PREGNANCY COMPLICATIONS OF WOMEN WITH SICKLE CELL ANEMIA AND RESULTS PERINATAL

INTERCORRÊNCIAS GESTACIONAIS DE MULHERES COM ANEMIA FALCIFORME E RESULTADOS PERINATAIS

INTERCORRÊNCIAS GESTACIONAIS DE MULHERES COM ANEMIA FALCIFORME Y RESULTADOS PERINATALES

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ABSTRACT

Objective: to identify the main pregnancy complications in women with sickle cell anemia and describe perinatal results in their babies. Method: descriptive study of a series of cases, retrospective, documentary with data collection from medical records of pregnant women with sickle cell anemia, accompanied by Service High Risk Pregnancy at a University Hospital in the period 2000 to 2009. Data were analyzed using descriptive statistics. The research project was approved by the Ethics Committee in Research, Protocol number 1781/2010. Results: two cases of painful crises were found in the 3rd trimester; one of sinusitis in the 3rd trimester and asymptomatic bacteriuria in the 2nd; obstetric complications consisted of two cases of pre-eclampsia in the 3rd trimester, when one had eclampsia and HELLP syndrome. Conclusion: perinatal morbidity and mortality of pregnant women and babies remained with unpredictable results, however, always with complications results in greater quantities when compared to pregnancies without the disease. Descriptors: Sickle Cell Anemia; pregnant women; newborn.

RESUMO

Objetivo: identificar as principais intercorrências gestacionais de mulheres com anemia falciforme e descrever os resultados perinatais em seus conceptos. Método: estudo descritivo de uma série de casos, retrospectivo, documental, com coleta de dados em prontuários de gestantes com anemia falciforme, acompanhadas pelo Serviço de Gestação de Alto Risco de um Hospital Universitário, no período de 2000 a 2009. Os dados foram analisados através da estatística descritiva. O projeto de pesquisa foi aprovado pelo Comitê de Ética em Pesquisa, Protocolo n°. 1781/2010. Resultados: foram encontrados dois casos de crises de dor no 3º trimestre gestacional; um de sinusite no 3º trimestre e um de bacteriúria assintomática no 2º; das complicações obstétricas constaram dois casos de pré-eclâmpsia no 3º trimestre, quando uma evoluiu para eclâmpsia e Síndrome HELLP. Conclusão: a morbidade e mortalidade perinatal das gestantes e os conceptos permaneceram com resultados imprevisíveis, entretanto, sempre com intercorrências em maior quantidade quando comparadas a gestações sem a doença. Descritores: Anemia Falciforme; Gestantes; Recém-Nascido.

REUMEN

Objetivo: identificar las principales intercorrelaciones gestacionales de mujeres con anemia falciforme y describir los resultados perinatales en sus bebés. Método: estudio descriptivo de una serie de casos, retrospectivo, documental, con recolección de datos en prontuarios de gestantes con anemia falciforme, acompañadas por el Servicio de Gestación de Alto Riesgo de un Hospital Universitario, no periodo de 2000 a 2009. Los datos fueron analizados a través de la estadística descriptiva. El proyecto de investigación fue aprobado por el Comité de Ética en Investigación, Protocolo n°. 1781/2010. Resultados: fueron encontrados dos casos de crisis de dolor en el 3º trimestre gestacional; un de sinusitis en el 3º trimestre y un de bacteriuria asintomática en el 2º; de las complicaciones obstétricas constaron dos casos de pre-eclampsia en el 3º trimestre, cuando una evolucionó para eclampsia y Síndrome HELLP. Conclusión: la morbilidad y mortalidad perinatal de las gestantes y los bebés permanecieron con resultados imprevisibles, entre tanto, siempre con intercorrelaciones en mayor cantidad cuando comparadas a gestaciones sin la enfermedad. Descriptores: Anemia Falciforme; Gestantes; Recién-Nacido.
Sickle cell anemia is the most common genetic disease in Brazil and involves a group of inherited hemoglobinopathies, of high clinical and epidemiologic importance. It is a genetically determined chronic disease with significant rates of morbidity and high prevalence in Brazil. In the United States of America (USA), it affects one in every 600 African Americans, constituting the most common hemoglobinopathy in the country.

