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**Original Research Article**

# Associated factors for maternal-foetal complications in pregnant women with sickle cell disease at the departmental University Hospital of Borgou and Alibori (Benin)

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## ABSTRACT

**Background:** Sickle cell disease is one of the most common genetic disorders in the world, with a high prevalence in Africa. It is a pathology that threatens the maternal-fetal prognosis in case of pregnancy. The objective of this study was to describe the maternal-foetal complications and to identify the factors associated with maternal-foetal complications in sickle cell pregnant women (SP).
**Methods:** This was a descriptive cross-sectional study with retrospective data collection over a period of 4 years (01 January 2015 to 31 August 2019). The study population was All SP who had given birth in the maternity ward of the UH of Borgou/Alibori.
**Results:** We recorded 130 SP out of 10087 admissions, either a frequency of 1.3%. There were 119/130 exploitable files. Maternal complications during pregnancy were: vaso-occlusive crises 79%; severe anaemia 27.7%; hyponatremia 10.1%; vasculo-renal syndromes 18.4%; infections 74.8%. The foetal complications during pregnancy were: Preterm births 38.6%, in utero deaths 17.6%, low birth weight 54.7%. Early neonatal mortality was 8.4% (8/95). There was a 4.2% (5/119) of maternal deaths. Low educational level of the SP, SS genotype, insufficient antenatal follow-up and antenatal follow-up outside the specialized center for the care of sickle cell pregnant women (SCCSP) were the factors associated with maternal-foetal complications in the SP.
**Conclusions:** The association of pregnancy and sickle cell disease is frequent in West Africa, particularly in Benin, and is characterised by numerous maternal-foetal complications that are associated with certain factors.

**Keywords:** Sickle cell disease, Pregnancy, Vaso-occlusive crises

## INTRODUCTION

Sickle cell disease is the world's leading genetic disease.[1] It is characterised by the presence of abnormal haemoglobin in high concentrations in the red blood cells. It is an autosomal recessive disease. The presence of the abnormal haemoglobin S is the result of a point mutation on the sixth codon of the globin ß gene carried on chromosome 11. There are 3 main sickle cell syndromes (SS, SC, and Sß thalassemia). Sickle cell disease, together with thalassaemia, is one of the most common genetic diseases in the world. Sickle cell disease is most prevalent in blacks.[2] The area of high prevalence for sickle cell disease extends from the 15$^{th}$ parallel of north latitude to the 20$^{th}$ parallel of south latitude and covers West Africa, equatorial Africa, Madagascar and southern India. This area is known as the sickle cell belt.[3] Sickle cell disease is a major public health problem.

In Benin, the prevalence of sickle cell disease is estimated at around 4%. Considerable scientific progress has made it possible to improve the life expectancy of patients with sickle cell disease, with the corollary of an increase in the number of pregnancies among women with sickle cell disease.[4]

This chronic pathology exposes to multiple complications. In pregnant women, the complications can jeopardise both the maternal and foetal prognosis. Pregnancy in women with sickle cell disease is characterised by high morbidity and mortality.[5] The main causes of maternal death were bone crises, infections and severe anaemia. (6) In the womb the morbidity and mortality are high.[6] It is a pathology whose specific management during pregnancy is still controversial among a large proportion of health professionals.

In Benin, few studies had been done on sickle cell disease during pregnancy. The objectives of this research work were: to describe maternal-fetal complications in pregnant women with sickle cell disease; and to identify the risk factors for maternal-fetal complications in pregnant women with sickle cell disease.

## METHODS

This was a descriptive cross-sectional study with retrospective and prospective data collection covering the period from 01 January 2015 to 31 August 2019: four years. Data collection was done from 01 March to 31 August 2019.

The study population was all pregnant women with sickle cell disease who had been treated at the maternity ward of the departmental University Hospital (UH) of Borgou/Alibori.

