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PRIMARY DYSMENORRHEA IN INDIVIDUALS WITH GENOTYPES :HbAA, HbAS and HbSS

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ABSRACT

Genotypes predispose individuals to various disease conditions. For instance, individuals with HbAA are more susceptible to malaria. On the other hand, individuals with abnormal Hb e.g HbAS do enjoy protection against infection by plasmodium falciparum. Individuals with HbSS suffer a common vasoocclusive crisis, which is characterized by osteo arthritic pains. However whether the pain of dysmenorrhea in these individuals deserve a special description is yet to be studied. This study was aimed at investigating the genetic predilection of genotypes; HbAA, HbAS and HbSS to dysmenorrhea and its effect on HbSS individuals. We carried out a cross sectional study on 90 subjects that were selected by multistaged sampling technique. Though the subjects knew their genotype, we confirmed genotype by standard hemoglobin electrophoresis . Subjects gave informed consent for the study and we gave them a semi-structured questionnaire for the study. The age range of subjects was 19-22 years. The mean age of subjects with dysmenorrhea was 19.1 ±1.9 years while 20.7±1.8 years was the mean age for the eumenorrhic subjects. The percentages of sufferers of dysmenorrhea with genotypes HbAS and HbAA were 53.6% and 63.3% respectively All the subjects (100%) with HbSS suffered dysmenorrhea although the grade of dysmenorrhea was essentially grade 1. The predominant effect of dysmenorrhea on subjects with HbSS was that of taking analgesics and continuing daily activities. Although dysmenorrhea has a genetic predilection for HbSS, it is not a cause of admission for subjects with HbSS because the pain of dysmenorrhea is mostly described as mild.

INTRODUCTION

Dysmenorrhea simply means menstruation that is associated with pain; it can be either primary or secondary. Primary dysmenorrhea occurs in the absence of pelvic pathology. Secondary dysmenorrhea on the other hand occurs in the presene of a pelvic disease. Pelvic pathologies that can cause secondary dysmenorrhea include endometrosis, pelvic inflammatory disease, adenomyosis etc. However, the mechanism of pain in both types of dysmenorrhea are the same. Genotype has been shown to predispose individuals to various disease conditions. For instance, individuals with abnormal hemoglobin do enjoy protection against infection by plasmodium falciparum[1, 2]. Sickle-cell disease, usually presenting in

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childhood, occurs more commonly in people (or their descendants) from parts of tropical and sub-tropical regions where malaria is or was common. One-third of all indigenous inhabitants of Sub-Saharan Africa carry the gene because in areas where malaria is common, there is a fitness benefit in carrying only a single sickle-cell gene (sickle cell trait). Those with only one of the two allelles of the sickle-cell disease, while not very resistant, are more tolerant to the infection and thus show less severe symptoms when infected[3]. This protection was suggested to be because of the sequestration of the infected cells, which lead to parasite death because of low oxygen tension [4]. It is also known that the intracellular decrease of K^+ in the HbAS erythrocyte under low oxygen tension is responsible for the suppression of parasetemia, since erythrocytic parasite require a high potassium ion environment for growth[5] . Subjects with sickle cell trait might have a higher cell mediated immune response to plasmodium falciparum soluble antigens than normal HbAA individuals [6]. Hypoxemia has been documented as the hallmark of pulmonary abnormality in SCD patients of all age groups[7]. Sickle cell disease SCD is an autosomal recessive, hemolytic disorder, which results from the substitution of a valine residue for glutamic acid at position six in the beta-subunit of the hemoglobin molecule [8]. It is prevalent especially among people with ancestry in malaria stricken areas such as Africa, the Mediterranean, India and the Middle East [9]. Although the molecular nature of the hemoglobin defect underlying SCD is well-established[8, 10], details of the pathophysiology are uncertain and treatment remains largely supportive [11]. Vasoocclusive crisis is a common crises amongst patients with hemoglobin SS. Severe pains, fever and dehydration characterize it. The pain of this crisis is a major reason for hospital visitation either on outpatient basis or as in-patient. Pains also characterize dysmenorrhea, which sometimes warrants hospital admission and disruption of academic activities. Acute chest syndrome characterized by chest pain and a variety of other symptoms is the most common cause of death[12,13] in adults with sickle cell anemia. It is the second most common cause of hospitalization of adults with sickle cell anemia [14]. Factors such as labor, postpartum and menstruation have been implicated as precipitators of crises in sickle cell disease patients [15]. This crisis usually warrants hospital admissions [16]. However, within the limits of our literature search, dysmenorrhea as a cause of hospital admissions amongst sickle cell disease patients is yet to be studied and fully documented. The purpose of this study is to examine the incidence of dysmenorrhea in HbAA, HbAS and HbSS. We will attempt to answer the following questions:

