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Original Research

Major Sickle Cell Disease in Pregnant Women at University Teaching Hospital of Cocody in Cote d'Ivoire, a Low Resources Country

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Abstract

Background: Sickle cell disease (SCD) is one of the most prevalent genetic disorders, including major SCD and SC Trait (SCT) genotypes. Many studies have shown a negative association between major SCD and pregnancy. However, they are underestimated in Cote d'Ivoire statistics. To provide consistent data on SCD in pregnancy, we compare outcomes between women with normal hemoglobin (Hb) genotype and major SCD. **Methods**: A retrospective, and case-control study in the University Hospital of Cocody, from 2015 to 2018, analyzed maternal and fetal outcomes, comparing the Cases Group: major SCD (HbSS, HbSC) and Control Group: normal hemoglobin (Hb) genotype A. Only pregnancies with gestations longer than 28 weeks were included. No cases of thalassemia or variant of hemoglobin were found. Local protocols recommended systematic use of vasodilators or analgesics, folic acid, and high concentrations of inhaled oxygen during labor, associated with fluid and/or blood transfusion. We excluded sickle cell trait (SCT) genotype AS (HbAS), and incomplete data. A logistic regression was exploited to gauge the risk factors. We used SPSS version 19 (IBM Corp., Armonk, NY, USA) for statistical analysis, and calculate the adjusted odds ratio and 95% confidence interval. **Results**: We registered 156 major SCD (0.92%), compared to 312 HbAA. In Cases Group 27.6% were multigravidas (>4), young aged (≤20) (16.0%), and well-educated (43.6%). Major SCD were HbSC (33.3%) and HbSS (66.7%). The commonest maternal antenatal complication in major SCD was anemia ($p < 0.0001$), vaso occlusive crisis ($p < 0.0001$), and pregnancy-induced hypertension ($p < 0.0001$). Blood transfusions were significant in the SCD group ($p < 0.0001$). No significant difference between the groups regarding stillbirths ($p = 0.3150$) was recorded. Moreover, a significant risk in the major SCD genotype was low birth weight (LBW) ($p < 0.0001$), negative Apgar in the 5th minute ($p < 0.0001$), vaso-occlusive crisis (VOC) ($p < 0.0001$), and acute chest syndrome (ACS) ($p < 0.0019$). **Conclusions**: The findings of the survey suggest better fetal and maternal prognosis in HbAA compared to major SCD. Multidisciplinary team management is necessary to improve those outcomes. Patient awareness and education, and early and effective prenatal care are useful to avoid those risks.

Keywords: major SCD; HbAA genotype; pregnancy maternal and fetal outcome; MTD

1. Introduction

Normal human hemoglobin (Hb) (HbAA) allows oxygen transfer in blood. Its chemical structure normally includes one pair of heme molecules (2α-type) and globin chains (2β-type) [1]. Globin represents the protein fraction in which many mutations can occur, leading to structural and physiological function alterations [1,2]. Abnormal hemoglobin corresponds to sickle (S) cell disease (SCD) and may be in the form of a homozygous or heterozygous genotype. Sickle cell disease (SCD) is the most prevalent genetic disorder in developing Sub-Saharan Africa, South America, Central America, Saudi Arabia, India, and Mediterranean countries [3–9]. This disorder is caused by a β-globin subunit gene mutation [3–9] and can be divided into 2 groups: major and minor SCD. Genotypically, homozygous hemoglobin S (SS) and heterozygous form (hemoglobin SC, hemoglobin Sβ+-thalassemia, and Sβ0-thalassemia) were predominant and considered major SCD. Infrequent forms include hemoglobin C, or even hemoglobin E (thalassemia β), or genotypes SD and SE [1–4]. Women with hemoglobin HbAS or SC trait (SCT) genotype suffer from minor diseases [5–7]. These abnormal structural variations result in oxygen delivery alterations, Hb molecule instability, and low oxidation resistance [1,4]. SCD is the most common hemoglobinopathy among humans, affecting approximately 5% of the world's population, and 7% of pregnant women [1,4]. The condition promotes susceptibility to severe infections, chronic inflammation, hypercoagulability disorders, damage to vital organs, renal and respiratory disorders, or bone marrow suppression [1,5–7]. Empirical evidence suggests that major SCD is negatively correlated with poor maternal and perinatal health outcomes [5–9]. Few studies in Cote d'Ivoire, have studied the negative outcomes of SCD in

