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RESEARCH ARTICLE

Sickle cell anemia and pregnancy: Profile of hemodynamic changes in sickle cell pregnant women in Kinshasa

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Abstract

Pregnancy is accompanied by hormonal changes. These relate mainly to progesterone and placenate growth factor. Hemodynamic changes are also observed. in a sickle cell pregnant woman, all these changes have a direct effect on hypoxia. This is responsible for the polymerization of HbS. The latter causes the sickling of sickle red blood cells. sickling of red blood cells is responsible for hemolysis and vasoocclusion, two major acute manifestations during pregnancy in a sickle cell patient.

KEYWORDS
changes, hemodynamics, pregnancy, sickle cell anemia

1 | INTRODUCTION

Sickle cell anemia (SCA) is a constitutional qualitative hemoglobinopathy characterized by the synthesis of an abnormal hemoglobin called HbS. Hemoglobin S is the consequence of a missense point mutation [Glu7Val] at the 7th codon of the beta globin gene on chromosome 11. Molecularly, the E7V mutation of SCA is characterized by a transversion of nitrogenous bases in which a purine base (adenine [A]) is replaced by a pyrimidine base (Thymine [T]) [1–4]. The consequence of this substitution is the synthesis of an abnormal Hb called HbS. Under conditions of hypoxia, metabolic acidosis, dehydration, and other stressful conditions, HbS precipitates, crystallizes, and polymerizes. This polymerization leads to sickling and hemolysis of the red blood cell [5, 6]. Clinically, SCA is characterized by acute manifestations including vaso occlusion crises (VOCs), chronic hemolysis and high susceptibility to infection [7, 8]. Acute manifestations are responsible in the long term for chronic multivisceral manifestations [7, 8]. The chronic manifestations will evolve in the medium and long term towards progressive and sometimes irreversible multivisceral failures. SCA is a disease that is accompanied by great morbidity and mortality [9, 10]. SCA with thalassemia represent the most widespread hemoglobinopathies in the world. Indeed, the WHO estimates that 300,000 new births of children with SCA each year worldwide, 80% of which are born in sub-Saharan Africa [11, 12]. SCA is therefore a public

health problem in several sub-Saharan countries where the prevalence of the beta S gene is high [13]. Early detection, the use of specific vaccines, prophylaxis with penicillin and especially the use of hydroxy urea have improved the quality of life and life expectancy of sickle cell patients [14–17]. This is why, currently in sub-Saharan countries, the association between SCA and pregnancy is frequent [9, 18]. Indeed, this high frequency of the association SCA and pregnancy is due to the fact that fertility is preserved in sickle cell patients. However, there is a negative reciprocal influence between pregnancy and SCA. Pregnancy aggravates SCA and SCA negatively influences the course of pregnancy [19–21]. This is why a sickle cell pregnant woman must be cared for by a multidisciplinary team. Maternal complications during pregnancy are: VOCs, worsening anemia, risk of infection, acute chest syndrome, thromboembolic accidents, caesarean and maternal death [21]. These maternal complications are associated with several fetal complications including: early abortions, hypotrophy or low birth weight, prematurity and fetal death in utero [22, 23]. Several hypotheses explain the worsening of sickle cell disease during pregnancy. Among these we can cite the hemodynamic changes during pregnancy [24], the hormonal hypothesis and placental growth factors [25].

Our study aimed to describe the hemodynamic changes (plasma volume and globular volume) that occur during pregnancy in sickle cell pregnant women living in a context of precariousness on the one hand and to establish the correlation between the frequency of acute complications SCA and hemodynamic changes during pregnancy on the other hand.

2 | METHODS

We conducted a cross-sectional and analytical study between 2010 and 2022. The study was conducted at the Sickle cell, a public center specializing in the care of sickle cell patients in Kinshasa, DRC. During the study period we followed 1112 sickle cell pregnant women. In the present study, 146 pregnant and women who gave birth fulfilled the inclusion criteria. A control group of homozygous AA pregnant women was formed to compare the hemodynamic changes. This control group included 120 homozygous AA pregnant women followed during the study period.

2.1 | Inclusion criteria

To be included in this study, the following inclusion criteria had to be met:

1. Being known to have SCA and regularly monitored at the Sickel cell center,
2. Have started prenatal consultations before 10 weeks of amenorrhea,
3. Have carried out all the blood tests requested during pregnancy,
4. Having regularly attended consultations and having given birth at the sickel cell center. The exclusion criteria were the same as those for pregnant women with sickle cell disease.

In this study, we excluded:

1. Any pregnant woman who was transfused during pregnancy,
2. Any pregnant woman who has developed preeclampsia.
3. Any pregnant woman who presented a complication such as acute chest syndrome.

