate to the nearest whole number

Disease severity scores

- ≤ 3 - mild
- 3 - ≤ 7 moderate
- 7 - severe

Statistical analysis

The statistical analysis was performed using analysis of variance (ANOVA). Values were deemed significant at $P < 0.05$. Correlation of the parameters with disease severity was performed using the Pearson’s correlation coefficient. Statistical analysis was carried out using SPSS version 22.0.

Results

Table 1 there was a significant difference in the mean serum level of testosterone in the different blood genotype groups ($P < 0.05$). No significant difference was observed in the mean serum levels of FSH and Progesterone in the different blood genotype groups ($P > 0.05$).

Groups	Number (n)	FSH (μIU/ml)	Progesterone (ng/ml)	Testosterone (ng/ml)
HbSS	30	8.11 ± 4.51	419.03 ± 163.90	2.37 ± 1.50
HbAS	30	6.95 ± 4.32	415.66 ± 126.02	4.16 ± 2.83
HbAA	30	5.63 ± 1.96	472.09 ± 194.77	4.31 ± 1.66
f-value		2.311	0.769	6.436
P-value		0.108	0.468	0.003

Table 1: Levels of FSH, progesterone and testosterone in different blood genotype groups (Mean ± SD).

Groups	FSH	Progesterone	Testosterone
HbSS vs HbAS	P = 0.957	P = 1.000	P = 0.014
HbSS vs HbAA	P = 0.107	P = 0.855	P = 0.007
HbAS vs HbAA	P = 0.845	P = 0.842	P = 1.000

Table 2: Variations of the serum levels testosterone, progesterone and FSH in HbSS, HbAS and HbAA Subjects.

Post-hoc analysis showed no significant difference in the mean serum levels of FSH and progesterone in homozygous sickle cell disease (HbSS) compared with that in the normal control group (HbAA) and in heterozygous sickle cell subjects ($P > 0.05$). Same pattern was observed when the mean serum level of FSH and pro-

gesterone in the control group (HbAA) was compared with that in heterozygous sickle cell disease subjects (HbAS) ($P > 0.05$). Furthermore, there was a significant decrease in the mean serum level of testosterone in homozygous sickle cell disease subjects (HbSS) compared with that in the control group (HbAA) and in heterozygous sickle cell subjects (HbAS) ($P < 0.05$). Contrarily, no significant difference was observed in the mean serum level of testosterone in the control group (HbAA) compared with that in heterozygous sickle disease subjects (HbAS) ($P > 0.05$).

Disease severity classification	Score
Total number of mild	13
Total number of moderate	12
Total number of severe	5

Table 3: Disease severity scores of homozygous sickle cell subjects in steady state.

Disease severity in HbSS sickle cell subjects was determined by adding anaemia score, complication score, WBC score, transfusion score and crisis score. The total score was then used to determine the level of severity for each subject. The total number of subjects that were mild, moderate or severe was then calculated.

