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Relationship between Blood Groups, Haemoglobin Genotypes and Menstrual Disorders in Female Undergraduate Students in Niger Delta University, Bayelsa State, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Menstrual Disorders (MDs) refers to as irregularities of menstruation, which is seen as one of most prevalent gynecological conditions affecting women interfering with the regular menstrual cycle, causing pain, irregularly light or heavy blood flow and missed periods.
Aim: The purpose of this study is to evaluate the association between ABO, Rhesus blood groups, hemoglobin genotypes, and menstruation disorders in female undergraduate students at Niger Delta University, Bayelsa State, Nigeria.
Study Design: A cross-sectional study design was carried out among undergraduate female students. The study was carried between September, 2023 to February, 2024.
Methodology: A total of five hundred and fifty-three (553) undergraduate students were recruited for the study. Questionnaires were administered randomly and data collected from the subjects from September, 2023 to February, 2024. Two milliliters of whole blood samples were collected into ethylene diamine tetra-acetic acid anticoagulant container which was used for the determination of ABO, Rhesus blood groups and haemoglobin genotypes using standard serological techniques and Haemoglobin electrophoresis method respectively. Statistical analysis was done using Special Package for Social Science (SPSS) version 23.0 and $p<0.05$ was considered statistically significant.
Results: The result revealed that out of the 553 participants, 64.3% had menstrual disorders, while 34.7% had normal or regular menstrual cycle. The result also showed that menstrual disorders are more common within blood group O-ve, +ve individuals with prevalence of 59.4%, followed by group A-ve, +ve (29.7%), B-ve, +ve (8.1%) and AB-ve, +ve (2.8%) (O>A>B >AB). For the haemoglobin genotypes, menstrual disorders were more common in HbAA (79.7%) individuals with prevalence pattern of HbAA>HbAS>HbSS. Furthermore, dysmenorrhea was found to be the commonest type of menstrual disorder in all blood group types and haemoglobin genotypes.
Conclusion: These findings can be considered to have established a potential nexus between blood groups, haemoglobin genotypes and menstrual disorders in women. Hence, emphasizing the relevance of considering blood group factors in the assessment and management of menstrual disorder.

Keywords: Menstrual disorders; female undergraduates; blood groups; hemoglobin genotypes.

1. INTRODUCTION

Menstruation is defined as the intermittent shedding of the endometrium accompanied by the discharge of blood from the endometrial arteries [1]. It occurs as a result of intricately intertwined systems that include the pituitary, ovaries, uterus, prostaglandins, and neuroendocrine factors [2]. Menstrual disorders (MDs) refer to as irregularities of menstruation, is seen as one of the commonest gynecological problems in reproductive health [3]. While some women experience only mild discomfort or anxiety before or during their monthly period, others suffer severe physical and psychological symptoms that can negatively impact their quality of life. These symptoms can range from heavy flow to missed periods, pains, mood swings, and painful menstruation [4].

The normal length of the menstrual cycle and menstruation (uterine flow of blood shed) of a woman is twenty-eight (28) days. Menstrual cycle less than twenty (21) days and more than thirty-five (35) days are indication of abnormal menstruation, which are referred to as oligomenorrhoea and polymenorrhoea, respectively [5]. The standard length of menstruation (uterine flow of blood shed) greatly varies among individuals. However, menstruation length that were not within 3 and 7 days were considered abnormal. In regards to menstrual blood volume, subjects that uses less than 2 and more than 5 sanitary pads, each total saturated with menstrual blood, it is referred to hypomenorrhoea and hypermenorrhoea respectively, which are referred to irregular menstrual cycle. The presence of dysmenorrhoea was taken as the occurrence before, during or after menstruation of lower abdominal pain that seriously affected the quality of life [5].

Menstrual disorders include; amenorrhea, irregular menstrual cycle, infrequent menstruation, dysmenorrhea, intermenstrual bleeding, heavy menstrual bleeding and premenstrual syndrome which are the most recorded [6,7]. Many factors can contribute to irregular menstruation, dysmenorrhea, and non-

menstrual vaginal bleeding; however, in women who are of reproductive age, pregnancy should always be suspected. Abnormal vaginal bleeding in non-pregnant women is assessed differently from vaginal bleeding in pregnant women due to the possibility that polycystic ovarian syndrome may present with symptoms similar to those of menstrual disorders [8].