Inclusion criteria control group (homozygous AA)

To be included in the control group, you had to:

1. Be homozygous AA
2. Have started prenatal consultations before 10 weeks of amenorrhea,
3. Have carried out all the blood tests requested during pregnancy,
4. The exclusion criteria were the same as those for pregnant women with sickle cell disease. The exclusion criteria were the same as those for pregnant women with sickle cell anemia.

2.2 | Operational definitions

In the present study: The corpuscular volume or hematocrit expressed as a percentage was calculated by the difference between the volume of whole blood and the plasma volume after centrifugation. VG or Ht (%) = VT of blood – VPL.

The plasma volume (PLV) expressed as a percentage was calculated by the difference between the volume of whole blood and the globular volume (hematocrit) after centrifugation.

$$\text{VPL}\,(\%) = \text{VT}\,\textit{blood} - \text{VG}$$

Weight gain during pregnancy was calculated as the difference between birth weight (Pf) and prepregnancy weight (Pi); ΔP (Kg) = Pf-Pi.

The globular volume or hematocrit and the plasma volume were determined with a hematocrit centrifuge of the brand REMI RM-12C, Remi Electrotechnik LTD, India.

2.3 | Laboratory tests

We had collected 2 ml of venous blood in a tube containing EDTA. The complete blood count was assayed with an H18 blood count analyzer. The diagnosis of SCA was made by the technique of capillary electrophoresis with an automaton brand Minicap, Sebia France. The diagnosis was confirmed by molecular testing using the Restriction Fragment Length Polymorphism (RFLP) technique.

2.4 | Care during pregnancy

Before pregnancy, all pregnant women regularly received folic acid (5 mg per day) and omega 3. None of the pregnant women received hydroxy urea. During pregnancy, all pregnant women benefited from

folic acid supplementation 10 mg per day, omega 3, magnesium pidolate, two courses of prophylactic antimalarials at the 22nd and 34th week of amenorrhea. The antimalarial course was made up of a combination of artemisinin (80 mg) and lumefantrine (480 mg). All pregnant women received a dose of vermifuge (anti-helminth) at 32 weeks. Prenatal consultations were followed according to the local protocol for the management of sickle cell pregnant women. This protocol provides for one consultation per month until the 20th week of amenorrhea, then one consultation every 3 weeks until the 32nd week of amenorrhea and finally one consultation every 2 weeks until the 35th week. The delivery is scheduled for the 37th week. During pain attacks, pain was assessed with the visual analogue scale. In this scale, the WHO classifies the pain in stage 4. At stage 4, the pain was treated with morphine subcutaneously. The pain treatment was associated with hyperhydration and systematic research of the etiology of the pain crisis.

2.5 | Variables of interest

In the present study, we studied the following variations: hemoglobin, corpuscular volume or hematocrit, plasma volume, mean corpuscular volume, and weight gain during pregnancy. These variations were analyzed from the 12th week of amenorrhea, then every 4 weeks until the 36th week. We then analyzed the frequency of vaso-occlusive crises during the different periods of pregnancy.

2.6 | Statistics

Our data were processed with SPSS 20 software. We calculated the means and standard deviations. The means were compared by the annova test. The value of $p < 0.05$ was considered as the level of significance. Logistic regression generalized linear latent and mixed models (GLLAMM) with the logit link and binomial family [26] that adjusted for clustering was used to measure the level of association between the incidence of Vaso-occlusive attacks (CVO) and explanatory variables (hematocrit and Log VPL). We have introduced log VPL because VPL was not normally distributed. The Shapiro-Wilk test was used to measure the normality of the distribution of continuous variables.

3 | RESULTS

3.1 | Socio-demographic and obstetrical characteristics of pregnant women

In the present study, the age of the pregnant women varied from 17 to 34 years with a median of 24 years. The average age of pregnant women was 23.84 ± 3.85 years. Parity varied from 1 to 3 with a mean of 1.2 ± 0.1. All the pregnant women were of SS genotype, however 12 pregnant women or 8.21% had AS heterozygous partners. In stady state, the average HbS level was 90.2%, HbF 7.6% and HbA2 2.2%. Regarding the mode of delivery, we recorded 102 or 69.86% of cesarean deliveries.

Table 1 above shows the evolution of hematological, biochemical, physiological, and pregnancy variables during pregnancy in the study population. We observe overall that the hemoglobin level, the hematocrit decreased progressively from the 12th week to the 36th week of pregnancy with a highly significant statistical difference ($p < 0.001$), on the other hand the plasma volume, the average globular volume have increased gradually from the 12th week of pregnancy until the 36th week of pregnancy with a statistically significant difference ($p < 0.001$).