Disease severity

- ≤ 3---mild
- >3-≤ 7---moderate
- 7---severe

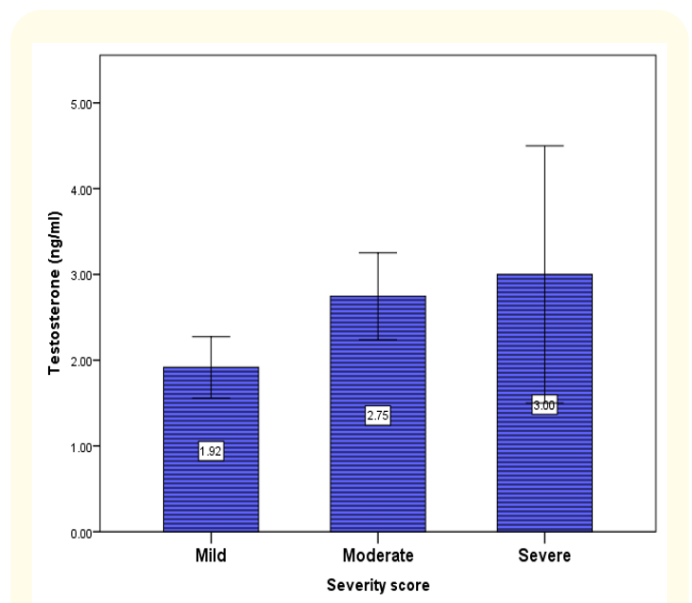


Figure 1: Relationship between mean serum level of testosterone and disease severity in HbSS subjects in steady state: A positive correlation existed between the serum levels of testosterone and disease severity in homozygous sickle cell disease subjects (HbSS) in steady state ($r = 0.287$) ($P > 0.05$). $P=0.165$ $r = 0.287$.

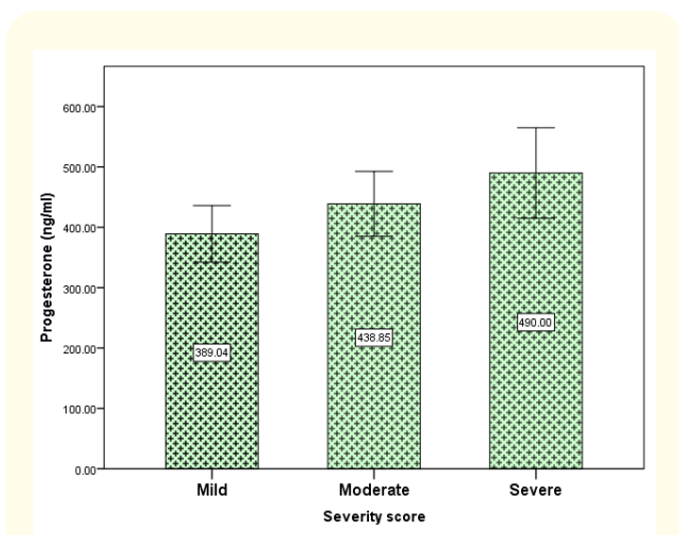


Figure 2: Relationship between mean serum level of progesterone and disease severity in HbSS subjects in steady state: A positive correlation existed between the serum level of progesterone and disease severity in homozygous sickle cell subjects (HbSS) in steady state ($r = 0.198$) ($P > 0.05$). $r = 0.198$ $p = 0.344$

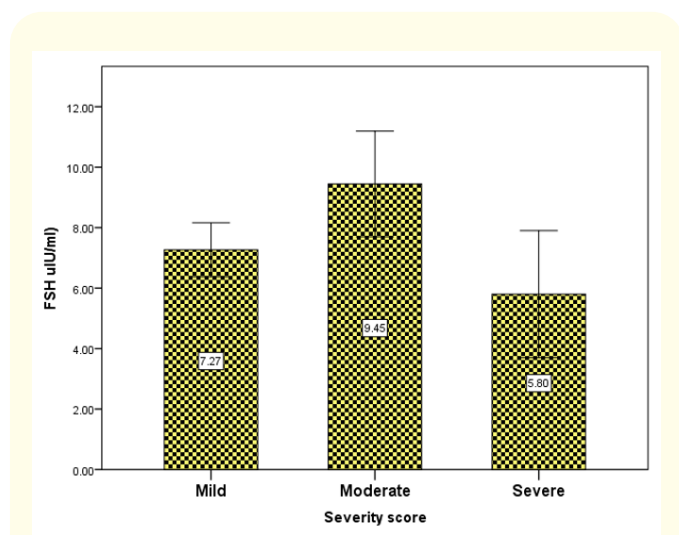


Figure 3: Relationship between mean serum level of FSH and disease severity in HbSS subjects in steady state: A positive correlation existed between the serum level of FSH and disease severity in homozygous sickle cell disease subjects (HbSS) in steady state ($r = 0.078$) ($P > 0.05$). $r = 0.078$ $p = 0.710$

Discussion

Sickle cell disease is the most common genetic disorder in persons of African origin [1] and the disorder comprises a spectrum of syndromes that range from the almost completely benign trait or carrier state (HbAS) to the most severe syndrome, the homozygous sickle cell anaemia (HbSS). However, up to 24% of men with sickle cell disease (SCD) is postulated to have hypogonadism, a clinical syndrome associated with poor testosterone production, infertility, erectile dysfunction and poor libido [21].

