Maternal and Foetal Outcomes of Pregnancy with Homozygous Sickle Cell Disease: A Case - Control Study at the Yaounde Central Hospital, Cameroon

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Abstract

Background: Sickle cell disease (SCD) is the most common genetic disease worldwide. Pregnancy and delivery in sickle cell women carry out high risk of materno-foetal morbidity and mortality. Our objective was to determine pregnancy outcomes in sickle cell women.

Methods: We carried out a retrospective case control study from January 2007 to December 2012 at the Yaoundé Central Hospital (YCH). Each of the 32 cases of SCD women had three controls non SCD women matched for age and parity.

Results: The prevalence of sickler women was 0.16%. The following maternal complications were more frequent in SCD women: vaso-occlusive crisis (40.6% Vs 0%; p < 0.05), severe anaemia (37.5% Vs 0%; p < 0.05), edema (15.6% Vs 3.1%; p < 0.05), pneumonia (6.2% Vs 0%; p < 0.05) and caesarean section (71.9% Vs 27.1%, p < 0.05). Maternal mortality was higher among SCD women but not significantly (3% Vs 0%; p = 0.082). The following foetal complications were more frequent in SCD women: acute foetal distress (43.7% Vs 10.4%; p < 0.05), intrauterine growth retardation (25% Vs 6.2%, p < 0.05), perinatal death (63% Vs 42%, p = 0.629).

Conclusion: Maternal and foetal outcomes of pregnancy in SCD women were poorer than in their non SCD counterparts. Clinicians should pay more attention to these women during antenatal care and delivery.

Keywords: Sickle Cell Disease; Pregnancy; Outcome; Morbidity; Mortality; Complications; Cameroon

Abbreviations


Background

Sickle Cell Disease (SCD) is the most common genetic disorder worldwide and Africa is the most affected continent. In Cameroon, 25 to 30% of the population carry the SCD gene while 1-2% is homozygous sicklers. Pregnancy in SCD patients is risky for the mother and the foetus [es] in both low and high income countries [1,3]. In Africa, sicklers account for 0.14 - 0.29% of pregnant women [2,4-6]. In 1981, Kaptue, et al. reported that 0.19% of pregnant Cameroon women were homozygous sicklers [2]. Given that life expectancy of homozygous sicklers has increased allowing more of them reach child-bearing age, it is awaited that our health systems will have to manage more and more pregnancies in homozygous sicklers [7]. Studies among black populations in United States of America (USA) and in Jamaica have demonstrated that higher complication rates in pregnancies in homozygous sicklers tend to increase rates of indirect maternal deaths [8,9]. To the best of our knowledge no study have evaluated pregnancy outcome among homozygous sicklers in Cameroon. Our goal is therefore to assess materno - foetal outcomes among homozygous sicklers. We hypothesized that the Cameroonian homozygous sicklers have poor pregnancy outcomes.

Methods

We carried out a retrospective case control study in the Gynaecology and Obstetrics unit of the Yaounde Central Hospital (YCH). We included complete files of women who gave birth at the YCH from January 1, 2007 to December 31, 2012 (six years). Sickle cell women were cases and for each, we considered three controls (non sickle cell women) matched for age and parity. Controls were women (without the sickle trait) who gave birth during the study period and whose files adequately matched those of cases. The following data were retrieved using a pretested technical form: socio-demographic characteristics (age, marital status, employment status, level of education), obstetrical characteristics (gestational age, gestity, parity, past history of miscarriage, the number of antenatal consultations), maternal complications (severe anaemia, vaso-occlusive crisis, eclampsia, infection, pyelonephritis, pneumonia, malaria, dystocia, premature rupture of membranes, maternal death, route of delivery) and foetal complications (acute foetal distress, intra-uterine growth retardation, intra-uterine foetal death, low birth weight (< 2500 grams), macrosomia (birth weight > 4000 grams), 5th minute Apgar score < 7, resuscitation at birth, prematurity and perinatal death).

Data were compiled on an Excel® spreadsheet and analysed with the software SPSS® 20. Frequencies and means were calculated. Chi square test was used to compare qualitative variables. Odds ratios with 95% confidence intervals were calculated. Differences are considered significant for p value < 0.05.