The ABO blood group system arises from the polymorphism of complex carbohydrate with diverse antigenic structures of glycoproteins and glycolipids expressed on the surface of erythrocytes, as glycan units of mucin glycoproteins [9]. According to Storry and Olsson, [10], the ABO locus's A and B alleles encode A and B glycosyltransferase activities, which in turn translate the precursor H antigen into A or B determinants. A and B antigens. On the other hand, having an additional saccharide unit to the O unit (N-acetylgalactosamine and galactose, respectively). The Rhesus blood group system is important because it is relevant to the haemolytic disease of newborn and to Rhesus D negative individuals in subsequent transfusions after they have developed Rhesus antibodies [11]. The clinical significance of ABO and Rhesus blood group systems is now known to extend beyond solid organ transplantation and blood transfusion, as it is linked to the pathophysiology of many systemic disorders [9].

Hemoglobin genotypes refer to the specific combinations of alleles inherited from both parents that determine an individual's hemoglobin composition. The main hemoglobin types are Hemoglobin A (HbA), Hemoglobin A2 (HbA2), and Hemoglobin F (HbF), with variations associated with different genetic conditions [12]. Abnormal hemoglobin genotypes arise when an individual inherits mutated globin genes from both parents, like hemoglobin S, C, D and E. The predominant abnormal hemoglobin genotypes among Nigerians are AS, AC, SC and SS. These genotypes are inherited in an autosomal codominant manner and result from various combinations [13].

In the past, several studies have established that both ABO and Rhesus blood groups are linked to many genetic and infectious diseases including; cardiovascular diseases [14], breast and gastric cancer [15, 16], parasitic and viral infections, diabetes mellitus [17], renal diseases and psychological disorders [18]. Authors in their previous studies identified the linking ABO blood category with infertility and functions of ovarian reserve. Antigen A has been identified to be a protective factor for ovarian reserve ability and blood group O has been reported detracts risk of ovaries broadness more than the forms of blood AB and A [19].

Despite numerous studies on the nexus between blood groups, haemoglobin genotypes and the risk of developing genetic diseases, there is a scarcity of information on the relationship between blood groups, haemoglobin genotypes and menstrual disorders. Therefore, this study was designed to determine the relationship between blood groups, haemoglobin genotypes and menstrual disorders in female undergraduate students in Niger Delta University, Bayelsa State, Nigeria.

2. MATERIALS AND METHODS

2.1 Study Setting and Population

A total of five hundred and fifty-three (553) female undergraduate students in College of Health Sciences, Niger Delta University, Bayelsa State, were recruited for the study. Out of the 553 subjects, 192 students had normal (regular) menstruation, which served as control group, while the remaining 361 subjects had one or more menstrual disorders (MDs), and were set as the experimental group. All the females had no biological relationship. A random sampling technique was used to select the 553 subjects. The study was carried between September, 2023 to February, 2024. All participants were not married, and subjects with daily intake of oral contraceptive pills were excluded for the study.

2.2 Data and Sample Collection

The questionnaires were co-designed with epidemiological, statistical and endocrinologist, and administered to the participants and filled under the guidance of the researcher which was retrieved immediately. The questionnaire consists of demographic details (age, marital status, religion) and menstrual features (amenorrhoea, oligomenorrhoea, dysmenorrhea and polymenorrhoea). Thereafter, two milliliters (2ml) of venous blood were collected under aseptic condition using venipuncture technique from each subject and dispensed into ethylene diamine tetra-acetic acid (EDTA) sample container. The blood sample was used for the determination of ABO, Rhesus blood groups and haemoglobin genotypes.