TABLE 1 Evolution of haematological, biochemical, physiological, and pregnancy variables during pregnancy in the study population.

Variables (mean ± SD)	12 w	16 w	20 w	24 w	28 w	32 w	36 w	*p*-Value
Hb (g/dl)	9.25 ± 0,06	8.83 ± 0.06	8.57 ± 0.05	8.14 ± 0.04	7.19 ± 0.04	6.46 ± 0.034	5.84 ± 0.04	<0.001
Ht (%)	27.45 ± 0.18	26.30 ± 0.17	25.22 ± 0.16	23.74 ± 0.14	21.14 ± 0.13	18.82 ± 0.12	16.81 ± 0.12	<0.001
VPL (%)	72.54 ± 0.17	73.69 ± 0.17	74.79 ± 0.15	76.27 ± 0.14	78.85 ± 0.13	81.13 ± 0.16	83.21 ± 0.12	<0.001
MCV (fl)	81.2 ± 0.17	82.71 ± 0.23	85.16 ± 0.21	87.99 ± 0.19	90.03 ± 0.20	92.06 ± 0.23	94.39 ± 0.25	<0.001
WBCs (/10^{-3} μl)	10.2 ± 2.1	9.5 ± 4.1	11.2 ± 3.4	12.5 ± 4.2	12.8 ± 5.2	13.2 ± 3.4	13.9 ± 6.4	<0.001
Platelets (/μl)	350 ± 72.7	365 ± 55.4	420 ± 58.9	452 ± 99.1	491 ± 47.9	520 ± 81.2	620 ± 79.2	<0.001
LDH	123.2 ± 29.6	135.6 ± 47.2	146.8 ± 45.4	154.3 ± 52.6	167.7 ± 65.4	188.3 ± 74.5	201.9 ± 98.7	<0.001
Reticulocytes (%)	12.1 ± 3.6	12.5 ± 4.2	13.5 ± 2.2	14.9 ± 3.3	16.6 ± 1.2	16.9 ± 4.1	17.1 ± 1.9	<0.001
D-dimer (mg/l)	1.5 ±	1.8 ±	2.2 ±	4.2 ±	7.2 ±	7.8 ±	8.2 ±	<0.001
ΔPWG (Kg)	52.6 ± 0.99	52.99 ± 1	53.1 ± 0.8	53.1 ± 0.7	54.4 ± 0.5	54.9 ± 0.91	55.1 ± 0.2	<0.2
O_2Sa (%)	98 ± 0.99	97 ± 0.91	96 ± 0.99	96 ± 0.4	95 ± 0.99	95 ± 0.1	94 ± 0.6	<0.001
Syst P (mm Hg)	90 ± 1	90 ± 1	90 ± 1	95 ± 1	95 ± 1	95 ± 1	95 ± 2	0.95
Diast P (mm Hg)	70 ± 1	70 ± 1	70 ± 1	75 ± 1	75 ± 1	75 ± 1	75 ± 1	0.92

Abbreviations: Diast P, diastolic blood pressure; Hb, hemoglobin; Ht, hematocrit; LDH, lactate deshydrogenase; MCV, mean corpuscular volume; O_2 Sa, oxygen saturation; Syst P, systolic blood pressure; w, week; WBC, whites blood cells; ΔWG, weight gain during pregnancy.