There was a significant difference in the mean serum level of testosterone in the different blood genotype groups. A significant decrease was also observed in the mean serum level of testosterone in homozygous sickle cell disease subjects (HbSS) compared with that in the normal control group (HbAA) and in heterozygous sickle cell subjects (HbAS). These findings were similar to the work done by [6,7,22] who observed a decreased serum testosterone level in subjects with homozygous sickle cell disease (HbSS). Similarly, [23] found that the values of mean serum testosterone were significantly lower in homozygous sickle cell subjects (HbSS) compared with subjects with heterozygous sickle cell disease (HbAS) and the normal control subjects (HbAA). The low levels of serum testosterone may be a reflection of hypogonadism secondary to hypopituitarism. This is because; hypopituitarism in HbSS disease may result from intravascular thrombosis and pituitary infarction [24]. Possible underlying patho-physiologic mechanisms of hypogonadism include disruptions in the hypothalamic-pituitary-gonadal axis leading to primary testicular failure. However, some studies are inconsistent as to whether primary testicular failure is the cause of the reduced level of testosterone [25] or secondary hypothalamic-pituitary dysfunction [21,6].

More so, [21] observed low serum testosterone level in eight of thirty-four men with SCD and all eight had low FSH and LH levels suggesting a central mechanism. Theories as to why these condition (hypogonadism) develop in males with SCD suggests zinc deficiency [25] and vaso-occlusion of testicular blood vessels [22], but the precise cause is unknown. The theory regarding vaso-occlusion of testicular vessels is interesting, given reports of recurrent testicular infarction in individuals with SCD [26]. Most importantly, primary testicular failure is marked by low levels of testosterone

and infertility resulting mainly from diseases or conditions that affect and destroy the testis [3]. The low levels of testosterone lead to fertility reduction, which is aggravated by impotence, secondary to earlier priapism [27]. However, a higher mean serum level of FSH was observed in homozygous sickle cell subjects (HbSS) compared with that in heterozygous sickle cell subjects (HbAS) and in the normal control subjects (HbAA). This conforms to the study carried out by [23] who observed that the serum FSH values were significantly higher in the homozygous sickle cell group (HbSS) in comparison with the heterozygous sickle cell subjects (HbAS) and normal control subjects (HbAA). In men, the pituitary gonadotrophins LH and FSH which serve to stimulate testosterone secretion and sperm production respectively have been reported to increase in serum concentration with age [28]. The rise in FSH and LH is consistent with the decline in sperm production and testosterone secretion considering that low testosterone and sperm levels signal the hypothalamic-pituitary-axis to release FSH and LH [29]. Therefore, an increased level of FSH in HbSS compared with HbAS and HbAA subjects could be as a result of compensatory mechanism resulting from reduced level of testosterone in HbAS and HbAA subjects. The result was consistent with the findings of the study carried out by (30), who observed that the mean serum level of progesterone was reduced in homozygous sickle cell disease (HbSS) compared with those with heterozygous sickle cell disease (HbAS) and the normal control group (HbAA).

A positive correlation existed between the serum levels of testosterone and disease severity in homozygous sickle cell disease subjects (HbSS) in steady state. In a study carried out by [31] it was observed that a significant positive correlation existed between serum testosterone levels and International Index of Erectile Function (IIEF) and aging Males Symptoms (AMS) scores, both in the controls and chronic kidney disease (CKD) patients. Also (31) recorded a positive correlation between the serum levels of testosterone and chronic kidney disease (CKD). Data from the Massachusetts Male Aging Study (MMAS) have demonstrated that there is a strong positive relationship between HDL and testosterone in men with cardiovascular disease (low total or free testosterone correlates with low HDL cholesterol) [32]. Anie., *et al.* [33] suggested that the positive correlation between serum testosterone level and disease severity may be as a result of intake of vitamin D supplement in the SCD subjects. It has been observed that vitamin D is essential to fertility because it is needed to help the body cre-