pregnancy [8,9]. These negative repercussions include maternal complications, such as chronic anemia, infection, painful vaso-occlusive crisis (VOC), preeclampsia, premature labor, and increased cesarean section (CS) rates [5–12]. On the other side, adverse perinatal outcomes include intrauterine growth restriction (IUGR), premature infants, and in-utero fetal distress or death (IUFD). High rates of maternal and fetal mortality were reported during pregnancy in major SCD compared to the general population [8–12]. This condition required better quality of management to improve the mother and child's prognosis [9]. There is a paucity of information about SCD making appropriate ante, prenatal and postnatal care challenging. In developing countries, lack of education in women, low access to prenatal care, lack of medical coverage, and low technical-level health facilities are obstacles to efficient management. Moreover, the development of guidelines for providing complete prenatal care to women with SCD has yet to be developed. The implementation of better management modalities should be instituted and would require a multidisciplinary team decision (MTD) of obstetricians, hematologists, pediatricians, anesthesiologists, and midwives. This study was conducted to report consistent data on the prevalence of this major hemoglobin disease, to evaluate prenatal and postnatal care, and to determine the maternal and fetal prognosis in a reference health center located in Cocody.

2. Material and Methods

We conducted a retrospective cross-sectional and retrospective case-control study of all hemoglobinopathies at the obstetrics department of the University Hospital of Cocody (Cote d'Ivoire), between January 2015 and December 2018 (4 years). We have obtained the approval of Felix Houphouet Boigny University for the publication of the results of this study. This study compared ante, intra and postnatal outcomes of women with major SCD (Cases Group), to those with normal hemoglobin genotype or HbAA (Control Group). The inclusion criteria are listed as following: Cases Group included the major SCD genotypes (HbSS, HbSC), and the Control Group consisted of pregnant women with HbAA. The exclusion criteria are listed as following: incomplet files lost of follow-up and non consent women. The genotype was specified by hemoglobin electrophoresis performed during antenatal care or known before pregnancy. We analyzed maternal and fetal outcomes. The Cases Group included the major SCD genotypes (HbSS, HbSC), and the Control Group consisted of pregnant women with HbAA. No cases of quantitative sickle cell disorders of globin chains (thalassemia), qualitative disorders of globin structure, or structural variant of hemoglobin (S-ßthalassemia, HbSF, HbSD, HbSO) were found in the population. In the same way, we did not find hemoglobin with decreased stability, and Hemoglobin with altered oxygen affinity as our laboratories are limited. We obtained consent from 468 pregnant women for this comparative retrospective study: 156 women with major SCD belonging (Cases Group); 312 pregnant women with HbAA genotype (Control Group). The comparison involved ante, intra, and postpartum data, and the selection of the patient pool was based on matching age, gravidity, and similar socioeconomic status. Emphasis was on obstetrical history and significant history of the underlying disease symptomatology. Preterm labor was considered as the onset of labor before 37 completed weeks of gestation (WG), while anemia was identified when the hemoglobin concentration level was below 110 g/dL. The World Health Organization (WHO) defined severe anemia as Hb $<$70 g/L in children under 5 years of age and Hb $<$80 g/L in all other age groups, though other definitions, including Hb $<$50 g/L, are used of particular importance clinically, as it can result in high-output heart failure and death. Pregnancy-induced hypertension (PIH) was a blood pressure higher than 140/90 mmHg in two instances six hours apart. Early neonatal death was determined as death within seven days of birth, whereas low birth weight (LBW) was defined as birth weight below 2500 grams. IUGR was diagnosed when the birth weight was lower than the 10th percentile of the average for gestational age. The patient's prenatal care was provided in conjunction with hematologists on an alternating bimonthly basis. Pregnant women's care was delivered under the aegis of MTD management, led by an experienced hematologist, neonatologist, nephrologist, pain management experts, and obstetricians. Local protocols recommended for major forms of hemoglobinopathies in pregnant women, systematic use of vasodilators (Trimetazidine Dihydrochloride 5 mg coated tablet daily, manufactured by Rakshit Pharmaceuticals Limited in Ahmedabad, Gujarat, India) or analgesic (manufactured by Sanofi-Aventis, Paris, France) three times per day (in case of painful crises), Folic acid tablet 5 mg daily 5 (manufactured by Versalya Pharma, Milan, Italia) until the postpartum period. High concentrations of inhaled oxygen were administered to prevent HbS polymerization during labor associated with fluid and blood transfusion if the hemoglobin level was less than 7 g/dL. We excluded women with HbAS, any other electrophoretic profile, and history of renal disease, pre-existing diabetes, incomplete data, and abortion as we only included pregnancy over 28 WG. A logistic regression was exploited to gauge the risk of pregnancy outcomes. Pregnant women with abnormal hemoglobin were compared (i.e., pregnant women with SCD versus SCT). Odds ratios were calculated by comparing SCT with SCD. We employed SPSS version 19 (IBM Corp., Armonk, NY, USA) for statistical analysis. The adjusted odds ratio (AOR) and 95% confidence interval (CI) were obtained with logistic regression in multivariate analyses adjusted for age, parity, and other variables in the study. The level of significance for the p value was set as 0.05 ($p < 0.05$).

