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Maternal and Perinatal Prognosis of Pregnancies in Women with Sickle Cell Disease at Chud-B/A from 2019 to 2023

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Abstract

Introduction: The association of sickle cell disease and pregnancy is a risky situation for the mother as well as the fetus and even the neonate. The objective of this work was to study the maternal and perinatal prognosis of pregnancies in women with sickle cell disease at CHUD-Borgou/Alibori from 2019 to 2023. **Patients and Methods:** This was a case-control study with a retrospective collection of data from January 1, 2019 to June 30, 2023. It covered sickle cell and non-sickle cell women and their neonates who having given birth at the maternity ward of CHUD-Borgou/Alibori. **Results:** The frequency of pregnant women with sickle cell disease was 1.36% (153/11212). The average age of the pregnant women with sickle cell disease was 26.77 years ± 5.03. Vaso-occlusive crisis (VOC) was the main complication observed in pregnant women with sickle cell disease during pregnancy (26%). Regarding the complications common to the 2 groups of pregnant women, urinary tract infections (18.1%), severe anemia (22.8%), and severe malaria (26.8%) were more reported in sickle cell patients with a statistically significant difference (p-value = 0.000). Delivery was premature in 61.9% of pregnant women with sickle cell disease compared to 18.5% in pregnant women without sickle cell disease, with a significant difference (p-value = 0.000). The main route of delivery among patients with sickle cell disease was cesarean section (94.4%), while it was vaginal delivery (50.4%) among non-sickle cell pregnant women. VOC (4.8%), severe anemia (39.7%), and acute pulmonary edema (2.4%) were the main complications reported among sickle cell pregnant women in the immediate postpartum period with a significant difference (p-value = 0.000). Three cases of maternal death (2.4%) were recorded in pregnant women with

sickle cell disease. The neonatal pathologies identified in the neonates of pregnant women with and without sickle cell disease were mainly neonatal bacterial infection (20.0% vs. 17.2%), hypotrophy (17.0% vs. 5.7%), prematurity (14.8% vs. 7.3%) with a significant difference (p-value = 0.000). The perinatal mortality rate was 57.14‰ in sickle cell women compared to 30‰ with a significant difference (p-value = 0.000). **Conclusion:** Pregnancy in women with sickle cell disease carries a high risk of maternal and perinatal morbidity and mortality. Information, awareness raising among populations and the adaptation of prenatal care are essential.

Keywords

Prognosis, Sickle Cell Disease, Pregnancy, Benin

1. Introduction

Sickle cell disease (SCD) is the most common monogenic disease worldwide [1] [2]. Over the past four decades, notable advances have made it possible to improve the survival of patients with sickle cell disease in both developed and low-resource countries. The corollary of this is a substantial increase in the number of subjects of childbearing age. However, the association between sickle cell disease and pregnancy is a risky situation for the mother, the fetus and even the neonate. Pregnant women with sickle cell disease are known to be at high risk of obstetric complications and perinatal mortality as well as sickle cell disease-related complications [1] [2]. Complications such as vaso-occlusive crises (VOC), acute chest syndrome (ACS), exacerbation of pre-existing anemia, and thromboembolic events are more important during pregnancy [2]. Fetal and neonatal complications include, among others: intrauterine growth retardation (IUGR), acute fetal asphyxia (AFA), prematurity and high perinatal mortality. Unlike in developed countries, the management of these pregnant women is a real challenge due to the increased risk of complications. In Africa, the prevalence of maternal mortality among pregnant women varies between 0.38 - 1.29/100,000 births and that of perinatal mortality between 1.21 - 2.5/100,000 births [3].

In Benin, the prevalence of major sickle cell disease (HbSS) is estimated at 4.18% [4] and 25% of subjects carry the S trait [3]. Taking into account factors predicting complications could improve patient care in order to reduce their mortality.

In Parakou, in a hospital study carried out at CHUD-Borgou/Alibori, the frequency of sickle cell disease among pregnant women was 1.3%, maternal mortality at 42‰ and perinatal mortality at 243.5‰ [3] [5]. The prognostic aspects of the maternal and perinatal prognosis have been addressed little in this previous study. That's why the objective of this work will be to study the maternal and perinatal prognosis in pregnant women with sickle cell disease.

Site and study methods

This was a case-control study, carried out in the maternity and neonatology

departments of the Regional Teaching Hospital of Borgou/Alibori (CHUD-B/A), from January 1, 2019 to June 30, 2023.

The study population consisted of all pregnant women with major sickle cell syndromes, those without sickle cell disease who gave birth at CHUD-Borgou/Alibori and their neonates.