2.3 Laboratory Investigation

ABO and Rhesus blood were determined using the Slide Haemagglutination Technique as described by Sadiq et al., [20]. A 2% suspension of red blood cell was prepared with normal saline, and a drop of red cell suspension was placed on three separate areas on a clean white tile. Each drop of red cell suspension was mixed with a drop of commercially prepared Anti-A, Anti-B, and Anti-D, and observed for agglutination for 60 seconds. Each mixture (blood plus antisera) was viewed microscopically to confirm agglutination. The ABO monoclonal reagent (Eryscreen Monoclonal ABO/Rh, Tulip Diagnostic Ltd. Goa, India) was used to assessed ABO blood groups [21]. Presence of agglutination established positive results, whereas absence of agglutination established negative results.

Haemoglobin genotypes was determined using Haemoglobin electrophoresis technique as described by Ajayi et al., [22]. A little quantity of haemolysate of venous blood from each of the subjects was applied on the cellulose acetate membrane and carefully introduced into the electrophoretic tank containing Tris - EDTA - Borate buffer at pH 8.9. The electrophoresis was then allowed to run for 15 minutes at an electro-motive force (emf) of 160 V. The results were read immediately.

2.4 Statistical Analysis

The results obtained were analyzed using the Chi square ($\chi 2$). Data presentation was in the form of tables and expressed in percentage. The statistically significant level was set at p-values <0.05.

3. RESULTS

The results in Fig. 1 shows the percentage distribution of normal (regular) and disorder menstrual cycle among female students in Niger Delta University. The result shows that out of the 553 participants in the study, majority (65.3%) of the female students had menstrual disorders, while 34.7% of the subjects had normal or regular menstrual cycle.

Fig. 2 shows that majority 47.6% of the females had more than one MDs, 30.7% had Dysmenorrhea, 6.9% had Menorrhagia and Oligomenorrhoea, 4.7% had Metrorrhagia, while 3.0% had Amenorrhea. However, the most predominant type of menstrual disorder found within the female students was Dysmenorrhea (menstrual cramp), as majority of the subjects had both dysmenorrhea with other type of menstrual disorders (MDs).

The distribution of ABO and Rhesus blood groups among the females with menstrual disorder revealed that, majority 212(57.6%) are of blood group O-ve, +ve, followed by group A-ve, +ve 110(34.4%), B-ve, +ve 30(8.3%) and AB-ve, +ve 09(2.0%) as shown in (Table 1). This suggests that blood group O-ve, +ve were the most predominant blood group with a prevalence of 57.6%. As shown in the result, high menstrual disorders were more common within group O+ve, -ve individuals as compared with the other blood types ($P<0.05$). In the females with normal (regular) menstrual cycle, the result revealed that majority 106(55.2%) were of blood group O-ve, +ve, followed by B-ve, +ve 48(25.0%), A-ve, +ve 23(12.0%) and AB-ve, +ve 15(7.8%). When the blood groups of females with menstrual disorders were compared with those of normal menstrual cycle, there was a statistical difference ($p<0.05$) observed in blood group O+ve and A+ve.

Table 2 revealed that majority 101(47.6%) of the group O+ve females had a greater prevalence of more than one menstrual disorder compared to other MDs. Blood group O-ve females had greater incidence of dysmenorrhea 14(6.6%) compared to other MDs. Blood group A+ve females had greater prevalence of more than one MDs 41(37.3%) compared to other MDs. Blood group A-ve females had greater prevalence of dysmenorrhea 11(10.0%) compared to other MDs. Blood group B-ve, +ve females had a higher prevalence of dysmenorrhea 13(43.4%) than other MDs. Also, blood group AB-ve, +ve females had a greater prevalence of dysmenorrhea (55.5%) when compared to other MDs.

Results in Table 3 revealed that majority 156(81.2%) of the subjects with normal (regular) menstrual cycle had HbAA, followed by HbAS 34(17.7%), and HbSS 02(1.1%). However, in the females with menstrual disorder, majority 259(71.7%) had HbAA, followed by HbAS 97(26.9%), and HbSS 05(1.4%). There was no prevalence of HbSC and HbAC among the study population. The study suggests HbAA to be the most predominant genotype with a percentage of 7I.7% in women with menstrual disorder cycle. This indicates that high menstrual disorders were more predominant in HbAA females as compared

with the other types of haemoglobin genotype (P < 0.05). When the haemoglobin genotypes of the women with menstrual disorder were compared with the women with normal menstrual cycle, there was a statistical difference (p<0.05) observed in those with HbAA.