All pregnant women with sickle cell disease who had given birth in the maternity ward of the UH of Borgou/Alibori, were included in the study. Patients whose files were incomplete were excluded from the study.

This was a systematic and exhaustive census of pregnant women who met our inclusion criteria. The variable of interest was maternal-fetal complications in pregnant women with sickle cell disease.

### *Independent factors*

*Sociodemographic characteristics*

It included age, occupation, education level, origin, sibling rank, ethnicity, religion, and monthly income.

Background included: gender, parity, medical and surgical history; and characteristics of current pregnancy.

Date of last menstrual period; term of pregnancy; number of prenatal visits, number of ultrasounds performed; type of pregnancy; temperature; haemodynamic constants; clinical parameters, complications during pregnancy (urinary tract infections, vaso-occlusive crises, acute chest syndrome, pre-eclampsia, severe anaemia (haemoglobin <7 g/dl), hyponatraemia (natraemia <135 meq/l), malaria, transfusion, premature rupture of membranes); number of hospital admissions; outcome of pregnancy (miscarriage, premature delivery, full term delivery, low birth weight, in utero death).

### *Definition of variables*

We considered a pregnancy to be well attended when the pregnant woman had completed the recommended number of antenatal visits for her term. A pregnancy followed to term must have had at least 8 antenatal visits.[7]

The data were collected from medical records in the archives of the UH of Borgou/Alibori maternity hospital.

## RESULTS

From 01 January 2015 to 31 August 2019, a proportion of 1.3% (130/10087) of pregnant women admitted to the maternity ward of UH of Borgou/Alibory were sickle cell. Of these, 119/130 had usable records. Heterozygous SC pregnancies were the most represented: 68.9% (82/119).

### *Socio-demographic characteristics and follow-up of sickle cell pregnant women*

A proportion of 59.7% (71/119) of the sickle cell pregnant women (SP) had been referred as shown in Table 1. The mean age of the SP was 25.81±6.17 years with extremes of 16 and 41 years. The SP with an age between 25 and 35 years were the most represented with 56.3%. A proportion of 79% (94/119) of the SP lived in Parakou. The SP had attained secondary school level in 26.9% of cases and 38.6% of them were housewives (Table 1).

A proportion of 57.1% (68/119) of the SP were primigravida, 24.1% were primiparous. We also noted that 42% (50/119) of them had a history of fetal loss: 17.6% (21/119) stillbirths, 24.4% (29/119) spontaneous miscarriages. Finally, 35.3% (42/119) of the SP had a history of caesarean section. One SP was infected with HIV.

A proportion of 87.4% (104/119) of the SP had not followed their pregnancy well. Most of the pregnant women with sickle cell disease who had not followed their pregnancy well had been followed outside the specialised center for the care of SP 96.10% (100/104) (Table 1).

### *Pregnancy and postpartum complications*

We noted complications in pregnant women with sickle cell disease during their pregnancy. Maternal complications included: vaso-occlusive crises 79% (94/119); infections 74.8% (89/119); severe anaemia

27.7% (33/119); hyponatraemia 10.1% (12/119); vasculo-renal syndromes 18.4% (22/119). Fetal complications included: premature deliveries 38.6% (46/119), low birth weight (LBW) 54.7% (52/119), in utero deaths 17.6% (21/119).

Table 2 shows the distribution of pregnant women with sickle cell disease according to the complications that occurred during pregnancy. A proportion of 58.8% (70/119) of the pregnant women with sickle cell disease had been hospitalised during their pregnancy. The average length of hospitalisation was 3.81±2.66 days with extremes ranging from 1 to 16 days. Pregnant women who had stayed between 1 and 7 days were the most represented: 72.8% (51/70).