Were included in the study:

-Cases: pregnant women suffering from major sickle cell syndrome (SS, SC, Sβ thalassemia), confirmed by hemoglobin electrophoresis, having given birth at the maternity ward of CHUD-Borgou/Alibori at the end of 22 weeks of amenorrhea (WA) or more or to a neonate alive or dead at birth weighing at least 500 g.

- Controls: pregnant women without sickle cell disease with a phenotype AA confirmed by hemoglobin electrophoresis, having given birth at the maternity ward of CHUD-Borgou/Alibori at the end of 22 WA or more or to a living or deceased neonate at birth weighing at least 500 g.

Were excluded from the study:

- Pregnant women whose medical records were unusable and incomplete;

- Pregnant women with comorbidities such as human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), diabetes and preconception hypertension.

- Matching criteria

Each pregnant woman with sickle cell disease was matched with two (2) non-sickle cell pregnant women according to age criteria (<20 years, 20 to 29 years; 30 to 39 years and ≥40 years); parity (nulliparous and primiparous, pauciparous, multiparous and grand multiparous) and gestational age (22 - 28 WA, 28 WA to 34 WA, 34 WA to 36 WA +6 days and ≥37 WA).

The pregnancy was considered well-monitored when the pregnant woman had completed at least 8 quality antenatal consultations as recommended by WHO [6].

Anemia in mothers was considered severe for a hemoglobin level below 7g/dl according to WHO criteria [6].

The sampling consisted of a systematic recruitment of all medical records of eligible pregnant women according to our inclusion criteria.

The minimum sample size calculated using the Schwartz formula was 62.

Maternal prognosis was the dependent variable. It is good or bad.

It was considered poor maternal prognosis, the occurrence of at least one complication and/or maternal death during pregnancy, delivery or after delivery.

The central tendency and dispersion parameters (mode, mean, median, standard deviation) were used to describe the quantitative variables. Proportions with their confidence interval (CI) were used for qualitative variables. The Chi (X^2) statistical test was used to compare the frequency of maternal and perinatal complications according to the modalities of the independent (qualitative) variables. The difference was statistically significant for a p-value less than 0.05. The protocol was submitted to the local ethics committee for biomedical research at the University of Parakou (CLERB-UP).

2. Results

Out of a total of 11,212 pregnant women admitted, 153 pregnant women with sickle cell disease were identified at the maternity ward of CHUD-Borgou/Alibori from January 2019 to June 31, 2023 and 127 had a usable medical record. The frequency of pregnant women with sickle cell disease was 1.36% (153/11212). Heterozygous pregnant women (HbSC) were the most represented, i.e., 77.2% (98/127).

Age of the pregnant women with sickle cell disease

The average age of the sickle cell pregnant women was 26.77 years ± 5.03 with extremes of 18 and 40 years. Pregnant women aged between 25 and 30 years were the most represented (37%). Pregnant women aged under 20 years, between 20 and 24 years, between 30 and 34 years and over 35 years old were 3.9%, 30.7%, 16.5%, and 11.8%, respectively.

Complications during the current pregnancy in the 2 groups of pregnant women

- **Complications specific to sickle cell disease**

VOC was the main complication observed in pregnant women with sickle cell disease during pregnancy (26%). No pregnant woman had an acute chest syndrome.

- **Non-specific complications of sickle cell disease**

Regarding the complications common to the two groups of pregnant women, urinary tract infections (18.1%), severe anemia (22.8%), severe malaria (26.8%) were more reported in sickle cell women than in non-sickle cell women in whom they represented 0.8%, 2% and 0.4%, respectively. The difference was statistically significant in all cases (p-value = 0.000).

In terms of fetal and adnexal complications, IUGR and the threat of premature birth (TPB) were predominant in sickle cell pregnant women with 3.9% and 4.7% of cases, respectively compared to 1.6% and 3.2% of cases, respectively in pregnant women without sickle cell disease. The difference is not significant (Table 1).

Table 1. Distribution of sickle cell and non-sickle cell pregnant women according to complications specific and non-specific to sickle cell disease occurring during pregnancy at CHUD-B/A from 2019 to 2023.