Table 1. Sociodemographic characteristics.

Data	Cases Group		Control Group		Total
	n = 156 (%)		n = 312 (%)		
Age (years)					
≤20	25	16.0	65	20.8	90
21–35	88	56.4	178	57.1	266
≥36	43	27.6	69	22.1	112
Education level					
Illiterate	88	56.4	212	67.9	143
Educated	68	43.6	100	32.1	157
Profession					
Informal sector	52	33.3	68	21.8	100
Student	36	23.1	132	42.3	104
Housewife	68	43.6	112	35.9	96
Gravidity (pregnancies number)					
Primigravida (1)	34	21.8	112	35.9	146
Paucigravida (2–3)	38	24.4	97	31.1	135
Multigravida (>4)	84	53.8	103	33.0	187
Parity (number of birth)					
Primiparous (1)	68	43.6	77	24.7	145
Pauciparous (2–3)	45	28.8	79	25.3	124
Multiparous (>4)	43	27.6	156	50.0	199
Delivery modalities					
Vaginal delivery	24	15.4	198	63.5	222
Cesarean section	132	84.6	114	36.5	246

3. Results

3.1 General Data of Pregnant Women

Over a 4-year-period, we recorded 16,924 deliveries, with 156 cases of major SCD (HbSS, 104; HbSC, 52) corresponding to a prevalence of 0.92%. Major SCD forms included heterozygous genotype (HbSC, 33.3%) and homozygous forms (HbSS, 66.7%). The mean gestational age at delivery was 36 ± 4 weeks. CS represents 52.6% in both Groups (n = 246), and included 246 in the Cases Group (84.6%). No twin pregnancies were recorded in HbAA either in major SCD. These major SCDs correspond to the Cases Group (n = 156), and were compared to 312 pregnant women without SCD (normal hemoglobin genotype, Control Group) (Table 1). The Control Group included women between the ages of 15 and 44 years (mean 26.9 ± 3.9). As for the Cases Group, the youngest and oldest were 16 and 40 years, respectively (mean 27.7 ± 4.1). The majority of women in the two groups were of the reproductive age, range between 21 and 35 years old. All women included in the Cases Group were below 40 years old Amongst the 468 women, 143 were primigravidas (30.6%), followed by 199 multigravida (>4) (42.5%) (Table 1). These data on pregnant general characteristics are highlighted in Table 1.