We observed that 78.2% of the SP (93/119) had been able to give birth with a new live baby, of which 89 (95.7%) by caesarean section: emergency caesarean section had been indicated in 55 (61.8%) pregnant women and prophylactic caesarean section in 34 (38.2%) pregnant women. The indications for emergency caesarean section were pre-eclampsia 18.2% (10), acute fetal distress 21.8%, and delivery dystocia 1.8%.[1] A proportion of 38.6% (46/119) of deliveries were preterm. Early neonatal mortality was 8.4% (8/95) of which 7 were within the first two hours. The main cause of death was perinatal asphyxia in 75% (6/8) of cases. During the post-partum period 45.4% (54/119) of the women had severe anaemia requiring transfusion and 35.3% (42/119) had suffered vaso-occlusive crises. Table 2 shows the distribution of sickle cell pregnancies according to maternal complications following childbirth. We recorded 4.2% (5/119) of maternal deaths, 3 of which occurred during pregnancy and 2 during childbirth. The causes of these deaths were acute chest syndrome (3 cases) and sepsis (2 cases).

***Factors associated with maternal-fetal prognosis***

The origin (outside Parakou), the low level of education of the SP, the low income professions (housewife, craftswomen, workers), the SS genotype, the insufficiency of prenatal follow-up, the mode of admission (referred/direct admission), the place of follow-up of the pregnancy were statistically associated with maternal-fetal complications in the sickle cell gestational carrier ($p<0,05$).

Table 3 presents the relationship between maternal-fetal prognosis, socio-demographic characteristics and prenatal follow-up of SP at UH of Borgou/Alibori.

In multivariate analysis, the low level of education of pregnant women, the SS genotype, the Insufficient of prenatal follow-up and the follow-up of the pregnancy outside the specialized center for the care of (SP) were the factors associated with maternal-fetal complications in SP as shown in Table 4.

**Table 1: Distribution of sickle cell pregnant women according to socio-demographic characteristics at the departmental University Hospital of Borgou and Alibori (N=119).**

| Variables | Average (N=119) | % |
|---|---|---|
| **Admission mode** | | |
| Reference | 71 | 59.7 |
| Functional symbol | 27 | 22.7 |
| Rendez-vous | 21 | 17.6 |
| **Age (years)** | | |
| <25 | 44 | 37 |
| 25 to 35 | 67 | 56.3 |
| >35 | 8 | 6.7 |
| **Educational level** | | |
| Primary | 26 | 21.8 |
| Secondary | 32 | 26.9 |
| High education | 11 | 09.2 |
| Literate | 20 | 16.8 |
| None | 30 | 25.2 |
| **Occupation** | | |
| Housewife | 46 | 38.6 |
| Craftswoman/worker | 22 | 18.5 |
| Tradeswoman/saleswoman | 16 | 13.4 |
| Civil servant | 27 | 22.8 |
| Pupil/student | 08 | 06.7 |
| **Place of pregnancy follow-up** | | |
| Sickle cell center | 17 | 14.29 |
| Maternity hospital | 08 | 06.72 |
| Peripheral public health center | 16 | 13.45 |

Continued.

| Variables | Average (N=119) | % |
|---|---|---|
| Private health center | 78 | 65.55 |
| **Number of PC[a]** | | |
| <the recommended number | 104 | 87.39 |
| ≥the recommended number | 15 | 12.61 |
| **Pregnancy term (WA) on admission** | | |
| <37 | 89 | 74.79 |
| ≥37 | 30 | 25.21 |

a: Prenatal consultation

**Table 2: Distribution of pregnant women with sickle cell disease at the University Hospital of Borgou and Alibori according to maternal-fetal complications.**