The origin of sickle cell disease is related to the erythrocyte membrane reflecting molecular changes within the cell. These mutations induce clinical manifestations like increased expression of adhesion molecules allowing the interaction of erythrocytes, granulocytes and platelets to vascular endothelium with consequent inflammatory phenomena culminating with vaso-occlusion; harden the entire erythrocyte membrane, reducing their survival in circulation and helps to install a hemolytic anemia picture; causes microvascular lesions; production of inflammatory intermediaries such as cytokines and nitric oxide depletion (NO), which contributes to vasoconstriction and activation of inflammation and coagulation.

A pregnant woman with sickle cell disease presents numerous uncertainties and unknowns about this phase of her life, therefore, she is not prepared to meet the clinical aspects of the disease. At this stage, the clinical complications can be serious and may create difficulties especially with regard to the feasibility of pregnancy. In this perspective, pregnancy in women with sickle cell anemia is defined according to the Ministry of Health, as a high-risk pregnancy, needing special care for its potential maternal-fetal gravity.

The diagnosis of sickle cell anemia does not contraindicate pregnancy, but requires a differentiated monitoring during prenatal to postpartum, since pregnant women with the disease tend to gain less weight than women with normal hemoglobin correlated with weight when born and compromise fetal development.

During the pregnancy period in women with sickle cell anemia, it is perceived an increase in maternal-fetal morbidity and mortality, as they have main complications, miscarriage, retarded intrauterine growth, urinary tract infections, congestive heart failure, thromboembolic phenomena, pre-eclampsia, toxemia of pregnancy and bone pain crises. In this context, it is expected that the early identification of gestational events of pregnant patients with sickle cell anemia reduce perinatal complications. Thus, this study aims to identify the main pregnancy complications in women with sickle cell anemia and describe perinatal results in their babies.

This is a descriptive study of several cases, retrospective documentary with data collection from medical records of pregnant women with sickle cell anemia, accompanied by High Risk Pregnancy Service in a University Hospital Maria Aparecida Pedrossian of the Federal University of Mato Grosso South, in the period 2000 to 2009.

The study population were all pregnant women followed by the service in the delimited period, applying the criteria of inclusion and exclusion.

Inclusion criteria were: having confirmed prepregnancy diagnosis of sickle cell anemia by hemoglobin electrophoresis, having at least one prenatal consultation and have evaluation of their newborn (NB). Those who had no prenatal care were excluded.

At the end, four pregnant women with sickle cell anemia patients, total of seven pregnancies were excluded from this study. In data collection, the independent variables were: age, obstetric history, early prenatal care, number of visits, number of transfusions, complications, established treatments, pregnancy, length of stay, type of delivery, perinatal result and days of postpartum hospitalization. The dependent variables were postpartum complications and perinatal results of the babies. Data were analyzed using descriptive statistics.

The research project was approved by the Ethics Committee in Research of the Federal University of Mato Grosso do Sul, under Protocol 1781/2010.

Four patients were found with sickle cell anemia and assisted at the studied period which together had four pregnancies. They were between 17 to 25 years old, average of 20.4 years old. Of them, three were classified as mulatto and white, according to data from their medical records. Only one case had only one pregnancy and the other cases had two each.

When considering all pregnancies, the average time to start prenatal consultations was 12.2 gestational weeks. The four patients were identified as cases 1 to 4. Case 1 showed...
only one pregnancy, no birth and no abortion (G1P0A0), with a number of 18 consultations, with no pregnancy complications and normal delivery with forceps. Case 2 presented two pregnancies, no birth, fetal death and an abortion (G2P0A1), with a total of eight prenatal consultations. Case 3 had two pregnancies, no childbirth and one missed abortion (G2P0A1), with a total of five prenatal consultations. Case 4 had two pregnancies, no childbirth and one missed abortion (G2P0A1), with a total of ten prenatal consultations.

It is worth noting that pregnant women cases 2, 3, 4 who had abortions in the first pregnancy did not attend any follow-up prenatal consultation in those cases.

With regard to blood transfusion, case 1 received three units of packed concentrate red cells (CH); cases 2 and 3 were given seven units each of CH and case 4 received thirteen units of CH. The average number of units transfused red blood cells was approximately 4.3 units per pregnancy.

During the seven pregnancies, among the complications presented, there were two cases of painful crises in the third trimester (cases 3 and 4), one sinusitis in the third trimester (case 2) and one asymptomatic bacteriuria in the second trimester (case 4). Regarding obstetric complications, two pre-

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eclampsia occurred in the third trimester (cases 3 and 4), when one progressed to eclampsia and HELLP syndrome (case 3).