3.2 Maternal Antenatal Complications

There was a significant association between major SCD and maternal antenatal complications, such as mild anemia (odds ratio (OR) = 64.20, 95% CI [29.62–130.15]; $p < 0.0001$), VOC (OR = 540.15, 95% CI [73.83–3951.59]; $p < 0.0001$), PIH (OR = 0.33, 95% CI [0.17–0.58]; $p < 0.0002$) (Table 2). Other significant morbidity factors were IUGR (OR = 96.73, 95% CI [44.16–211.82]); $p < 0.0001$) ; Preterm labor (OR = 5.51, 95% CI [3.42–8.85]; $p < 0.0001$), and painful crisis (OR = 272.01, 95% CI [16.72–4425.09]; $p < 0.0001$) (Table 2).

3.3 Intrapartum and Neonatal Data

Logistic regression analysis did not confirm a statistically significant association between the major SCD group and HbAA, concerning CS ($p < 0.0001$) and intrapartum hemorrhage ($p = 0.0002$; Table 2). The occurrence of maternal death (MD) was not significant in the Cases Group (OR = 0.20, 95% CI [0.04–0.84]; $p = 0.0320$; Table 2). Emergency CS was realized for acute fetal distress (AFD) in major SCD (80.0%). The mean birth weight was 2825 g in the Control Group, while in the major Cases Group it was 1876.79 g. No significant association was observed between both Groups, regarding perinatal mortality ($p = 0.2110$), stillbirths ($p = 0.3150$), acute fetal distress ($p = 0.9308$), Intrauterine fetal death ($p = 0.7194$), and neona-

Table 2. Logistic regression analysis of maternal outcomes among pregnant women.

Adverse outcomes for mothers	Cases Group n = 156 (%)	Control Group n = 312 (%)	Odds Ratio, 95% CI	*p*
Antenatal complications				
Mild anemia	98 (62.8%)	8 (2.6%)	64.20, [29.62–130.15]	$p < 0.0001$
Preterm births	64 (62.8%)	35 (11.2%)	5.51, [3.42–8.85]	$p < 0.0001$
VOC	99 (41.0%)	1 (0.6%)	540.15, [73.83–3951.59]	$p < 0.0001$
IUGR	112 (71.8%)	8 (2.6%)	96.73, [44.16–211.82]	$p < 0.0001$
PIH	15 (9.6%)	77 (24.7%)	0.33, [0.17–0.58]	$p < 0.0002$
Preeclampsia	11 (7.1%)	33 (10.6%)	0.64, [0.31–1.31]	$p = 0.2210$
Eclampsia	7 (4.5%)	28 (9.0%)	0.47, [0.20–1.12]	$p = 0.0880$
Intrapartum complications				
Hemorrhage	22 (14.1%)	89 (28.5%)	0.366, [0.22–0.62]	$p = 0.0002$
IUFD	82 (52.6%)	16 (5.1%)	20.50, [11.33–37.09]	$p < 0.0001$
CS	132 (84.6%)	165 (52.9%)	4.90, [0.48–1.41]	$p < 0.0001$
Vaginal delivery	24 (15.3%)	147 (47.1%)	0.29, [0.12–0.33]	$p < 0.0001$
Maternal death (MD)	2 (1.3%)	19 (6.1%)	0.20, [0.04–0.84]	$p = 0.0320$
Postpartum hemorrhage (PPH)	27 (17.3%)	75 (24.0%)	0.66, [0.40–1.08]	$p = 0.0978$
Morbidity				
Severe anemia	55 (35.3%)	24 (7.7%)	6.53, [3.84–11.10]	$p < 0.0001$
Urinary tract infection	18 (11.5%)	16 (5.1%)	2.25, [1.11–4.54]	$p = 0.0235$
Painful crisis	65 (41.7%)	0 (0.0%)	272.01, [16.72–4425.09]	$p < 0.0001$
Blood transfusion	67 (42.9%)	65 (20.8%)	373.32, [22.87–6093.85]	$p < 0.0001$
Acute chest syndrome	12 (7.7%)	1 (0.3%)	25.91, [3.33–201.23]	$p = 0.0019$

VOC, vaso-occlusive crisis; IUGR, intrauterine growth restriction; PIH, pregnancy-induced hypertension; CS, cesarean section; CI, confidence interval; IUFD, in-utero fetal distress or death.