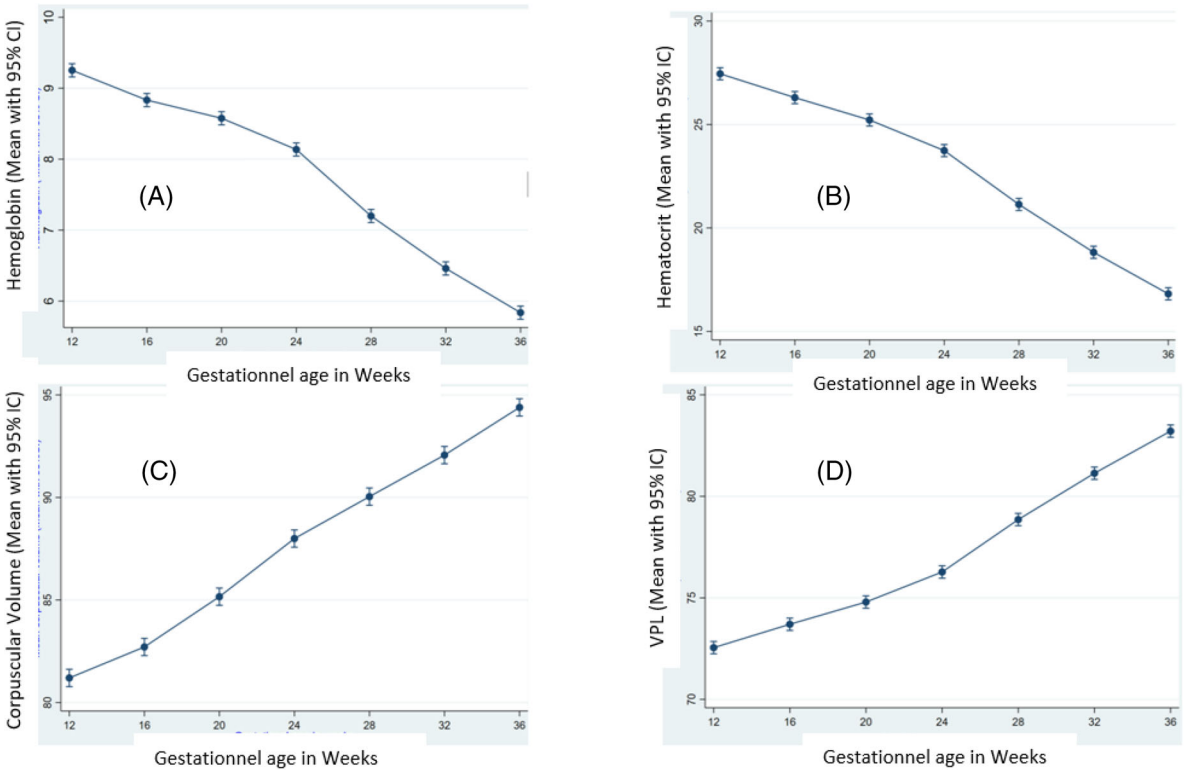

FIGURE 1 (A–D) Evolution curves of hemoglobin, hematocrit, mean corpuscular volume, and plasma volume during pregnancy in our study population.

Other hematological markers like white blood cells, reticulocytes, platelets, and D-dimer have seen a significant increase during pregnancy. On the other hand, the oxygen saturation experienced a significant drop. Blood pressure remained stable.

Figure 1(A–D) above shows how hemoglobin, hematocrit, mean corpuscular volume, and plasma volume changed during pregnancy in our study population. We observe a progressive decrease in hemoglobin and hematocrit from the 12th week to the 36th week; conversely the corpuscular volume and the plasmatic plasma increase expansively during the same period.

Figure 2 above shows the curves of hemodynamic changes during pregnancy in sickle cell pregnant women versus AA homozygotes. We observe that in sickle cell pregnant women (Figure 2A), we observe an opposite evolution of plasma volume and globular volume. Haemodilution anemia is significant from the 24th week of amenorrhea. However, in pregnant AA homozygotes (Figure 2B), we observe a slight increase in plasma volume and a slight decrease in globular volume. Haemodilution anemia is less severe than in AA homozygotes.

Figure 3 above shows the evolution of the erythrocyte concentration of HbS in our study population. It appears that the concentration of HbS increases during pregnancy, thus going from 90% to nearly 96% to the detriment of HbF, which decreases.

Figure 4 above shows the frequency of VOCs during pregnancy. We observe a progressive increase in the frequency of VOCs during pregnancy. The most frequent and severe attacks are observed between the 32nd and 36th week of amenorrhea (Table 2).

TABLE 2 correlation between vaso occlusion crises (VOCs), hematocrit, and plasma volume (VPL).

	Exp(b)	Std.err	95CI	*p*-Value
Week				
Week 12	Ref			
Week 24	3.72	1.30	1.87–7.39	<0.001
Week 32	9.32	5.14	3.21–27.42	<0.001
Week 36	8.63	5.56	2.48–30.44	<0.001
hematocrit	0.89	0.15	0.64–1.23	0.482
Log VPL	0.0000023	0.00002	0.000–71092.82	0.292

We looked at the incidence of VOCs over time as shown in Figure 4 above. Overall, the risk of vaso-occlusive crises increased with gestational age. Compared to the 12th week of pregnancy, the risk was multiplied by 4 at the 24th week. At the 32nd and 36th week of pregnancy, the risk was multiplied by 9 compared to the 12th week. Hematocrit level and PVL did not independently influence the risk of VOCs.