Table 4 shows the Percentage Distribution of Menstrual Disorders within Haemoglobin Genotype among female students under study. The result revealed that majority 102(34.6%) of the HbAA subjects experienced a combination of two or more menstrual disorders, 97(32.8%) had dysmenorrhea, 25(8.5%) had oligomenorrhea, 21(7.1%) had Menorrhagia, while 04(1.4%) had amenorrhea prevalence. Majority 44(45.4%) of HbAS subjects experienced a combination of two or more menstrual disorders, 35(36.1%) had dysmenorrhea, 08(8.2%) had Amenorrhea, 6(6.2%) had metrorrhagia, 04(64.1%) had metrorrhagia, while none of them with HbAS had oligomenorrhea. For HbSS individuals, 40% experienced dysmenorrhea, while 20% experienced amenorrhea.

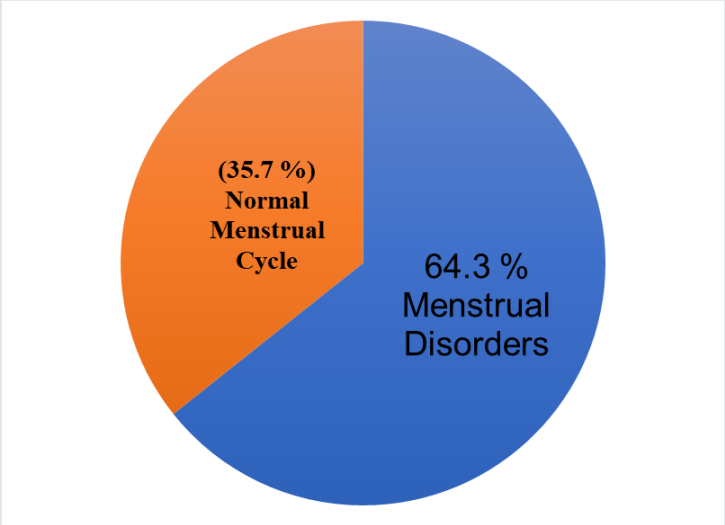

Fig. 1. The percentage of normal and menstrual disorders among female students in Niger Delta University