Table 3. Logistic regression analysis of perinatal outcomes among pregnant women.

Adverse outcomes for the fetus	Cases Group n = 156 (%)	Control Group n = 312 (%)	Odds ratio, 95% CI	*p*
Live birth	142 (91.0%)	220 (70.5%)	4.24, [2.32–7.74]	$p < 0.0001$
Low birth weight (LBW)	112 (71.8%)	24 (7.7%)	30.54, [17.74–52.58]	$p < 0.0001$
Apgar score at <7 at 5 min	62 (39.7%)	43 (13.8%)	4.12, [2.61–6.49]	$p < 0.0001$
Stillbirth or neonatal mortality	8 (5.1%)	15 (4.8%)	0.34, [0.27–1.53]	$p = 0.3150$
Acute fetal distress (AFD)	27 (17.3%)	53 (17.0%)	1.02, [0.61–1.70]	$p = 0.9308$
Intrauterine fetal death (IUFD)	6 (3.8%)	10 (3.2%)	1.21, [0.43–3.39]	$p = 0.7194$
Neonatal infection	7 (4.5%)	25 (8.0%)	0.53, [0.23–1.28]	$p = 0.1600$
Perinatal mortality	12 (7.7%)	15 (4.8%)	1.65, [0.75–3.61]	$p = 0.2110$

tal infection ($p = 0.1600$; Table 3). Moreover, major SCD genotypes were significantly associated high risk of low birth weight (LBW; $p < 0.0001$) and an Apgar score of less than 7 in the 5th minute ($p < 0.0001$; Table 3).

3.4 Postpartum Period Data

The main morbidity was severe anemia in major SCD (35.3%) when compared to HbAA (7.7%) ($p < 0.0001$); urinary tract infection ($p = 0.0235$), VOC ($p < 0.0001$), blood transfusion ($p < 0.0001$), and acute chest syndrome (ACS) ($p = 0.0019$) (Table 2).

4. Discussion

Sickle cell disease (SCD), first described three centuries ago in Africa [6,11], is an autosomal recessive disorder with higher maternal and fetal risk during pregnancy [12,13]. People who inherited one copy of the HbS allele, and one normal HbA allele (HbAS), also called sickle cell trait (SCT), are typically asymptomatic, with no serious adverse outcomes [12]. The homozygous form of the HbS gene (HbSS) characterizes sickle cell anemia, the most prevalent monogenic condition worldwide [1,2,13–18]. However, other genotypes causing SCD can be identified, corresponding to the uniparental inheritance of the βS allele in concomitance with mutations for other HbA variants, such as Sβ0-thalassemia, Sβ+-thalassemia, and HbSC [1,2,9]. The abnormal HbSS and heterozygous variants are considered major SCD [6,7,12–16], and the leading main consequences are the formation of falciform cells [15–17] and chronic anemia [2,6,9,15]. Falciform cells