1. Is there any genotypic predilection to dysmenorrhea?
2. Are there variations in the severity of dysmenorrhea in HbAA, HbAS and HbSS?

MATERIALS AND METHOD: A total of ninety subjects in three groups were used for the study. Each group had thirty subjects. Group A was made up of subjects with genotype HbAA; Group B was made up of subjects with genotype HbAS; and Group C was made up of subjects with HbSS. The HbSS subjects were selected randomly from the sickle cell clinic in the Sickle Cell Disease Center in Edo State. We used a multistage sampling technique to select subjects who knew their genotypes into Groups A and B. These subjects were students of St Philomena's school of midwifery. Their genotypes were verified

using standard hemoglobin electrophoresis. Subjects who volunteered to participate in the study gave informed consent. We administered a pretested semi structured questionnaire containing both open and closed ended questions to each volunteer. The questionnaire extracted basic demographic data, genotypes and menstrual cycle history (age at menarche, duration of menses, length of menstrual cycle and dysmenorrhea). We measured the severity of dysmenorrhea using verbal multidimensional scoring system[17].This scoring system grades pain as none, mild, moderate and severe and takes into account the effect of pain on daily activity, systemic symptoms and anagelsic requirement.

The results were presented in tables. Data were analysed using the Student's t-test. $P<0.05$ was considered significant.

RESULTS

A total of 90 subjects were used for the study, only 82 filled their questionnaires correctly and returned making a retrieval rate of 91.1%. The age range of subjects was 19-22 years. The mean age of subjects with dysmenorrhea was 19.1 ±1.9 years while 20.7±1.8 years was the mean age for the eumenorrhic subjects; $p>0.05$. The age range for menarche in this study was between 9 to 16 years.The modal age of menarche in this study was 13 years for all the genotypes studied. However 13.3% of subjects with genotype HbAA had menarche at the age of 9 years while 7.1% of subjects with genotype HbAS had their menarche at the age of nine years. None of the subjects with HbSS had menarche at 9 years. The duration of menstrual flow in the subjects used for the study is shown in table1. It is longer for subjects with HbSS ($P<0.05$).Table 2 shows the incidence of dysmenorrhea in HbAA, HbAS and HbSS. Table 3 shows the effect of dysmenorrhea on subjects HbSS, HbAS and HbAA More than half of the subjects with HbAA and HbAS had dysmenorrhea that will only involve use of analgesics and continue with daily activities. Table 4 shows the grades of dysmenorrhea in genotypes HbAA, HbAS and HbSS.

Table 1: Duration of menstrual flow in genotypes HbAA, HbAS and HbSS

DURATION OF MENSES (DAYS)	Genotypes n (%)			TOTAL
	HbAA	HbAS	HbSS	
Three	03 (10.0%)	11 (40.0%)	18 (76.9%)	32
Four	11 (36.7%)	16 (57.3%)	6 (23.0%)	33
Five	09 (30.0%)	01 (2.67%)	0.(0.0)	10
Six	07(23.3%)	0 (0.0)	0 (0.0)	07
Total	30(100.0%)	28(100.0%)	24 (100.0%)	82

TABLE 2: Incidence of dysmenorrhea/eumenorrhea in genotypes HbAA, HbAS and HbSS.