Ethical Considerations

Prior to data collection, ethical clearance was obtained under the following reference: N’2013/048/CIE-UdM/Pr from the ethical committee of “Université des Montagnes” (Cameroon) as well as from the management of the study site. Data collection and handling were done with strict confidentiality.
Results and Discussion

We have retrieved 19,940 files during the study period; out of them 32 are sickle cell disease cases (0.16%).

Socio-demographic characteristics of study participants

Table 1 describes the socio-demographic profile of the study participants. The mean age of sickle cell disease mothers are 24.1 ± 4.5 years (range from 17 to 34 years). Only 21.7% (seven out of 32) are married. Secondary school is the most frequent highest level of education (71.9% [26 out of 32]) and there is no significant difference with controls. Twenty five out of 32 (78.1%) SCD mothers are employed and there is no significant difference with controls.

Obstetrical profile of participants

The obstetrical profile of the study participants is presented in table 2. Mean gestational age at delivery is 5 ± 2.0 weeks for diseased and 37.7 ± 1.9 weeks for control with a significant difference (p = 0.002). Among diseased, 40% [13 out of 32] gave birth prematurely (before 37 completed weeks) versus 16.7% (16 out of 96) among controls, with a significant difference (Odds Ratio = 3.4; 95% CI: 1.4 - 8.3; p = 0.005). History of spontaneous abortion is significantly more present in diseased than in controls: 37.5% versus 13.5% (Odds Ratio = 1.5; 95% CI: 1.5 - 9.6; p = 0.011). Moreover, the Odds of eclampsia in sickers are 5.7 times that of controls. (OR = 5.7; 95% CI: 1.2 - 25.5; p = 0.011). Maternal death rate among sickers is higher than in controls but not significantly (31% Vs 0%; p = 0.082).

Maternal complications

Maternal complications are presented in table 3. The following maternal complications are significantly more frequent in SCD women: Vaso-Occlusive Crisis (40.6% Vs 0%; p = 0.000); severe anaemia (37.5% Vs 0%; p = 0.000); eclampsia (15.6% Vs 3.1%; p = 0.011) and pneumonia (6.2% Vs 0%; p = 0.014). Moreover, the Odds of eclampsia in sickers are 5.7 times that of controls. (OR = 5.7; 95% CI: 1.2 - 25.5; p = 0.011). Maternal death rate among sickers is higher than in controls but not significantly (31% Vs 0%; p = 0.082).

Foetal complications

Foetal complications are presented in table 4. The following foetal complications are significantly more frequent among sickers: acute foetal distress (43.8% Vs 10.4%; p = 0.000) and Intra-uterine growth retardation (25% Vs 6.2%; p = 0.003). Incidence of foetal complications are significantly higher in cases than in controls (34.4% Vs 76.0%; p = 0.003).

Route of delivery

The different routes of delivery are presented in table 5. Cesarean section is the main route of delivery among SCD women and the differences with controls are significant (71.9% Vs 27.1%; Odds ratio is 6.8; 95% CI: 2.8 - 6.7). Among women who delivered by caesarean section, the proportion of emergency interventions are significantly higher in sicklers (62.5% Vs 21.9%; p = 0.000).

Newborn parameters

Table7 shows the distribution of participants according to newborn parameters. Mean birth weight of children born to sickers (2661.4 ± 534 grams) is inferior to that of children born to non sickers. That

Table 1: Socio-demographic profile of participants (SD: Standard Deviation; CI: Confidence Interval. There is no significant difference between the two groups concerning the socio demographic profiles).

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cases n = 32 (%)</th>
<th>Controls n = 96 (%)</th>
<th>Odds Ratios</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD)</td>
<td>24.1 ± 4.5 (17 - 34)</td>
<td>24.1 ± 4.5 (17 - 34)</td>
<td>1</td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>7 (21.9)</td>
<td>35 (36.5)</td>
<td>0.4</td>
<td>0.1 - 1.2</td>
<td>0.128</td>
</tr>
<tr>
<td>Single</td>
<td>25 (78.1)</td>
<td>61 (63.5)</td>
<td>2</td>
<td>0.8 - 5.2</td>
<td>0.128</td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>4 (12.5)</td>
<td>12 (12.5)</td>
<td>1</td>
<td>2.0 - 33</td>
<td>1.000</td>
</tr>
<tr>
<td>Secondary</td>
<td>23 (71.9)</td>
<td>66 (68.7)</td>
<td>1.1</td>
<td>0.4 - 2.8</td>
<td>0.741</td>
</tr>
<tr>
<td>University</td>
<td>5 (15.6)</td>
<td>18 (18.8)</td>
<td>0.8</td>
<td>0.2 - 2.3</td>
<td>0.683</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>7 (21.9)</td>
<td>25 (26.0)</td>
<td>0.7</td>
<td>0.3 - 2.0</td>
<td>0.637</td>
</tr>
<tr>
<td>Employed</td>
<td>25 (78.1)</td>
<td>71 (74.0)</td>
<td>1.2</td>
<td>0.4 - 32</td>
<td>0.637</td>
</tr>
</tbody>
</table>