formation is supported by conditions like hypoxia, dehydration and acidosis, anemia, adhesion, and vasoconstriction [7,13]. The main consequences inherent to this structural change are vascular disorders, painful crises, intercurrent infection, retinopathy or stenosis of the proximal portions of the large arteries, and cerebrovascular complications [7,11,15–18]. A retrospective analysis conducted in Cote d'Ivoire gives new insights into the prevalence of SCD among patients suffering mild malaria, and found a national prevalence higher than these findings [18]. This study revealed limited prevalence, reflecting only hospital dimensions of the disease. These findings were consistent with published data in Sub-Saharan Africa literature, describing lower frequencies of around 1% to 2% of pregnancies [5–7,18–27]. In Asia and North Africa, some authors reported higher prevalence rates [3,4,7,12,16]. In the current study, young women were predominant, and that was consistent with sub-Saharan African authors' findings [6,8–10,13,17–20,24], and those in high-income countries [21,22,28–31]. The majority of African populations are characterized by early sexual activity, due to early marriage, which was in perfect adequation with customs and traditions [6,8–10,13,17–20,24,31]. Those populations lived usually in precarious socio-economic conditions, and are unaware of family planning methods [9,13,18–20,23,24,30,31], which can explain the low rate of antenatal monitoring reported in this study and the fact that nearly half of the pregnant women did not know their hemoglobin genotype before the antenatal screening [6,13,17–20,31–33]. In this study, the commonest SCD was HbSS, which was consistent with literature findings [3,5,7,8,17–20,27–32]. In low- and middle-income countries (LMIC), the HbSS genotype was commonly associated with high rates of spontaneous miscarriage and IUFD [3,5,7,10,18–31]. The severe maternal and fetal complications of this association have been documented [3,6,18,21,22,25,31]. The implementation of ante, intra, and postpartum monitoring, managed by the obstetrician-led team (obstetricians, interns, and midwives) was essential [17,27–29,32]. The contribution of a hematologist is also required in all inpatient and outpatient pregnant women with SCD. Laboratory blood analysis, fetal Doppler ultrasound examination, fetal biometry, and Doppler velocimetry were necessary after 34 WG. A bi-weekly fetal monitoring until 34 WG, and weekly thereafter was necessary until delivery. This MTD provided all outpatient medical care for efficient care as vascular trouble during pregnancy, such as gestational thrombocytopenia, coagulation disorders and development of abnormal blood cells that can occlude blood vessels can be observed [11,15,17,27,32–37]. According to previous studies [10–12,19–23,31,32,34,37], we also found significant maternal morbidity rates associated to PIH ($p = 0.0002$) and VOC ($p = 0.0001$). As such, we considered that MTD is essential to provide efficient care, and reduced maternal and perinatal mortality rates amongst pregnant women with SCD compared to pregnant women without SCD [16,17,27]. Its implementation is essential [17], but depends on the country's medical possibilities and resources. There was no standard care protocol for outpatient and inpatient, and a hematologist consult was sought using the hospital's procedures for internal referrals [17]. As described in the literature [11,15,17,32–38], we recorded severe maternal morbidity in people with SCD compared with deliveries among people without SCD, especially for severe hemolytic anemia ($p < 0.0001$) and blood transfusions ($p < 0.0001$). Blood transfusions were the main treatment for the HbSS genotype as consistent in the literature, and the hematologist's contribution is essential in its monitoring [38,39]. Additional morbidity factors have been highlighted, in particularly painful VOC, postpartum hemorrhage [13,14,31,40]. Severe chronic anemia and painful VOC are commonest in HbSS compared to HbSC [10,38,39]. All those morbidity factors increased the rate of hospitalization [15,26]. MTD care using blood coagulation monitoring during the antenatal period, including accurate testing and appropriate implementation, is necessary to contribute to early diagnosis and treatment [17,27,37]. The possibility of the appearance of disorders of the vital organs demonstrates the need for multidisciplinary management [17,23,27]. The crucial period of these complications' development is during the third trimester and postpartum period [33–36]. In this study, no cases of COVID-19 infection were recorded because the study was conducted before the epidemic crisis. However, it is well-known that SCD is considered to have a greater risk of severe illness and death from respiratory infections, including COVID-19, compared to normal hemoglobin. VOC in SCDs and severe SARS-CoV-2 infection are both characterized by thrombo-inflammation mediated by endothelial injury, complement activation, inflammatory lipid storm, platelet activation, platelet-leukocyte adhesion, and activation of the coagulation cascade [39,40]. In this study, pregnancy in women with SCD was not associated with increased rates of MD. The same constatations have been recorded by Oppong *et al.* [17] regarding MD compared to Controls Group. Cardiopulmonary complications were the commonest cause of MD [33], even if more than half of the deceased women had ACS [38]. For all these reasons, it was recommended establishing multidisciplinary care to reduce maternal and perinatal mortality rates amongst pregnant women with SCD compared to pregnant women without SCD [17,27,39]. Our findings concerning neonatal findings, confirmed the evidence that major SCD is not significantly associated with preterm labor ($p = 0.0572$), IUGR ($p = 0.0001$), LBW ($p < 0.0001$), and Apgar <7 at 5 min ($p < 0.0001$). HbSS genotype had higher rates of perinatal morbidities compared to pregnant women with HbSC, as described by Oppong *et al.* [17]. As reported in the research literature, SCD increased the risk of adverse perinatal and maternal outcomes in both LMIC of Africa [10,12,15,16,31] or Asia [3,5,16], and high-income