	Type of patient				
	With SCD		Without SCD		p-value
	n	%	n	%	
Complications specific to SCD					
VOC	33	26.0	-	-	
ACS	0	0.0	-	-	
Non-specific complications of SCD					
Gestational hypertension	18	14.2	45	17.9	0.621
Premature rupture of membranes	16	12.6	35	13.9	0.749

Continued

Oligohydramnios	2	1.6	22	8.8	0.007
Pre-eclampsia	10	7.9	19	7.6	0.916
Transversely contracted pelvis	0	0.0	13	5.2	0.116
TPB	6	4.7	8	3.2	0.533
Eclampsia	1	0.8	8	3.2	0.148
IUGR	5	3.9	4	1.6	0.158
Placenta previa	0	0.0	3	1.2	0.216
Urinary tract infection	23	18.1	2	0.8	0.000
Malaria	34	26.8	1	0.4	0.000
Abruptio placenta	0	0.0	1	0.4	0.365
Pulmonary Infection	3	2.4	0	0.0	0.476
Salmonellosis infection	1	0.8	0	0.0	0.172
Moderate anemia	63	49.5	10	3.9	0.000
Severe anemia	29	22.8	5	2.0	0.000

Pregnancy outcome in women with sickle cell disease and in women without sickle cell disease

➢ **Modalities of delivery**

The average gestational age at delivery in sickle cell women was 36.04 WA ± 2.04 with the extremes of 27 WA and 40 WA. In non-sickle cell women, it was on average 37.48 WA ± 4.20 with the extremes of 22 WA and 41 WA. This difference between the two groups was statistically significant (p = 0.000).

Delivery was premature in 61.9% of pregnant women with sickle cell disease compared to 18.5% in pregnant women without sickle cell disease. This difference between the two groups was also statistically significant with a p-value equal to 0.000. The main route of delivery among sickle cell women was cesarean section (94.4%) while it was vaginal delivery (50.4%) among non-sickle cell pregnant women. It was prophylactic in 83.2% of pregnant women with sickle cell disease compared to 38.9% in those without sickle cell disease (Table 2).

Table 2. Distribution of sickle cell and non-sickle cell pregnant women according to the modalities of delivery at CHUD-B/A from 2019 to 2023.

	Type of patient				p-value
	With SCD		Without SCD		
	N	%	n	%	
Term at delivery (WA)					0.000
<37	78	61.9	47	18.5	
≥37	48	38.1	207	81.5	

Continued

Route of delivery					0.000
Caesarean section	119	94.4	126	49.6	
Vaginal	7	5.6	128	50.4	
Type of cesarean					0.000
Planned cesarean section (Prophylactic)	99	83.2	49	38.9	
Urgent cesarean section	20	16.8	77	61.1	

➢ **Pre-partum and peri-partum complications**

Among pregnant women with sickle cell disease, 5 (4.0%) gave birth to a still-born neonate compared to 6 (2.4%) among those without sickle cell disease. This difference between the two groups was statistically insignificant. Pregnancies resulted in preterm deliveries in 61.9% of cases in pregnant women with sickle cell disease compared to 18.5% in pregnant women without sickle cell disease. This difference was statistically significant with a p-value equal to 0.000 (Table 3).

Table 3. Distribution of sickle cell and non-sickle cell pregnant women according to pre-partum and peri-partum complications at CHUD-B/A from 2019 to 2023.

	Type of patient				
	With SCD		Without SCD		p-value
	N		N		
Antepartum fetal death					0.379
No	121	96.0	248	97.6	
Yes	5	4.0	6	2.4	
Preterm birth					**0.000**
No	48	38.1	207	81.5	
Yes	78	61.9	47	18.5	

➢ **Postpartum complications**

VOC (4.8%), severe anemia (39.7%), postpartum hemorrhage (PPH) (1.6%) and acute pulmonary edema (APE; 2.4%) were the main complications reported in pregnant women in the immediate postpartum period (Table 4).

➢ **Vital prognosis of mothers**

In total, among sickle cell pregnant women, 3 (2.4%) of them died. The maternal mortality rate was 23.6‰ in pregnant women with sickle cell disease compared to 0‰ in pregnant women without sickle cell disease. There were 2 deaths after pregnancy and one during pregnancy at the end of 27 WA. The causes of death were: hemorrhagic shock, disseminated intravascular coagulation and acute pulmonary edema (APE).

Table 4. Distribution of sickle cell and non-sickle cell pregnant women according to postpartum complications at CHUD-B/A from 2019 to 2023.

	Type of patient				p-value
	With SCD		Without SCD		
	N		N		
VOC	6	4.8	0	0.0	**0.001**
Severe anemia	50	39.7	7	2.8	**0.000**
PPH	2	1.6	1	0.4	0.223
APE	3	2.4	0	0.0	**0.014**
Anemia (Mild/Moderate)	0	0.0	4	1.6	0.679
High blood pressure	0	0.0	1	0.4	0.324
Severe preeclampsia	1	0.8	0	0.0	0.247
Postpartum psychosis	0	0.0	1	0.4	0.578

Characteristics relating to neonates in the 2 groups of pregnant women

➢ **Anthropometric parameters and morphological characteristics**

In total, there were 396 neonates, i.e. 135 for pregnant women with sickle cell disease and 261 for pregnant women without sickle cell disease. Low birth weight (weight < 2500 g) and birth length below the normal (50 cm) were significantly more observed in neonates born of sickle cell mothers compared to those born of non-sickle cell mothers with p-values of 0.002 and 0.000, respectively (Table 5).