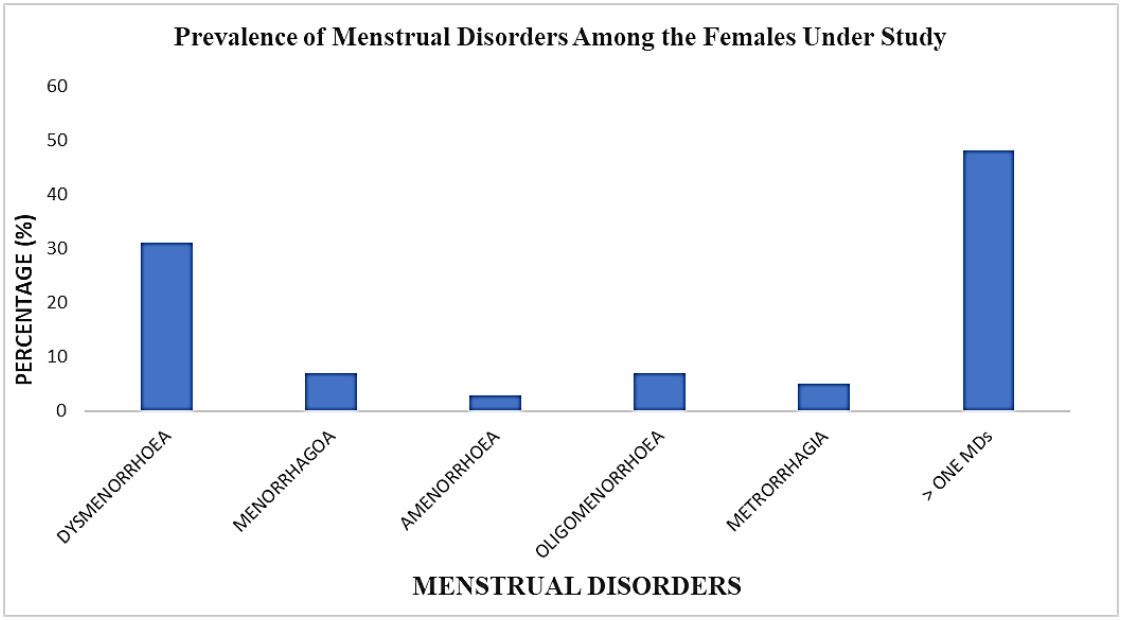

Fig. 2. Distribution of menstrual disorders among the female undergraduate students under study

Table 1. Comparison of percentage distribution of the blood groups among female students with regular and disorder menstrual cycle under study

Blood group	Normal Menstrual Cycle	Disorder Menstrual Cycle	χ2	P-value
	n(%)	n(%)		
Group O^+	86(44.8%)	168(46.5%)	41.21	0.001*
Group O^-	20(10.4%)	44(11.1%)	3.11	0.357
Group A^+	18(9.4%)	85(23.5%)	51.72	0.000*
Group A^-	05(2.6%)	25(6.9%)	6.34	0.101
Group B^+	43(22.4%)	20(5.5%)	6.21	0.429
Group B^-	05(2.6%)	10(2.8%)	5.14	0.511
Group AB^+	11(5.7%)	06(1.7%)	6.91	0.107
Group AB^-	04(2.1%)	03(0.3%)	5.11	0.149
	192(100%)	361(100%)		

**Significant difference P-Value < 0.05.*

Table 2. Percentage distribution of menstrual disorders according to blood groups among female students under study

Blood Group	Dysmenorrhea n(%)	Menorrhagia n(%)	Amenorrhea n(%)	Oligomenorrhea n(%)	Metrorrhagia n(%)	>one disorder n(%)
Group O^+	49(23.1%)	15(7.1%)	07(3.3%)	12(5.7%)	11(5.2%)	101(47.6%)
Group O^-	14(6.6%)	04(1.9%)	02(0.9%)	08(3.8%)	00(0.0%)	10(4.7%)
Group A^+	19(17.3%)	03(2.7%)	00(0.0%)	03(2.7%)	00(0.0%)	41(37.3%)
Group A^-	11(10.0%)	00(0.0%)	02(4.5%)	00(0.0%)	00(0.0%)	10(9.1%)
Group B^+	11(36.7%)	02(6.7%)	00(0.0%)	01(3.3%)	06(20.0%)	07(23.3%)
Group B^-	02(6.7%)	00(0.0%)	00(0.0%)	00(0.0%)	00(0.0%)	02(6.7%)
Group AB^+	03(33.3%)	01(11.1%)	00(0.0%)	01(11.1%)	00(0.0%)	01(11.1%)
Group AB^-	02(22.2%)	00(0.0%)	00(0.0%)	00(0.0%)	00(0.0%)	01(11.1%)

Table 3. Comparison of the percentage distribution of haemoglobin genotypes among female students with normal and disorder menstrual cycle under study

Blood group	Normal MC	Disorder MC	χ2	P-value
	n(%)	n(%)		
HbAA	156(81.2%)	259(71.7%)	31.72	0.010*
HbAS	34(17.7%)	97(26.9%)	5.01	0.278
HbSS	02(1.1%)	05(1.4%)	6.12	0.341
HbSC	00(0.0%)	00(0.0%)	-	-
HbAC	00(0.0%)	00(0.0%)	-	-
	192(100%)	361(100%)		

**Significant difference P-Value < 0.05*

Table 4. Percentage distribution of menstrual disorders according to haemoglobin genotypes among female students under study