countries [33–38]. The perinatal mortality rate was comparable in women with and without SCD ($p = 0.211$) but a small sample size of maternal (n = 2) and perinatal (n = 12) deaths, in both the women with and without SCD [12,19]. HbSS had higher rates of perinatal morbidities compared to HbSC disease [19,20,23,32,38,39,41]. Implementation of the MTD care team significantly helps to decrease the perinatal mortality rate from 60.8 per 1000 births to 23.0 per 1000 births, representing a relative risk reduction of 62.2% ($p = 0.20$) [34,39]. The authors also showed that the decline in the mortality rate was not significantly different, so additional preventive measures are probably required. According to our study, pregnancy complications can be severe, more frequently in pregnant women with major SCD compared to other genotypes [10,20,34,37,41]. Indeed, women with SCD had a higher risk of intrapartum stillbirth compared to normal hemoglobin but the real pathological mechanism is still not elucidated [40]. A few studies point out vasoconstriction in the placenta, placental infarction, and placental insufficiency due to reduced nutrient supply and poor metabolic exchange responsible for IUFD and IUGR [30,32,41]. Similar reports were found in the literature and suggested the implementation of common therapeutic measures during pre and postnatal care [6–8,28,29].

5. Limitations

There are some limitations in the present study. This was a retrospective study based on patients' data collected at a hospital and further analyzed. Our study did not cover women with SCD who delivered at home or other health care facilities in the territory, as well as the cause of the perinatal mortality rate of 4.4% observed in the Control Group ($p = 0.50$). Therefore, the findings of this study may not be generalized to all the women in Cote d'Ivoire. Prospective data collection could increase the quality and credibility of the presented results. Nevertheless, our results were reported according to statistical standards that would minimize potential bias. Also, we did not perform a statistical comparison between data of the different sickle cell genotypes which could have allowed us to determine prognostic factors. This will soon be done in a prospective cohort multi-centric study.

6. Conclusions

The findings of the present survey suggest better fetal and maternal prognosis in HbAA, than in major SCD. The latter is associated with maternal complications, such as severe anemia, low birth weight, and prematurity. Multidisciplinary team management is required during these pregnancies to improve maternal and fetal prognosis. Patient awareness and education, and early and effective prenatal care are useful to avoid those risks.

Availability of Data and Materials

Data supporting the results of this study are available from the corresponding author, but restrictions apply to their availability. The data were used under license for the current study, and are therefore not publicly available. However, the data are available from the authors upon reasonable request and with permission from Mian *et al*.

Author Contributions

VAA, JK, KHY contributed to the extraction and drafting this manuscript; data analysis, design and editing. DBM, VAA, CJN, JK, KNG, SB have made the final statistical analysis and manuscript revision. All authors have read and approved this final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Felix Houphouet Boigny University (N245354-CI/2020). All subjects gave their informed consent for inclusion before they participated in the study.

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Conflict of Interest

The authors declare no conflict of interest.

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