Table 2: Obsetetrical profile of participants. Mean gestational age at delivery is 5 ± 2.0 weeks for cases and 37.7 ± 1.9 weeks for control with a significant difference (p = 0.002). Among cases, 40% [13 out of 32] gave birth prematurely (before 37 completed weeks) versus 16.7% (16 out of 96) among controls, with a significant difference (Odds Ratio = 3.4; 95% CI: 1.4 - 8.3; p = 0.005). History of spontaneous abortion was significantly more present in cases than in controls: 37.5% versus 13.5% (Odds Ratio = 1.5; 95% CI: 1.5 - 9.6; p = 0.003). Cases had more antenatal consultations than controls (6.5 ± 2.0 versus 3.2 ± 0.9) with a significant difference (p = 0.000).
difference is statistically significant ($p = 0.000$). The rate of newborns with 5th minute Apgar’s scores ≥ 7 was 68.8% among SCD women and 86.4% among controls ($p = 0.024$). The risk of having a newborn with fifth Apgar’s score between 1 and 6 is 5.3 higher in SCD women than in controls. Prematurity is significantly more frequent in sicklers (43.8% Vs 16.7%; $p = 0.000$) and Intra-uterine growth retardation (25% Vs 6.2%; $p = 0.003$). Incidence of foetal complications was significantly higher in cases than in controls (34.4% Vs 76.0%; $p = 0.003$).

**Table 6**: Distribution of participants: Indications of Cesarean section (PROM: Premature Rupture of Membranes)

<table>
<thead>
<tr>
<th>Indications of cesarean sections</th>
<th>Cases n = 32 (%)</th>
<th>Controls n = 96 (%)</th>
<th>Odds Ratios</th>
<th>95% CI</th>
<th>p - values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cephalo-Pelvic Disproportion</td>
<td>4 (12.5)</td>
<td>6 (6.2)</td>
<td>2.1</td>
<td>0.5 - 8.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Ecclampsia</td>
<td>3 (9.4)</td>
<td>3 (3.1)</td>
<td>3.2</td>
<td>0.6 - 16.7</td>
<td>0.1</td>
</tr>
<tr>
<td>Acute fetal distress</td>
<td>7 (21.9)</td>
<td>7 (7.3)</td>
<td>3.5</td>
<td>1.1 - 11.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Contracted pelvis</td>
<td>2 (6.2)</td>
<td>0 (0.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transverse lie</td>
<td>1 (3.1)</td>
<td>3 (3.1)</td>
<td>1</td>
<td>0.1 - 9.9</td>
<td>1.0</td>
</tr>
<tr>
<td>Breech presentation in primiparous</td>
<td>2 (6.1)</td>
<td>2 (2.1)</td>
<td>3.1</td>
<td>0.4 - 23.2</td>
<td>0.2</td>
</tr>
<tr>
<td>Ecclampsia + Acute fetal distress</td>
<td>2 (6.2)</td>
<td>0 (0.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROM / poor Bishop’s score</td>
<td>1 (3.1)</td>
<td>0 (0.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe pre-ecclampsia + poor Bishop's score</td>
<td>1 (3.1)</td>
<td>0 (0.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Failure of trial of scar</td>
<td>0 (0.0)</td>
<td>2 (2.1)</td>
<td>0</td>
<td></td>
<td>0.4</td>
</tr>
<tr>
<td>Pre-rupture of uterus</td>
<td>0 (0.0)</td>
<td>1 (1.0)</td>
<td>0</td>
<td></td>
<td>0.6</td>
</tr>
<tr>
<td>Macrosomia</td>
<td>0 (0.0)</td>
<td>2 (2.1)</td>
<td>0</td>
<td></td>
<td>0.4</td>
</tr>
</tbody>
</table>
Discussion