Table 5. Distribution of sickle cell and non-sickle cell pregnant women according to the anthropometric and morphological characteristics of neonates at CHUD-B/A from 2019 to 2023.

	Type of patient				p-value
	With SCD		Without SCD		
	N		N		
Condition of the neonate at birth					0.361
Normal	114	84.4	223	85.4	
Neonate with respiratory distress	16	11.8	32	12.3	
Stillborn neonates	5	3.7	6	2.3	
Weight					**0.002**
<2500	53	39.3	54	20.7	
2500 - 3800	82	60.7	198	75.9	
>3800	0	0.0	9	3.4	
Length					**0.000**
<50 cm	117	91.4	177	70.8	
≥50 cm	11	8.6	73	29.2	

Continued

Apgar at the 5th minute					0.248
<7	4	3.1	7	2.8	
≥7	124	96.9	243	97.2	
Relationship between gestational age and birth weight					**0.001**
Hypotrophy	43	31.9	49	18.8	
Normal growth	90	66.7	191	73.2	
Macrosomia	2	1.5	21	8.0	
Resuscitation					0.907
Yes	15	11.3	28	10.7	
No	120	88.9	233	89.3	

➢ **Early neonatal morbidity and mortality**

In total, 120 (88.9%) neonates of pregnant women with sickle cell disease were transferred to the neonatology unit compared to 143 (54.8%) for those without sickle cell disease. The difference was statistically significant with a p-value equal to 0.000. In both cases the predominant reason for transfer was the delivery by cesarean section (70.8% vs 58.0%). In pregnant women with sickle cell disease, other more frequent reasons for transfer were low birth weight, prematurity and immediate neonatal distress.

The neonatal pathologies identified in neonates of pregnant women with and without sickle cell disease were mainly neonatal bacterial infection (20.0% vs 17.2%), hypotrophy (17.0% vs 5.7%), prematurity (14.8% vs 7.3%) with a significant difference. Early neonatal mortality was higher in neonates born of mothers with sickle cell disease, compared to those born of mothers without sickle cell disease, but the difference was not statistically significant (Table 6).

Table 6. Distribution of sickle cell and non-sickle cell pregnant women according to information relating to the transfer of neonates to neonatology at CHUD-B/A from 2019 to 2023.

	Patient type				
	With SCD		**Without SCD**		**p-value**
	N		**N**		
Transfer to the neonatology unit					**0.000**
No	15	11.1	118	45.2	
Yes	120	88.9	143	54.8	
Neonatal pathology					
Low birth weight	53	39.3	54	20.7	**0.000**
Neonatal bacterial infection	27	20.0	45	17.2	**0.003**

Continued

Hypotrophy	23	17.0	15	5.7	**0.000**
Prematurity	21	15.6	20	7.7	0.605
Perinatal asphyxia	9	6.7	17	6.5	0.962
Neonatal jaundice	6	4.4	3	1.1	0.386
Respiratory distress	5	3.7	14	5.4	0.074
Anemia	2	1.5	2	0.8	0.633
Hypoglycemia	1	0.7	4	1.5	0.198
Malaria	1	0.7	1	0.4	0.199
Evolution of neonates					0.218
Living neonates	132	97.8	259	99.2	
Deceased neonates	3	2.2	2	0.8	

In terms of perinatal deaths, pregnant women with sickle cell disease had 5 intrauterine fetal deaths and 3 early neonatal deaths, i.e. 8 perinatal deaths out of 140 total births, i.e. a perinatal mortality rate of 57.14‰. The stillbirth rate was 35.71‰ and that of early neonatal mortality was 21.4‰. On the other hand, pregnant women without sickle cell disease had 6 intrauterine fetal deaths and 2 early neonatal deaths, i.e. 8 perinatal deaths out of 267 total births, i.e. a perinatal mortality rate of 30‰. The stillbirth rate was 22.5‰ and that of early neonatal mortality was 7.5‰.