| Complications | Average (N=119) | % |
|---|---|---|
| **Maternal pregnancy** | | |
| Severe anaemia | 33 | 27.7 |
| Crise vaso-occlusive | 94 | 79.0 |
| Infections | 89 | 74.8 |
| Urinary tract infection | 50 | 42.0 |
| Digestive infection | 03 | .. |
| Pneumonia | 02 | .. |
| Typhoid fever | 02 | 1.7 |
| Malaria | 32 | 26.9 |
| Hyponatraemia | 12 | 10.1 |
| Vasculo-renal syndromes | 22 | 18.4 |
| Preeclampsia | 10 | 8.4 |
| Gestational hypertension | 11 | 9.2 |
| Chronic high blood pressure | 01 | 0.8 |
| Hyperuricaemia | 06 | 5.0 |
| **Fetal/adnexal** | | |
| Death in womb | 21 | 17.6 |
| Placenta previa | 01 | 0.8 |
| Premature rupture of the membranes | 19 | 16.0 |
| Oligohydramnios | 12 | 10.1 |
| Premature delivery | 93 | 78.1 |
| Acute foetal distress | 12 | 10 |
| Low birth weight | 52 | 54.7 |
| Spontaneous miscarriage | 02 | 1,6 |
| **Layer suites** | | |
| Severe anaemia | 54 | 45.4 |
| Vaso-occlusive crisis | 42 | 35.3 |
| Acute lung edema | 03 | 2.5 |
| Postpartum haemorrhage | 02 | 1.7 |
| Genital infection | 02 | 1.7 |
| Urinary tract infection | 01 | 0.8 |
| Acute thoracic syndrome | 09 | 7.6 |

*: High blood pressure

**Table 3: Relationship between maternal-fetal complications, socio-demographic characteristics and follow-up of sickle cell pregnant Women at the University Hospital of Borgou and Alibori.**

| Variables | Maternal-fetal complications | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Total | Present | | Absent | | | | |
| | | n | % | n | % | RR | IC 95% | P |
| **Educational level** | | | | | | | | |
| Secondary/superior | 43 | 33 | 76.74 | 10 | 23.25 | 1 | [1.04-8.55] | 0.0354 |

Continued.

| Variables | Maternal-fetal complications | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Total | Present | | Absent | | | | |
| | | n | % | n | % | RR | IC 95% | P |
| Primary/literateor not | 76 | 69 | 90.79 | 07 | 09.21 | 1.67 | | |
| **Profession** | | | | | | | | |
| Civil servant/pupil/student | 35 | 26 | 74.28 | 09 | 25.72 | 1 | [1.14-9.41] | 0.0404 |
| Housewife/craftswoman/worker | 84 | 76 | 90.48 | 08 | 09.52 | 3.29 | | |
| **Genotype** | | | | | | | | |
| SC | 82 | 66 | 80.49 | 16 | 19.15 | 1 | [1.07-1.36] | 0.0207 |
| SS | 37 | 36 | 97.30 | 01 | 02.70 | 1.21 | | |
| **Number of PCa** | | | | | | | | |
| Sufficient | 15 | 07 | 46.67 | 08 | 54.33 | 1 | [1.13-1.37] | 0.0001 |
| Insufficient | 104 | 95 | 91.35 | 09 | 08.655 | 1.95 | | |
| **Admission mode** | | | | | | | | |
| Appointments | 21 | 11 | 52.38 | 10 | 47.62 | 1 | [1.17-2.67] | 0.0001 |
| Signs/referrals | 98 | 91 | 92.86 | 07 | 07.14 | 1.77 | | |
| **Place of follow-up** | | | | | | | | |
| Specializedb HCc | 30 | 18 | 60.00 | 12 | 40.00 | 1 | [1.16-2.11] | 0.0001 |
| Non-specialized HCc | 89 | 84 | 94.38 | 05 | 05.62 | 1.57 | | |

a: Prenatal consultation, b: specialized center for the care of sickle cell pregnant women; University Hospital of Borgou/Alibory; private obstetrics practice, and c: health center