Genotype	Dysmenorrhea (%)	Eumenorrhea (%)	TOTAL (%)
AA	19(63.3%)	11 (36.7%)	30(100.0%)
AS	15 (53.6%)	13(46.4%)	28(100.0%)
SS	24 (100.0%)	0 (0.0%)	24(100.0%)
Total	58 (70.7%)	24 (29.3%)	82(100.0%)

Table 3: Effects of dysmenorrhea on subjects based on genotype

Effects	Genotypes n (%)			TOTAL
	HbAA	HbAS	HbSS	
1.Take drugs and continue daily activities	10 (33.3%)	09 (32.1%)	20 (83.3%)	42
2.Take drugs and stay indoors	06 (20.0%)	04 (14.3%)	04 (16.7%)	38
3.Hospitalized	03 (10.0%)	02 (7.1%)	0 (0.0%)	02
Total	30(63.3%)	28(53.5%)	24 (100.0%)	82

Table 4: Grades of dysmenorrhea in genotypes HbAA, HbAS and HbSS.

Grades	Genotypes		
	HbAA	HbAS	HbSS
Grade 0 (nil pain)	11 (36.7%)	13(46.4%)	0(0.0%)
Grade1 (mild pain)	10 (33.3%)	09(32.1%)	20(83.3%)
Grade2 (moderate pain)	06(20.0%)	04(14.3%)	04(16.7%)
Grade 3 (severe pain)	03(10.0%)	02(7.1%)	0(0.0%)
Total	30	28	24

Discussion

Dysmenorrhea is a common gynecological problem among women especially the young ones. This problem is as old as humanity as most women at a particular point in their reproductive lives have suffered this unpleasant condition [17]. The incidence of certain diseases like malaria has been shown to be a function of one's genotype. For instance individuals with abnormal hemoglobin do enjoy protection against infection by plasmodium falciparum.[1,2] From this study the sickle cell trait seems to have an effect on the age of menarche. For instance in this study the minimum age for menarche was 9years; 7.1% of subjects with HbAS had menarche at this age while none of the subjects with HbSS had menarche at this age of nine. However, 13.3% of subjects with HbAA had menarche at the age of nine years. Dysmenorrhea is most common among adolescents and younger women affecting about 67.2% of adolescent females[18]. However, another study has revealed 53.3% [19] as the incidence of dysmenorrhea. The incidence for dysmenorrhea in this study was 63.3% for HbAA and 53.6% for HbAS and 100% for HbSS. This amounts to about 72% on the average. The reason for the variation from previous studies may due to the fact that those studies did not take note of the propable influence of genotype on dysmenorrhea. However, further studies that will include a larger sample size is needed to establish this influence. The incidence of dysmenorrhea in this study was highest in HbSS subjects and this corroborates with the study done by Joy and Scott in 1985 [15]. They also observed that the periods of sickle cell disease subjects were heavier and they have shorter menstrual cycles than their HbAA counterpart. Dysmenorrhea can be of three grades: grade l which is mild pain, grade ll which is moderate pain and grade lll which is severe pain.[20] The grade lll pain will usually warrant hospital admission. Patients with sickle cell disease have an unpredictable course that range from mild to severe disease. Severe disease has frequently been associated with a debilitating clinical course that decreases quality of life; causes frequent hospitalizations and results in both work and school absenteeism from painful episodes, stroke, acute chest syndrome, and sepsis, avascular necrosis of the fermur, retinopathy and osteomylitis. Stroke is often recurrent and can lead to major functional deficit. Although from this study the incidence of dysmenorrhea amongst subjects with HbSS genotype was highest compared to subjects with HbAA and HbAS, none of the HbSS subjects with dysmenorrhea had grade lll dysmenorrhea. In other words, dysmenorrhea per se is not a cause of hospital admission amongst subjects with HbSS. However one would have expected that with their low hemoglobin concentration the functional competence of blood to supply oxygen to tissue [21]will be compromised. This hypoxic senerio should have made them more prone to severe forms of dysmenorrhea which warrants hospital admission. Since this is not the case, it is possible that the recurrent acute episodes of pains which is the hallmark of sickle cell disease may have increased the pain threshold of these subjects, making the pain of dysmenorrhea to be described as grade l. Since acute painful episodes in HbSS, increase with age and peaks in the third and fourth deacades of life [22], chances are that painthreshold will also increase with age in these subjects. This study revealed that dysmenorrhea has a relatively high predeliction for HbSS, but the pain for them does not warrant hospital admission. This study is however limited by the small sample size.

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