4 | DISCUSSION

The association of SCA and pregnancy is a major challenge in the management of sickle cell pregnant women. Hemodynamic changes during

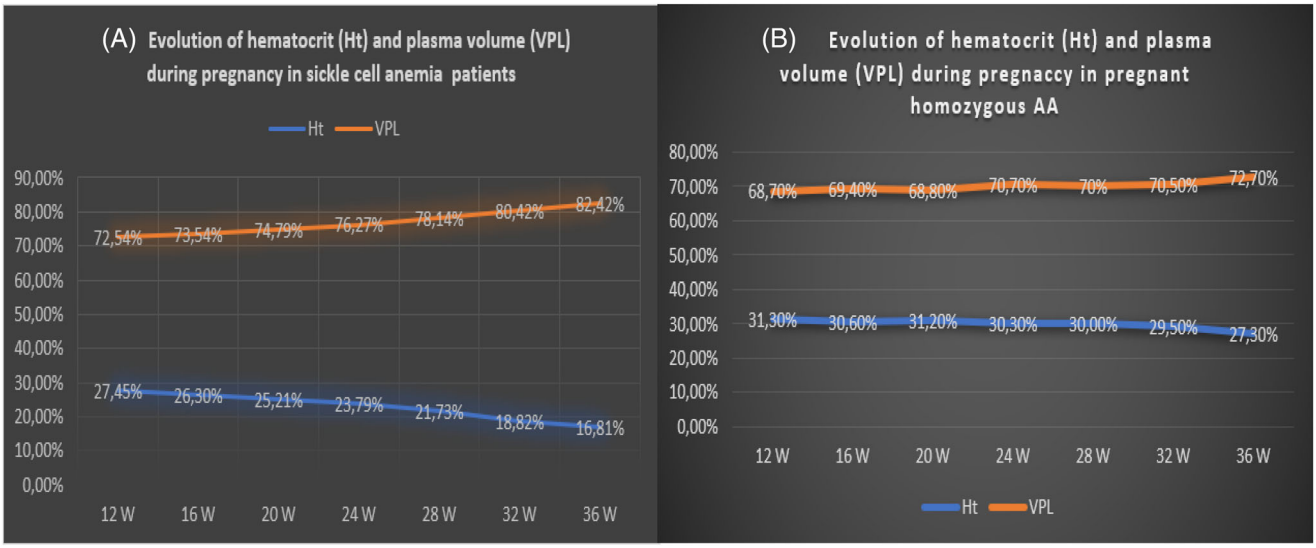

FIGURE 2 Curves of hemodynamic changes between hematocrit and plasma volume during pregnancy in sickle cell patients versus AA homozygotes.

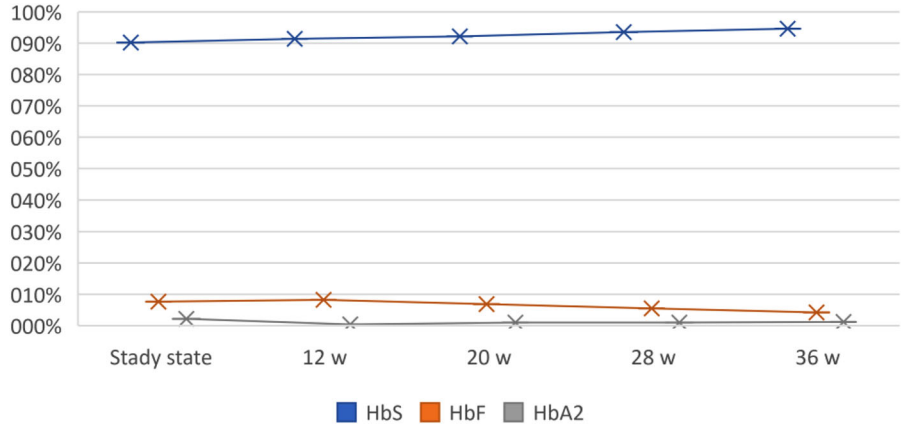

FIGURE 3 Evolution of erythrocyte HbS concentration during pregnancy.

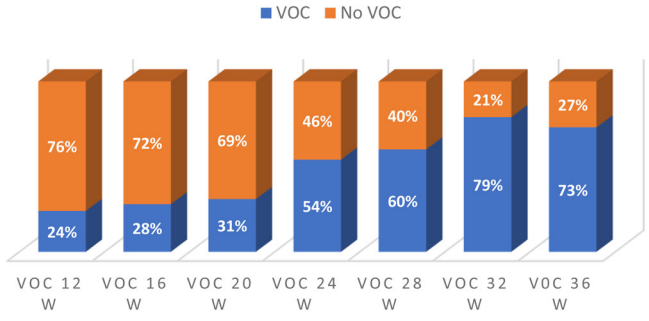

FIGURE 4 frequency of vaso occlusion crises (VOCs) during pregnancy.