**Table 4: Factors associated with maternal-fetal complications in pregnant sickle cell patients at the departmental University Hospital of Borgou and Alibori.**

| Variables (modalities) | $OR_{ajusted}$ | $IC_{95\%}$ | P |
|---|---|---|---|
| **Origin (outside Parakou)** | 1.46 | [0.77-1.69] | 0.467 |
| **Education level (low)** | 1.49 | [1.06-2.26] | 0.006 |
| **Occupation (low income)** | 1.04 | [0.47-1.51] | 0.297 |
| **SS genotype** | 2.34 | [1.47-6.53] | 0.045 |
| **Insufficient prenatal care** | 2.38 | [1.43-3.22] | 0.005 |
| **Mode of admission (referral)** | 1.01 | [0.92-1.90] | 0.930 |
| **Place of follow-up (outside the specialised centre for sickle cell disease pregnancy)** | 2.49 | [0.39-4.92] | 0.009 |

## DISCUSSION

Our work was carried out at the departmental University Hospital of Borgou/Alibori. We had hospital data. Our sampling was exhaustive, which reduced the possible selection bias of the files. The analytical aspect allowed us to highlight the factors associated with the occurrence of complications.

The mean age of sickle cell pregnancies was 25.8±6.17 years. This result is similar to those reported by Omo et al in Nigeria and Wilson et al in Ghana with 25 and 27.7 years respectively.[8,9] In our study, we observed a predominance of the SC genotype (68.9%) in pregnant sickle cell patients. This finding is the same as that of Rahimy et al in Cotonou (Benin).[10]

The majority of SP were primigravida (57.1%). This finding is similar to that of Kavitha et al in India and Wilson et al in Ghana who found 58% and 53.1% primigravida in sickle cell gestations respectively.[9,11] This is lower than the rate reported by Faye et al in Senegal in 2018 which was 48.6%.[12] With regard to parity, 48.7% of pregnant women were nulliparous. Kuo et al in the United State found a similar result with 46.2%.[13] Faye et al in Senegal reported a higher proportion of nulliparous (74.6%).[12] These results could be explained by the difference in study populations.

A proportion of 24.3% (29/119) of pregnant women with sickle cell disease had a history of spontaneous miscarriage. This result is similar to that of Leborgne et al in Guadeloupe.[14]

Most of the sickle cell gestational carriers who had not followed their pregnancy well had been followed outside the specialized center for the care of SP 96.10% (100/104). This may be the reason why most of them had experienced complications. A proportion of 79% (94) of the sickle cell pregnancies had had at least one vaso-occlusive crisis during their pregnancy. This proportion is lower than that of the study by Leborgne et al in Guadeloupe (88%) but higher than that of Burgo et al in Colombia (54%) and Rahimy et al in Benin (55%).[10,14,15] These differences could be related to the quality of antenatal care.

We observed a proportion of 74.8% of infections in the SP. These results are higher than those of Burgo et al in Colombia (66.6%).[15] This difference could be related to the endemic presence of malaria in our region.

We recorded 42% of urinary tract infections. This result is similar to that of Kavitha et al in India (47.05%).[11] In the United Kingdom , Oteng-Ntim et al reported a lower proportion of urinary tract infections (21.8%) in pregnant women with sickle cell disease.[16] This difference may be related to better monitoring of these women.

We recorded a proportion of 8.4% (1/119) of pregnant sickle cell patients who had had pre-eclampsia. This result is similar to those reported by Al Kahtani et al in Saudi Arabia and Wilson et al in Ghana, respectively 9.7%, 7.6%.[9,17] Vascular and kidney lesions caused by falciform disease are the major contributors.[6]

In our series there was a proportion of 31.7% (33/119) of severe anaemia. This result is similar to those of Kahansim et al in Nigeria and Kavitha et al in India with 31.4% and 29.41% severe anaemia respectively.[11,18] This rate of severe anaemia is higher than that reported in the general population of pregnant women by Koura et al in Ouidah (Benin) who noted 1.7%.[19] There is a high frequency of anaemia in sickle cell patients because of the frequent haemolytic crises they often present.[6]

There was a 38.6% (46/119) preterm delivery rate. This is lower than Desai et al in India 45%, and higher than Leborgne et al in Guadeloupe and Kathani et al in Saudi Arabia 21% and 15% respectively.[14,17,20] This could be explained by the lack of follow-up of pregnancies, the high frequency of complications during pregnancy, but also the practice of prophylactic caesarean section at 36 weeks of amenorrhoea in SP at the departmental University Hospital of Borgou and Alibori because of premature placental ageing with the alteration of foeto-placental exchanges, which is characteristic of sickle cell disease.