With regard to delivery, there were two vaginal deliveries, two cesarean sections and three curettage due to abortions. The average of gestational age at delivery was 32 weeks and one day and the average in performing curettage was 17 weeks.

In perinatal maternal results, case 3 was admitted to the Intensive Care Unit (ICU) during three days because of a transvaginal bleeding and severe dyspnea, diagnosed as pneumonia and acute pulmonary edema, when 11 more days remained hospitalized. Case 4 presented in the immediate postpartum hematomata subaponeurotic in surgical incision and remained hospitalized four days.

Three pregnant women had abortions in the first pregnancy. One miscarriage (case 2, 15 gestational weeks and three days), two abortions retained of cases 3 and 4 (14 weeks and four days, 20 gestational weeks, respectively). Regarding pregnancies interrupted by abortions, the average was 17 weeks.

The general data of the four cases are described in Table 1:

<table>
<thead>
<tr>
<th>Variables</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
<th>Case 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years old)</td>
<td>17</td>
<td>24</td>
<td>25</td>
<td>17</td>
</tr>
<tr>
<td>Obstetric history</td>
<td>G1</td>
<td>G1</td>
<td>G2P0A1</td>
<td>G1</td>
</tr>
<tr>
<td>Prenatal starting</td>
<td>11 weeks and 4 days</td>
<td>15 weeks and 3 days</td>
<td>6 weeks</td>
<td>14 weeks and 4 days</td>
</tr>
<tr>
<td>Number of prenatal consultations</td>
<td>18</td>
<td>7</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td>Transfusions (units)</td>
<td>3</td>
<td>-</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>Complications</td>
<td>Miscarriage, bleeding</td>
<td>Cough with yellow sputum, fever, Blood Pressure Elevation</td>
<td>Abortion retained</td>
<td>Sickling pre-eclampsia crisis de falcização</td>
</tr>
<tr>
<td>Treatment</td>
<td>Curettage</td>
<td>Amoxacillin</td>
<td>Curettage</td>
<td>Methylodopa, nifedipine dolantina, Plasili, tramadol</td>
</tr>
<tr>
<td>Hospitalized days</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Type of delivery and perinatal result</td>
<td>Vaginal delivery with forceps, Apgar 5/7**</td>
<td>Cesarean delivery, Apgar 3/7</td>
<td>Normal birth, fetal death</td>
<td>Cesarean delivery, Apgar 9/10</td>
</tr>
<tr>
<td>Postpartum complications</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Postpartum hospitalization days</td>
<td>5</td>
<td>4</td>
<td>14</td>
<td>4</td>
</tr>
</tbody>
</table>

*G = Number of pregnancies, P = Number of deliveries, A = Number of abortions. ** Apgar scores achieved in the first and fifth minutes after birth.
With respect to perinatal results of the babies, in NB of the case 1, birth was via vaginal delivery with a gestational age of 40 weeks and 3 days, had Apgar score 5 at 1st minute and 7 at 5th minutes, rated in moderate and mild asphyxia.

The NB of case 2 was born by cesarean section at 36 weeks of gestation, Apgar score of three obtained in the first minutes and seven in the fifth minute and it was classified into mild and severe asphyxia. Case 2 reported an abortion in the first pregnancy.

The stillbirth NB of case 3 gave birth by cesarean section performed at 27 weeks and our days and it is emphasized that in this case, an abortion was retained in the first pregnancy. In NB of case 4, born by cesarean section at 36 weeks and one day, got Apgar score of nine in the first minute and ten at fifth minutes; also highlights an abortion in first pregnancy.

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**DISCUSSION**

Maternal results showed increased perinatal morbidity and mortality in relation to the fetus and newborns in this study, the same as found in another study, when comparing pregnant women with sickle cell disease and pregnant women with sickle cell trait, found in maternal and perinatal results in higher morbidity group with sickle cell disease. However, another study found satisfactory results in the population studied, but all pregnant women in the study were followed from before fertilization by hospital sector and hematology were clinically well when they became pregnant.

Regarding consultations in prenatal, results obtained in this study suggest that the largest number of prenatal reduces complications, findings in accordance with the recommendations to the Ministry of Health (MOH), in which queries in pregnant women with sickle cell anemia is generally held every two weeks until the twenty-eighth, and weekly after this period.