pregnancy are implicated in the aggravation of the disease during pregnancy. Our objective was to evaluate the hemodynamic changes during pregnancy in order to establish the correlation between these changes and acute sickle cell manifestations during pregnancy, in particular vaso-occlusive crises and the risk of worsening anemia during pregnancy. Our study showed that hemoglobin and hematocrit decrease gradually from the 12th week to the 36th week. Conversely, the plasma volume and the mean globular volume gradually increase until the 36th week. The progressive decrease in hemoglobin, hematocrit and plasma volume is responsible for the aggravation of anemia by hemodilution during pregnancy. This physiological change [25] worsens the anemia of sickle cell pregnant women from the 24th week. We also observed a gradual decrease in oxygen saturation. The progressive decrease in oxygen saturation coupled with hemodilution anemia are responsible for hypoxia [1, 27, 28]. Indeed, hypoxia is one of the factors responsible for exposing to the risk of vaso occlusion [29, 30]. It promotes deoxygenation and polymerization of hemoglobin S. The polymerization of HbS will promote the sickling of red blood cells. Sickle-formed red blood cells are responsible for acute sickle cell complications including vaso occlusion and hemolysis [31, 32]. In the present study, this risk begins around the 24th week and increases gradually until the

36th week. Several studies have shown that acute sickle cell manifestations, particularly vaso-occlusive crises, increase in frequency and severity with gestational age [33–37]. This aggravation of the anemia exposes to the increased risk of transfusions during pregnancy. This study also showed that during pregnancy, other actors of vasooclusion intervene, these are the white blood cells, the reticulocytes, the platelets which experience a progressive increase with gestational age. White blood cells and reticulocytes promote vasoocclusion through adhesion molecules expressed on the surface of their membranes, while activated platelets secrete thrombospondin. Finally, our study also showed that the risk of thrombosis during pregnancy was also linked to the increase in D-dimer which increases the hypercoagulability of the blood and the increase in the erythrocyte concentration of HbS. In this study, we observed a progressive increase in mean corpuscular volume during pregnancy. This observation proves that folate requirements increase during pregnancy [38]. This increased folate requirement must be compensated by effective folic acid supplementation during pregnancy. The risk of hypoxia secondary to hemodilution and the decrease in oxygen saturation, the increase in vasooclusion actors mentioned above, the increase in hypercoagulability are responsible for the occurrence of acute sickle cell complications during pregnancy: vasooclusion and haemolysis. Our study showed that the frequency of vaso-occlusive crises is directly proportional to hemodilution anemia. Indeed, vaso-occlusive crises increase progressively with gestational age. The most severe VOCs are observed between the 32nd and 36th week. This period of pregnancy is reported as a critical period of pregnancy in sickle cell disease.

5 | CONCLUSION

Our study showed that the hemodynamic changes during pregnancy, essentially the progressive decrease in hematocrit and the increase in plasma volume, are responsible for anemia by hemodilution. These changes are responsible for hypoxia during pregnancy. This hypoxia exposes to the risk of polymerization of hemoglobin S and vaso-occlusive crisis. The frequency of vaso-occlusive crises increases proportionally with the worsening of anemia by hemodilution. Finally, the gradual increase in globular volume during pregnancy proves the increase in folate needs during pregnancy.

AUTHOR CONTRIBUTIONS

Topic design, data collection, manuscript writing, and interpretation of results: MTM. *Data collection*: KNC. *Data collection*: MEKB. *Sample analysis*: KTI. *Data analysis and interpretation of results*: APZ. *Supervising*: LPT.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

FUNDING INFORMATION

This study has not received funding from any institution, government or donor.

ETHICAL STATEMENT

The study was approved by the ethical committee of the school of public health of the University of Kinshasa (approval reference: ESP/CE/079/2016), DRC. Informed consent was obtained from all patients before their inclusion in the study.

PATIENT CONSENT STATEMENT

Informed consent was obtained from all individual participants included in the study. A verbal informed consent was obtained from all patients before their inclusion in the study. The informed consent form written in French and translated into the four national languages (Lingala, Swahili, Tshiluba, and Kikongo) was given and explained to the patient in the language of his choice. An appointment was fixed for the return of the form and obtaining the response of the person concerned. Taken the local cultural context into account, a verbal response was sufficient to be included in the study.

CLINICAL TRIAL REGISTRATION

The authors have confirmed clinical trial registration is not needed for this submission.

DATA AVAILABILITY STATEMENT

The data supporting the conclusions of this study are freely available.