We recorded a high proportion of caesarean sections: 95.7% of deliveries with live newborns. Leborgne et al also report a high caesarean section rate among SP in Guadeloupe: 48%.[14] The high caesarean section rate in our study could be explained by the mode of admission of our pregnant women who were mostly complicated cases referred (59.7%), and by the practice of prophylactic caesarean section at 36 weeks of amenorrhoea.

In the postpartum period, 45.4% (54/119) of the women had been transfused. This rate is similar to those reported by Desai et al in India: 50% transfusion in the postpartum period.[20] It is lower than that observed by Al Farsi et al in the Middle East where 90% of parturients were transfused.[21]

In our study, low birth weight infants were the most represented at 49.5%. This is lower than the 70.2% found by Desai et al in India.[20] However, this rate is higher than that reported by Oteng-Nim et al in the United Kingdom: 16%.[16] This difference could be linked to the quality of care for sickle cell gestational carriers, which differs from one study to another, to chronic anaemia, placental hypoxia and frequent infectious episodes in sickle cell gestational carriers.[6]

The maternal death rate in our series was 4.2%. This rate of maternal death is similar to those of Burgo et al in Colombia and Omo-Aghoja et al in Nigeria who found respectively 4% and 4.6% maternal death in SP.[8,15] This is lower than the result of Mugayanzi et al in Tanzania in 2013 (11.4%).[5] However, this rate is higher than those reported by Rahimy et al in Cotonou (Benin) in 2000 (1.8%) and Faye et al in Senegal in 2018 who had no maternal deaths.[10,12] This difference could be explained by the quality of management. In our study, the majority of patients were not well followed for sickle cell disease.

In our study, we noted a proportion of 17.6% (21/119) of deaths in utero. This result is similar to those observed by Faye et al in Senegal and Silva et al in Brazil, respectively 18.6% and 15%.[12,22] Rahimy et al in Cotonou (Benin) reported a lower rate of 11.7%.[10] This could be explained by the fact that the majority of our pregnant women had not followed their pregnancy well and had infectious complications and anemia responsible for placental hypoxia.

Early neonatal mortality was 8.4% (8/95). The main cause of death was perinatal asphyxia (75%). This mortality is similar to that reported by Asaré et al in Accra (Ghana) in 2017: 6.08%.[23] It is lower than the fetal and neonatal mortality reported by other authors: 50 to 80%.[24]

In our study, the SS genotype was statistically associated with the occurrence of maternal-fetal complications p=0.030. This observation has been made by several authors, notably Silva et al in Brazil, and Leborgne et al in Guadeloupe.[14,22]

Indeed, Silva et al in their study of 89 sickle cell pregnancies, noted a proportion of 15% of in utero deaths which occurred only in SS sickle cell patients.[22] They also found that transfusion was more frequent in SS than SC with p=0.007.

We also observed that low educational level was statically associated with the occurrence of maternal-fetal complications. This could be explained by the lack of awareness of the risks of sickle cell disease by uneducated pregnant women who, as a result, undergo less monitoring during their pregnancy than educated women.

The limitations of our study were related to the sample size. Some pregnant women with sickle cell disease were probably not recruited into the sample because their records were not usable or their biological diagnosis of sickle cell disease was not made due to lack of financial resources.

## CONCLUSION

Pregnancy in women with sickle cell disease is a frequent clinical association at the Departmental University Hospital of Borgou and Alibori. The evolution of this association is often marked by complications. Certain factors are associated with the occurrence of these complications. Taking these factors into account in the management strategy will certainly improve the prognosis of sickle cell pregnancies.

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