Blood Group	Dysmenorrhea n(%)	Menorrhagia n(%)	Amenorrhea n(%)	Oligomenorrhea n(%)	Metrorrhagia n(%)	>one disorder n(%)
HbAA	97(32.8%)	21(7.1%)	04(1.4%)	25(8.5%)	10(3.4%)	102(34.6%)
HbAS	35(36.1%)	04(4.1%)	08(8.2%)	00(0.0%)	06(6.2%)	44(45.4%)
HbSS	02(40.0%)	00(0.0%)	01(20.0%)	00(0.0%)	00(0.0%)	02(20.0%)
HbSC	00(0.0%)	00(0.0%)	00(0.0%)	00(0.0%)	00(0.0%)	00(0.0%)
HbAC	00(0.0%)	00(0.0%)	00(0.0%)	00(0.0%)	00(0.0%)	00(0.0%)

4. DISCUSSION

Human fertility plays a crucial role in public health and overall human well-being (Didem et al., 2010). Menstrual Disorders, a prevalent gynaecological condition, not only impact the health and well-being of females but also elevate the susceptibility to various gynaecological diseases such as endometrial and breast cancer, as well as cardiovascular diseases, as noted by Tao et al. [3]. This present study confirmed that there is an association between menstrual disorders (MDs) and distribution of blood groups and haemoglobin genotypes.

Results from this study revealed that out of the 553 females that participated in the study, majority 65.3% had menstrual disorders (MDs), while 34.7% had normal (regular) menstrual cycle. This finding suggests that majority of the female students had menstrual disorders. The high prevalence of menstrual disorders (MDs) observed in this study could be connected with diet intake and lifestyle of the female students, as most of them are involved in the consumption of caffeinated beverages [23]. This is consistent with the previous work by Amu and Bamidele [24], and inconsistent with Huda and Rajaa, [25] who reported a percentage prevalence of 65.9% for regular menstrual cycles and 34.1% for Disorder menstrual cycle group in Iraq.

Majority (47.6%) of the subjects experienced a combination of two or more MDs, 30.7% had dysmenorrhea, 6.9% had Menorrhagia and Oligomenorrhoea, 4.7% had Metrorrhagia, while 3.0% had Amenorrhea. However, the most predominant type of menstrual disorder found within the female students was Dysmenorrhea (menstrual cramp), as majority of the subjects experienced both dysmenorrhea with any other type of menstrual disorders (MDs). The high incidence of dysmenorrhea (menstrual cramps) observed in this study could also be due to the dietary intake and lifestyle of the females [23]. This is in consonance with Amu and Bamidele [24], which reported a high prevalence of dysmenorrhea as 77.8%, menorrhagia 57.4% and metrorrhagia 18.6% in Osogbo, South-West, Nigeria.

The present study showed that, O-ve, +ve was the most predominant blood group (57.6%), followed by group A-ve, +ve (34.4%), B-ve, +ve (8.3%), and the least blood group was AB-ve, +ve 09(2.0%) in the females with menstrual disorders, with a distribution of O>A>B >AB. While the distribution of the population based on blood groups in the regular menstrual cycle females was O>B>A>AB. When the blood groups of the females with disorder menstrual were compared with the women with normal menstrual cycle, there was a statistically significant difference ($p<0.05$) observed in females with blood group O. This finding confirmed that there is an association between menstrual disorders (MDs) and blood group distribution. This may be due to the fact the position of the responsible ABO-blood gene is located on a chromosome 9q34.2, and the gene for blood type and the TRAF2 allele could be a gene for the reason of menstrual disorders [1]. Certain genetic markers related to menstrual disorders could be connected to the ABO gene and situated in proximity to chromosome 9q34.2. An unidentified genetic variation near the ABO gene could potentially be linked to MDs, providing a theoretical explanation for the association between the ABO blood group system and irregularities in menstrual and reproductive functions [1]. According to the findings presented by experts from Yale University and Albert Einstein Medical College at the 66th ASRM Annual Meeting in 2010, blood type O has been linked to infertility. Studies conducted by Mahammed et al., [26] and Uwem et al., [27] have also shown a higher prevalence of blood group O in infertile male and female patients compared to other ABO blood groups. Additionally, Nejat et al., [19] reported that antigen A may serve as a protective factor for ovarian reserve capacity, while type O blood was associated with a decreased risk of ovarian reserve capacity compared to blood types A and AB.