Out of the 19940 deliveries recorded during the study period, 32 are from homozygous SCD women giving an incidence of 0.16%. In 1981, Kaptue, et al. [2] found an incidence of 0.19% in Cameroon. In 2013, Boulet, et al. [9] Of the 335,348 black women with a delivery during 2004 - 2010, 1,526 had a diagnosis of SCD (0.5%) in USA. This lower prevalence of delivery among homozygous sicklers in Cameroon may be explained by the fact that a small proportion of them reach childbearing age in Cameroon. Mean age was 24.1 ± 4.5 years among sicklers in our series, (range 17 to 34 years). Diallo, et al. [10] reported similar findings in Dakar in 2009 with a mean age of 23 years (range 15 - 35 years).

Pregnancies in homozygous sicklers lasted significantly shorter in controls (36.5 weeks Vs 37.5 weeks p = 0.002). Nomura, et al. [11] found that mean pregnancy duration was 35.2 weeks among Brazilian sicklers in 2010. In our series, 59.4% of homozygous sicklers gave birth at term; a proportion which is similar to that of 53.1% reported in Saudi Arabia by Zia, et al. [12]. The risk of premature birth is significantly higher among sicklers (OR: 3.4; 95% CI: 1.4 - 8.3). Most cases of prematurity were induced because of chronic fetal distress.

Mean gestity and parity among homozygous sicklers in our series were 1.7 ± 0.9 and 1.2 ± 0.7 respectively. These findings are similar to those published by Leborgne - Samuel, et al. [13] for a group of 33 homozygous sicklers (mean gestity of 2.7 and mean parity of 1.3 parity). Diallo, et al. [10] reported a mean gestity of 1.5 and a mean parity of two among homozygous sicklers in Dakar. In Jamaica, Asnani, et al. [8] reported a mean gestity of two among homozygous sicklers. Given that life expectancy of homozygous sicklers has increased worldwide in recent years and with progress in reproductive medicine, they may be more prone to childbearing.

We found that pregnant women with homozygous SCD are significantly more antenatal consultations than controls (6.5 ± 2.0 Vs 3.2 ± 0.9; p < 0.05). This may be explained by the higher prevalence of complications during pregnancy in homozygous sicklers. Asnani, et al. [8] reported similar findings in Jamaica in 2011 (3.3 Vs 7.3; p - value: 0.01).

Maternal complications among homozygous sicklers were significantly more frequent than in controls. This is in accordance with results published by Leborgne - Samuel in Guadeloupe [13].

Vaso-Occlusive Crisis (VOC) was the most frequent maternal complications in our series, accounting for 40.6% of cases. This rate of VOC is closed to the rates of 43.3% and 46% of VOC reported by Al Khataini, et al. [14,15] in Saudi Arabia and by Howard et al. in United Kingdom respectively. The rate of VOC reported by Leborgne - Samuel, et al. [13] in Guadeloupe in 2000 was higher (88%). In our series, homozygous sicklers were six fold more likely to have eclampsia than controls (OR: 5.7; 95% CI: 1.2 - 25.5). This is less than the Odds Ratio of 10.6 (95% CI: 3.6 - 30.9) reported by Wilson, et al. [16] in 2012 in Ghana on a larger sample. In a systematic review of studies from both low and high income countries in 2015, Boafor, et al. [3] reported a pooled Odds Ratio of 3.02, (95% CI: 1.20 - 7.58) for eclampsia among SCD women. Pyleonephritis is significantly more frequent in homozygous sicklers than in controls in our study; this is in accordance with results by Odum, et al. [17] in Nigeria in 2002. In our series maternal mortality rate was 31% among sicklers. Sonwane, et al. [10] reported a rate of 40% in India in 2005. In Jamaica, Asnani, et al. [8] found that maternal mortality ratio among homozygous sicklers was 7 - 11 times higher than non sicklers. Similarly, Boafor, et al. [9] reported a pooled Odds Ratio for maternal mortality of 10.9 (95% CI: 1.8 - 65.1, p = 0.009).

Health staff in antenatal care units should keep those facts in mind when care for homozygous sicklers.