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REFERENCES

1. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. Lancet. 2010;376:2018–31. [PubMed: 21131035]
2. Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, Williams TN, et al. Global distribution of the sickle cell gene and geographical confirmation of the malaria hypothesis. Nat Commun. 2010;1:104. [PubMed: 21045822]
3. Ingram VM. A specific chemical difference between the globins of normal human and sickle-cell anaemia haemoglobin. Nature. 1956;178:792–94. [PubMed: 13369537]
4. Ingram VM. Gene mutations in human haemoglobin: the chemical difference between normal and sickle cell haemoglobin. Nature. 1957;180:326–28. [PubMed: 13464827]
5. Bunn HF. Pathogenesis and treatment of sickle cell disease. N Engl J Med. 1997;337:762–69. [PubMed: 9287233]
6. Barabino GA, Platt MO, Kaul DK. Sickle cell biomechanics. Annu Rev Biomed Eng. 2010;12:345–67. [PubMed: 20455701]
7. Williams NT, Thein LS. Sickle cell anemia and its phenotypes. Annu Rev Genomics Hum Genet. 2018;19:113–47. https://doi.org/10.1146/annurev-genom-083117-021320
8. Sundd P, Gladwin TM, Enrico M, Novelli EM. Pathophysiology of sickle cell disease. Annu Rev Pathol. 2019;14:263–92. https://doi.org/10.1146/annurev-pathmechdis-012418-012838