3. Discussion

The frequency of sickle cell disease among pregnant women admitted to CHUD-B/A during the period was 1.36%. This frequency is similar to that reported by Agbeille *et al*. in the same department in 2019 [3]. On the other hand, Nwafor *et al*. [4] in 2019 in Nigeria and Nkwabong *et al*. [7] in 2020 in Cameroon found lower frequencies of 0.69% and 0.1%, respectively. This difference could be explained in part by the variability of the study population, but also by the variability in the prevalence of sickle cell disease depending on the regions of the world. The average age of the pregnant women was 26.77 years ± 5.03. This result is similar to 27.5 and 27 years reported by Nkwabong *et al*. [7] in Cameroon in 2020 and Galiba *et al*. [8] in Congo Brazzaville in 2020, respectively. The most represented age group was 25 to 30 years old (37%). Women of this age group are young, sexually active and capable of procreation.

Regarding specific complications, vaso-occlusive crisis was the most common (26%). This result is similar to that of Marielle *et al*. [9] in Gabon in 2022 who reported 27.3% of vaso-occlusive crisis. Dangbemey *et al*. [10] in Benin in 2018 reported in their study that the proportion of vaso-occlusive crises was 19.5%. This could be explained by the irregularity of follow-up of pregnant women.

In terms of non-specific complications, they were dominated by severe anemia (22.8%), malaria (16.5%), urinary tract infection (17.3%), gestational hypertension (14.2%). These complications were more frequent in pregnant women with sickle cell disease. Pregnant women with sickle cell disease were more likely to suffer from anemia (72.4%) than those without sickle cell disease (5.9%). This result was comparable to that of Haseeb *et al*. [11] in Saudi Arabia who reported 89.4% and 11.6% in sickle cell and non-sickle cell pregnant women, respectively. Anemia was found in 83 (65.3%) pregnant women with sickle cell disease. Among these 83 pregnant women with sickle cell disease, 42.5% had moderate anemia and 22.8% had severe anemia. Dangbemey *et al*. [10] reported 19.2% in Benin in 2020. Pregnancy is a factor that aggravates anemia in women with sickle cell disease. This anemia is the result of several factors including deficiency and infectious causes (bacterial infections and malaria). Urinary tract infection was more significant in pregnant women with sickle cell disease than in those without sickle cell disease (p-value < 0.001 in both cases). Haseeb *et al*. [11] in Saudi Arabia in 2019 and Babah *et al*. [12] in Nigeria in 2019, reported a statistically higher urinary tract infection in pregnant women with sickle cell disease compared to those without sickle cell disease (p-value of 0.001). Nkwabong *et al*. [7] in Cameroon in 2020, reported a higher frequency of urinary tract infection in pregnant women with sickle cell disease compared to those without sickle cell disease but the difference was not significant (p-value equal to 0.106). Bacterial infections are more common in women with sickle cell disease. They are the consequence of early functional asplenia with greater vulnerability to infections linked to encapsulated germs. But other factors have been identified as predisposing to bacterial infections, namely: neutrophil dysfunction, impaired cell-mediated immunity, impaired phagocytosis and the presence of ischemia, which constitute an environmental conducive to bacterial proliferation [13]. In our pregnant women, other factors may be associated with it, namely: the irregularity of pregnancy follow-up which does not make it possible to detect and treat these infections early. Hence the need to emphasize the education of patients and health care providers on pregnancy-related complications, the management of pregnancies, the benefits of early antenatal care according to protocol provided by a multidisciplinary team [14] [15].

Maternal death was observed in 3 pregnant women, including one during pregnancy and two after childbirth, bringing the maternal death rate to 2.4%. This rate was close to those reported by Dangbemey *et al*. [10] in Benin in 2020 and Oppong *et al*. [16] in Ghana which were 1.3% and 1.3%, respectively. This rate is lower than 11.4% and 6.2% reported by Galiba *et al*. [8] in Congo in 2020 and Faye *et al*. [17] in Senegal in 2018, respectively. Nwafor *et al*. [4] in Nigeria in 2019 reported 0% of maternal deaths. This difference could be explained by the quality of sickle cell disease management. In our study, the majority of pregnant women had a poor follow-up and developed severe complications during pregnancy and peripartum period. This suggests that the mainstay of antenatal care should include the follow-up and prevention of general and specific complications of sickle cell

disease [18]. Indeed, it has been shown that improving antenatal care specific to pregnant women with sickle cell disease considerably reduces the maternal mortality rate which can be comparable to that among pregnant women without sickle cell disease [15].

4. Conclusion

Pregnancy among women with sickle cell disease is a clinical association. It remains common at the Regional Teaching Hospital of Borgou and Alibori. The course of pregnancy in pregnant women with sickle cell disease is often marked by multiple maternal and perinatal complications. Better follow-up of pregnancy, especially by specialized care centers, could improve the prognosis of pregnancy in this category of pregnant women.

Conflicts of Interest

None.

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