In this study, that majority (47.3%) of females with the blood group O+ve experienced a combination of two or more menstrual disorders (MDs). Blood group O-ve females had greater prevalence of dysmenorrhea 14(6.6%). Blood group A+ve females had greater prevalence of more than one MDs (37.3%). Blood group A-ve females had greater prevalence of dysmenorrhea 11(10.0%) compared to other MDs. Blood group B-ve, +ve females had a higher prevalence of dysmenorrhea 13(43.4%) than other MDs. Also, blood group AB-ve, +ve females had a greater prevalence of dysmenorrhea (55.5%) when compared to other MDs. This finding suggests that majority of the subjects in all blood types experienced more than one type of menstrual disorders (MDs). However, dysmenorrhea (menstrual cramp) is the most common type of

menstrual disorder found within the subjects, but highest prevalence occurs in the blood group O individuals. This could be attributed to regular consumption of caffeinated beverages [23]. This confirmed the reported by Amu and Bamidele, [24] who indicated a high dysmenorrhea prevalence of 77.8% among adolescents.

Several authors have documented that genotypes predispose individuals to several medical illness [28]. It is reported that individuals with HbAA are more susceptible to malaria, while individuals with HbAS have protection against infection by Plasmodium falciparum. Individuals with HbSS suffer a common vasoocclusive crisis, which is characterized by osteo arthritic pains (Anisa and Kwabena, 2014) [29]. This study has revealed that majority (71.7%) of the subjects with menstrual disorders had HbAA, followed by HbAS (26.9%), while the least haemoglobin genotypes was HbSS (1.4%). The distribution of the population based on haemoglobin genotypes was HbAA>HbAS>HbSS. The study suggests that HbAA was the most predominant genotype with an incidence of 7I.7% in females with menstrual disorders. This indicates that high menstrual disorders were more predominant among HbAA females as compared with the other types of abnormal haemoglobin genotype variants ($P < 0.05$). The 71.7% documented for HbAA in this study is consistent with the previous work by Jeremiah, [30], which recorded 50-75% for Africa, while the 26.9% reported for HbAS in this study is in consonance with the works of Ajayi et al., [22], which reported 21-30% recorded for Nigeria. The 1.4% reported for HbSS in this study confirmed the works by Ajayi et al., [22], which reported 1.0% for HbSS in a previous study in Nigeria. However, in this study, there was no prevalence of HbSC and HbAC among the study population.

This study reveals that majority (34.6%) of HbAA subjects experienced a combination of two or more menstrual disorders, (32.8%) had dysmenorrhea, (8.5%) had oligomenorrhea, (7.1%) had Menorrhagia, while (1.4%) had amenorrhea prevalence. Also, majority (45.4%) of HbAS subjects experienced a combination of two or more menstrual disorders, (36.1%) had dysmenorrhea, (8.2%) had Amenorrhea, (6.2%) had metrorrhagia, (64.1%) had metrorrhagia, while none of them with HbAS had oligomenorrhea. For HbSS individuals, 40% experienced dysmenorrhea, while 20% experienced amenorrhea. This confirmed the works of Ghafuri et al., [31], which reported that adolescents with HbAA had significantly higher rates of dysmenorrhea than HbAS.

5. CONCLUSION

The study has established that menstrual disorders are prevalent among the undergraduate students in the study area. It also shows that there is an association between menstrual disorders (MDs) and distribution of blood groups and haemoglobin genotypes. It was seen from the study that high menstrual disorders was more common within individuals with blood group O-ve, +ve with a prevalence of 59.6%, while for haemoglobin genotypes, menstrual disorders was more common in individuals with HbAA with a prevalence of 79.7%. Furthermore, the study confirmed that dysmenorrhea is the most prevalent type of menstrual disorder in all blood groups types and haemoglobin genotypes.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declared that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

CONSENT

All authors declare that ‘Written informed consent was gotten from all the subjects prior to the data collection.

ETHICAL APPROVAL

Ethical approval was obtained from the Ethics Committee of College of Health Sciences with Reference No NDU/CHS/CHSEC/2023/0187, in the Niger Delta University.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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