9. Mikobi TM, Lukusa PT, Muamba JMM, Rhama T. Homozygous deletion alpha-thalassemia and hereditary persistence of fetal hemoglobin, two genetic factors predictive the reduction of morbidity and mortality during pregnancy in sickle cell patients. A report from the democratic republic of congo. Mediterr J Hematol Infect Dis. 2019;11(1):e2019039. https://doi.org/10.4084/MJHID.2019.039
10. Makani J, Cox SE, Soka D, Komba AN, Oruo J, Mwamtemi H, et al. Mortality in sickle cell anemia in Africa: a prospective cohort study in Tanzania. PloS One. 2011;6(2):e14699. Epub 2011/03/02. https://doi.org/10.1371/journal.pone.0014699 PMID: 21358818; PubMed Central PMCID: PMC3040170
11. Piel FB, Hay SI, Gupta S, Weatherall DJ, Williams TN. Global burden of sickle cell anaemia in children under five, 2010–2050: modelling based on demographics, excess mortality, and interventions. PLoS Med. 2013;10(7):e1001484. https://doi.org/10.1371/journal.pmed.1001484 PMID: 23874164; PubMed Central PMCID: PMC3712914
12. Weatherall DJ. The inherited diseases of hemoglobin are an emerging global health burden. Blood. 2010;115(22):4331–36. Epub 2010/03/18. blood-2010-01-251348 [pii] https://doi.org/10.1182/blood-2010-01-251348 PMID: 20233970; PubMed Central PMCID: PMC2881491
13. Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bull World Health Organ. 2008;86(6):480–87. Epub 2008/06/24. S0042-96862008000600017 [pii]. PMID: 18568278; PubMed Central PMCID: PMC2647473
14. Piety NZ, Yang X, Julie Kanter J, Vignes SM, Alex George A, Shevkoplyas SS. Validation of a low-cost paper-based screening test for sickle cell anemia. PLoS One. 2016;11:e0144901. https://doi.org/10.1371/journal.pone.0144901
15. Platt OS, Orkin SH, Dover G, Beardsley GP, Miller B, Nathan DG. Hydroxyurea enhances fetal hemoglobin production in sickle cell anemia. J Clin Investig. 1984;74:652–56. [PubMed: 6205021]
16. Williams TN, Thein SL. Sickle cell anemia and its phenotypes. Annu Rev Genomics Hum Genet. 2018;19:113–47. https://doi.org/10.1146/annurev-genom-083117-021320
17. Russell EW. How I use hydroxyurea to treat young patients with sickle cell anemia. Blood. 2010;115(26):5300–5311. https://doi.org/10.1182/blood-2009-04-146852
18. Mikobi TM, Kamuanya NC, Akilimali PZ, Lukusa PT. Sickle cell disease and pregnancy profile of complicated malaria in 982 pregnancies in Kinshasa. PLoS ONE. 2022;17(10):e0275115. https://doi.org/10.1371/journal.pone.0275115
19. Habibi A, Cannas G, Bartolucci P, Voskaridou E, Joseph L, Bernit E, et al. Outcomes of pregnancy in sickle cell disease patients: results from the prospective ESCORT-HU cohort study. Biomedicines. 2023;11:597. https://doi.org/10.3390/biomedicines11020597
20. Rust OA, Perry KG Jr. Pregnancy complicated by sickle hemoglobinopathy. Clin Obstet Gynecol. 1995;38:472–84.
21. Hassell K. Pregnancy and sickle cell disease. Hematol Oncol Clin N Am. 2005;19:903–16.
22. Elenga N, Adeline A, Balcaen J, Vaz T, Calvez M, Terraz A, et al. Pregnancy in sickle cell disease is a very high-risk situation: an observational study. Obstet Gynecol Int. 2016;2016:9069054.
23. Jain D, Atmapoojya P, Colah R, Lodha P. Sickle cell disease and pregnancy. Mediterr J Hematol Infect Dis. 2019;11:e2019040.
24. Kazma JM, Anker van den J, Allegaert K, Dallmann A, Ahmadzia KH. Anatomical and physiological alterations of pregnancy. J Pharmacokinet Pharmacodyn. 2020;47(4):271–85. https://doi.org/10.1007/s10928-020-09677-1
25. Cathey AL, Watkins DJ, Rosario ZY, Vega CMV, Mukherjee B, O'Neill MS, et al. Gestational hormone concentrations are associated with timing of delivery in a fetal sex-dependent manner. Front Endocrinol. 2021;12:742145. https://doi.org/10.3389/fendo.2021.742145
26. Skrondal A, Rabe-Hesketh S. Generalized latent variable modeling: Multilevel, longitudinal, and structural equation models. London, UK: Chapman and Hall/CR; 2004.
27. Novelli EM, Gladwin MT. Crises in sickle cell disease. Chest. 2016;149:1082–93. [PubMed: 26836899]
28. Gutsaeva DR, Montero-Huerta P, Parkerson JB, Yerigenahally SD, Ikuta T, Head CA. Molecular mechanisms underlying synergistic adhesion of sickle red blood cells by hypoxia and low nitric oxide bioavailability. Blood. 2014;123:1917–26. [PubMed: 24429338]
29. Yale SH, Guthrie T. Approach to the vaso-occlusive crisis in adults with sickle cell disease. Am Fam Physician. 2000;61(5):1349 e1357.
30. Kord Valeshabad A, Wanek J, Gaynes B, Saraf SL, Molokie R, Shahidi M. Conjunctival microvascular hemodynamics following vaso-occlusive crisis in sickle cell disease. Clin Hemorheol Microcirc. 2015;62(4):359–67. https://doi.org/10.3233/CH-151977 PMID: 26444608
31. Rees DC, Williams TN, Gladwin MT. Sickle cell disease. Lancet. 2010;376:2018–31.
32. Darbari DS, Wang Z, Kwak M, Hildesheim M, Nichols J, Allen D, et al. Severe painful vaso-occlusive crises and mortality in a contemporary adult sickle cell anemia cohort study. PLoS ONE. 2013;8:e79923.
33. Poddar D, Maude GH, Plant MJ, Scorer H, Serjeant GR. Pregnancy in Jamaican women with homozygous sickle cell disease. Fetal and maternal outcome. Br J Obstet Gynaecol. 1986;93:727–32. https://doi.org/10.1111/j.1471-0528.1986.tb08059.x10
34. Dare FO, Makinde OO, Faasuba OB. The obstetric performance of sickle cell disease patients and homozygous hemoglobin C disease patients in Ile-Ife, Nigeria. Int J Gynecol Obstet. 1992;37:163–68. https://doi.org/10.1016/0020-7292(92)90376-T11
35. Vijay C, Fernandes N, Kanavi JV, Teena TM. Maternal and neonatal outcomes with sickle cell disease (SCD) in a tertiary health care hospital in a south Indian population. Ann Obstet Gynecol. 2021;4:1032.
36. Rajauria S, Atreja C, Mujalda A, Mujalda J, Yadav S, Kundal RK. The effect of sickle cell hemoglobinopathy on pregnancy, labor, puerperium, and fetal outcome: a retrospective cohort study from a single centre. Cureus. 2023;15(1):e34318. https://doi.org/10.7759/cureus.34318
37. Smith-Whitley K. Complications in pregnant women with sickle cell disease. Hematology Am Soc Hematol Educ Program. 2019;2019(1):359–66. https://doi.org/10.1182/hematology.2019000039 PMID: 31808864; PMCID: PMC6913482
38. Kazma JM, Anker VDJ, Allegaert K, André Dallmann A, Ahmadzia HK. Anatomical and physiological alterations of pregnancy. Pharmacokinet Pharmacodyn. 2020;47(4):271–85. https://doi.org/10.1007/s10928-020-09677-1

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