Acute Fetal Distress (AFD) and Intra Uterine Growth Restriction (IUGR) were the most frequent foetal complications among homozygous sicklers and were significantly more frequent than in controls (43.8% Vs 10.4%; p = 0.000). Concerning AFD, Nomura, et al. [11] had similar findings in Brazil in 2010, with a higher rate among homozygous SCD patients (56.9% Vs 43.7%). Our rate of IUGR (25%) is superior to that of 15% reported by Leborgne - Samuel, et al. among a cohort of 68 homozygous sicklers Guadeloupe [13].

The Odds ratio for AFD in our series (OR = 6.6; 95% CI: 2.5 - 17.4) is higher than that reported by Wilson et al. in Ghana (OR = 3.3; 95% CI: 1.4 - 7.4) [12]. Similarly the Odds ratio for IUGR in our series (OR = 5.0; 95% CI: 1.5 - 15.7) is higher that reported by Wilson, et al. (OR = 4.0; 95% CI: 1.4 - 11.6) [16]. This difference in effect sizes can be explained by the larger sample size in the study by Wilson et al. (131 cases Vs 32). Indeed in their meta-analysis, Boafor et al. reported a smaller OR (pooled OR 2.79, 95% CI 1.85 - 4.21) [3]. The rate of intra-uterine death among homozygous sicklers is higher when compared to controls but not significantly. This may be due to the more intensive antenatal care they received. Indeed they had more quality antenatal Consultations than controls as
stated earlier (6.5 ± 2.0 Vs 3.2 ± 0.9 (1-6); p = 0.000). Nevertheless, perinatal mortality is known to be roughly 4 times higher among homozygous sicklers [3].

The mode of delivery among homozygous sicklers is caesarean section and the rate is significantly higher than controls (OR = 6.8; IC: 2.8 - 16.7). Ngo, Sonwane, et al. had similar findings [18, 19]. The mean birth weight is significantly lower in homozygous sicklers (2661.4 ± 534 grams Vs 3249.9 ± 576 grams; p = 0.000). Leborgne - Samuel, et al. had similar findings with a mean birth weight of 2553 ± 534 grams among SCD women [13]. This may be explained by the fact that chronic anaemia is a feature of homozygous SCD. Indeed, the rate of severe anaemia is significantly higher in homozygous SCD women than in controls (37.5% Vs 0%). Leborgne - Samuel, et al. reported similar findings [13]. The rate of newborns with less than 2500 grams is higher in homozygous sicklers but not significantly (28.1% Vs 17.7%; p = 0.204). Diallo, et al. had a similar proportion (27.3%) in Senegal while Boafor, et al. reported a pooled OR of OR 2.00, 95% CI 1.42 - 2.83 [3, 10]. The rate of prematurity is significantly higher among SCD women (40.6% Vs 16.7%; p = 0.005; OR: 3.4; 95%CI: 1.4 - 8.3). Ashish, et al reported a rate of prematurity of 56% of SCD patients [20]. Resuscitation at birth is done for 18.7% of babies born to SCD women against 12.5% in controls but the difference was not statistically significant (p = 0.378). Ngo, et al. found that 13% of newborn to homozygous sicklers were resuscitated [19]. We recorded two early neonatal deaths (due to prematurity) among sickle (63%) and one in controls (42%); The difference is not statistically significant (p = 0.629). This may be explained either by the smallness of our sample size or by the high level of care delivered in the tertiary maternity in which the study is conducted because perinatal mortality is known to be roughly 4 times higher among homozygous sicklers [3].

What does this Study Add?

Our study is the first (to the best of our knowledge) to assess outcome of pregnancy among homozygous sicklers in Cameroonian population. Our hypothesis is confirmed that the pregnancy outcome is poor in sickle cell disease patients.

Limitations of the Study

The value of this study is limited by the smallness of the sample size. Another major limitation is retrospective data collection. Finally the study is carried out in a single centre and participants are from a narrow geographic area.

Conclusion

Though rare (0.16% of all pregnancies), pregnancy in homozygous sickle cell disease women carries out higher risk of complications. We therefore recommend high level antenatal care for homozygous sicklers.

Competing Interests

The authors declare that there are no competing interests.

Authors’ Contributions

FJH conceived the study, participated in the study design, data collection, drafting and editing of the manuscript. FYF and FTJ participated in the study design, data collection and analyses, drafting and editing of the manuscript. PNN, HJF, REM supervised the study from the beginning to the manuscript. All authors read and approved the final manuscript.

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