ate sex hormones [34]. Rohit., *et al.* [35] suggested that the positive correlation between testosterone level and disease severity might result from effects of hydroxyurea. Hydroxyurea intake has been reported to increase the levels of HbF and haemoglobin in addition to other benefits [35]. However, [36] observed that intake of hydroxyurea has little or no effect on spermatogenesis and hence testosterone and such negative effects result from nitric oxide (a metabolite of hydroxyurea), a suppressor of testosterone biosynthesis. Testosterone plays a role in red blood cell development and may modulate iron bioavailability [37]. Also, Albert., *et al.* [38] suggested that the continuous intake of folic acid and a new treatment called omega-3 has an effective role in prolonging reproductive lifespan and improving sperm quality. Furthermore, acute alcohol intoxication in normal men results in a fall in serum levels of testosterone. In a large series of clinical studies, reduced serum testosterone levels have been found in chronic alcoholics [38]. Several factors affect the testicular biosynthesis caused by alcohol. Ethanol and its metabolite acetaldehyde have a direct toxic effect on Leydig cells but, on the other hand, there is a disruption on the hypothalamic-pituitary-gonadal-axis [39]. Chronic alcohol exposure decreases circulating LH levels and the response of LH to GnRH is reduced in alcoholics [39]. As a result, disturbance of the hypothalamic-pituitary-gonadal-axis persists over months of abstinence, with sustained increases in serum free and total testosterone levels in the presence of inadequate raised LH concentrations [40]. Several studies have documented a primary testicular pathology, which could be secondary to vaso-occlusion of testicular vessels [22,36]. Other possible mechanisms have been postulated, including abnormal binding of pituitary hormones to testicular receptors and abnormality of testicular steroidogenesis [7]. However, several studies have also reported secondary hypogonadism, secondary to possible pituitary infarction [6]. In addition, [38] theorized that androgen deficiency in patients with SCD may be related to zinc deficiency.

A positive correlation existed between the serum levels of FSH and disease severity in homozygous sickle cell disease subjects (HbSS) in steady state. This is in agreement with the study carried out by [41] who observed that a positive correlation existed between age and serum levels of FSH. Radu., *et al.* [42] had a similar result in a study he carried out in which he observed that patients with the severe form of sickle cell disease showed more frequent abnormalities (increase) of FSH in comparison with patients with

mild disease. However, some studies [43,44] did not observe significant differences of FSH level in serum of normal and infertile patients. This present study also recorded a positive correlation between the serum levels of progesterone and disease severity in homozygous sickle cell subjects (HbSS) in steady state. Men produce approximately 5 to 15mg of progesterone in their testicles each day which in turn increases oestrogen levels [9]. According to Sharma, [45] and in addition to the natural production process of the hormone, environmental factors and activity levels can increase the progesterone and oestrogen levels. Nilsson, *et al.* [46] observed a positive correlation between the serum progesterone and disease severity in which he observed an increased serum level of progesterone in association with the occurrence of congestive heart failure (CHF). In the elderly men, increased physiologic concentrations of progesterone were found to be associated with an increased prevalence of CHF, independent of inflammatory factors, markers of renal function, and insulin metabolism [46]. We therefore hypothesize that single nuclear polymorphism (SNP) distribution does not matter for male reproductive function. However, the theory regarding vaso-occlusion of testicular vessels is increasingly suggestive of recurrent testicular infarction in individuals with SCD [26], thus could be the reason behind the positive correlation recorded in this present study.

Conclusion

The significantly decreased serum level of testosterone in homozygous sickle cell disease subjects (HbSS) compared with the heterozygous sickle cell disease (HbAS) and control groups (HbAA) suggests that there is an increased risk of infertility in male individuals with sickle cell disease.

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