Regular prenatal care with frequent consultations, healthy diet, vitamin supplementation before pregnancy, use of folic acid and preventing dehydration are the main precautions that should be considered in pregnant women with sickle cell anemia. Another highlight is the importance of the tests that accompany fetal development as Doppler and ultrasound to measure blood flow.

In the investigated cases, abortions occurred in the first pregnancy in cases that did not undergo any prenatal care. Furthermore, there was a miscarriage and two abortions retained. A cohort of 94 pregnancies in 52 women with sickle cell disease and 157 pregnancies in 68 controls reported that 80% of abortions occurring before 12 weeks suggest that many of these mothers did not attend any prenatal follow-up.

Abortions are phenomena of unknown etiology and with higher incidence in homozygous patients, when there is a correlation between the microvascular lesions of the placenta due to be sickle.

Another study complements that placental microcirculation is an environment with a high degree of deoxygenation of hemoglobin, causes sickling of red blood cells, polymerization, vaso-occlusion, microinfarcts and injury of the microvasculature. These are factors that reduce blood flow to decrease in the supply of nutrients to the fetus and placental membrane abnormalities such as fibrosis in the villi, microcalcifications with risk of developing miscarriage, intrauterine growth restriction, placenta previa, and premature birth (Cehmob, 2009).

Blood transfusion was also a treatment used in pregnant women in the study, since adequate prenatal care aims to reduce the number of sickled red blood cells to a smaller percentage than 40%, obtained by repeated blood transfusions in anemic patients and exsanguination transfusion.

Blood transfusion is important reducing risks during pregnancy, but should be performed with caution and as an individualized therapy. In addition, blood transfusion may benefit some women by improving oxygen delivery adduced with consequent decrease in the number of sickled cells. Attention should be paid to the importance of screening for antibodies during blood transfusion, as these can affect the fetus and enable the development of other complications.

Regarding complications presented, there was emphasis on pain episodes, when two cases were recorded in the third trimester. The painful crisis is a serious complication of sickle cell anemia and requires interventions such as blood transfusions, hydration, analgesia and oxygen therapy, however, one factor often limiting their treatment is the lack of a standardized approach, harming therefore further clinical picture of the pregnant woman.

Regarding the complications found, a pregnant woman had asymptomatic bacteriuria in the second trimester by *Escherichia coli*. Infections of the urinary tract...
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severe maternal morbidity or near miss due to transcervical bleeding, severe dyspnea and pulmonary edema, with fetal death when born.³

Among the perinatal results of babies in the present study, one of the three live births obtained the Apgar score of nine in the first minutes and ten in the fifth minute, by way of cesarean delivery with a birth weight of 2245 kg and 42 cm. A study conducted in Campinas/SP, with respect to NB, revealed the average birthweight of 2647 ranging between 1950 kg to 3380 kg. Six cases had higher Apgar seven in the first and fifth minutes. One NB had Apgar five in the first minute and nine in the fifth minute. The days of postpartum hospitalization ranged from two to ten days with an average of 4.8 days. One patient required intensive care.¹²

A mortalidade perinatal em gestações de mulheres com anemia falciforme tem diminuído ao longo das últimas décadas devido a vários fatores, principalmente pelo cuidado adequado da gestante, avaliação do bem-estar fetal, acompanhamento do crescimento intrauterino por meio de ultrassonografia, a monitorização contínua durante o trabalho de parto que ajuda a identificar o feto em risco, além do uso racional das transfusões de sangue, fundamentais em todo o processo.⁷

The perinatal mortality in pregnancies of women with sickle cell anemia has declined over the past decades due to several factors, mainly the proper care of the pregnant woman, evaluation of fetal well-being, monitoring intrauterine growth via ultrasound, continuous monitoring during delivery work that helps to identify the fetus at risk, beyond the rational use of blood transfusions, fundamental throughout the process.⁷

CONCLUSION

The results showed that maternal perinatal maternal-fetal morbidity and mortality were high. This perinatal result in women with sickle cell disease and their babies remain with unpredictable results and points to the need to investigate a larger number of cases.

Regarding abortion in primigravidae, we highlight the importance of early initiation of prenatal care. Furthermore, perinatal complications presented may be reduced if pregnant women with sickle cell anemia are properly oriented to seek immediate follow-up with the multidisciplinary team in pregnancies.
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