Pregnancy Outcomes for Women with Homozygous Hemoglobinopathy Diagnosis

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Abstract: Purpose of the study is to highlight pregnancy and delivery in major hemoglobinopathies.

Design setting and participants: Twenty four clinical cases of pregnant women are investigated; 22 suffered from homozygous sickle cell anemia and 2 from major thalassemia. Patient age, parity served as baseline characteristics and delivery way, infant average weight at birth were studied as primary and secondary outcomes. The 24 women, subjects of the study, gave birth within the time frame of 1992-2013.

Results: These past two years, for the first time in "Mbreteresha Geraldine", the Obstetric-Gynecology University Hospital of Tirana, there were two pregnant women with Thalassemia major. Both patients delivered their babies through cesarean section due to fetal suffering. They have had blood transfusion every three weeks during the pregnancy.

The other 22 patients being studied had a frequency of blood transfusion of 4.5 times during pregnancy. Out of 22, 10 women had vaginal delivery, while for the other 22 cesarean section was performed. A total of 15 pregnant women were primiparous (62.5%), 6 (25%) were secondiparous and only 1 terciparous case (4.2%). The other 2 patients with thalassemia major diagnosis were nuliparous (8.3%). The average babies' weight at birth of the women with hemoglobinopathy diagnosis (24) x= 2425.32±59.74 was compared with average babies' weight at birth of healthy mothers (46 women) x=3309.78±78.69. Results were statistically significant (p<0.01)

Conclusion: Pregnant women with homozygous hemoglobinopathy diagnosis followed with multidisciplinary and contemporary therapy are able to give birth, but multiple complications for mother and the baby must be taken into consideration.

Hemoglobin is a complicated protein, composed of a protein group, known as globin and 4 prosthetic or heme groups. It is proven now that hemoglobin A, known as Adult Hemoglobin, is the main constituent of the healthy human blood, that consists of 2 Alpha chains and 2 Beta chains. There are also 2 small fractions of hemoglobin F composed of 2 alpha polypeptide chains and 2 gamma polypeptide chains and A2 hemoglobin made of 2 alpha polypeptide chains and 2 delta polypeptide chains.

Hemoglobin A, being the most common human hemoglobin, is present at a level of 96-98 % in the blood of a healthy adult, hemoglobin A2 is approximately 1-3% present and hemoglobin F 0-1%. The content of hemoglobin fractions may change depending on different Hemoglobin pathologies. The main function of the hemoglobin is the Oxygen transport from the lungs to all the body tissues and to return the carbonic dioxide from the tissues to lungs, this is the reason that it is often referred as molecular lungs.
Hemoglobinopathies diverge in two big groups:

1. Thalassemia syndromes, where amino acids chains are in correct order, but deficient. The main types are thalassemina alpha and Beta, the latter being the most common and associated with a deficiency of beta globin chains.

2. The structural hemoglobin variant (abnormal hemoglobin), where there is a sufficient production of amino acid chains, but abnormality of individual hemoglobin chains arises due to mutations of the corresponding genes. There are about 300 types of structural hemoglobin variants, the most important being sickle cell anemia, where Valine at sixth position on the amino acid Beta chain is substituted with Glutamic acid(5,14).

In case of hemoglobinopathies, erythrocytes have a lower capacity to bind Oxygen, their life cycle is decreased due to hemolysis or sequestration from blood stream as in case of homozygous drepanocytosis.(5)

Prognosis becomes even worse in case of pregnancies, where major complications may arise for the mother and her fetus as well(3,9, 13). Pregnant women diagnosed with hemoglobinopathy have an increased need for hemotransfusion along with an increased risk for preeclampsia distacco placente(5,13,14). On the other hand there is also an increased risk for premature birth, fetal hypotrophy and feto morto in utero due to hypoxia(1,5,13).

Methods

Study subjects were pregnant women with hemoglobinopathy that gave birth within the time frame of 1992-2015 in Maternity of Lushnja and "Mbreteresha Geraldine" maternity. Out of 24 women with homozygous hemoglobinopathy, 22 had diagnosis of homozygous sickle cell anemia and 2 had thlassemia major diagnosis. Age of the patients, infant weight at birth, delivery way and the frequency of hemotransfusion were also taken into consideration.

47 pregnant women with normal hemoglobin electrophoresis served as a control group.

Results and Discussion

24 pregnant women with hemoglobinopathy were divided according to the parities as expressed below:
Sickle cell anemia

- Primipare --- 15 (62.5%)
- Secondipare ---6 (25%)
- Tercipare---- 1 (4.2%)

Major Thalassemia

- Primiparous ----2 (8.3%)
Delivery cases according to the following years;

| Year | HbSS | Major Thalassemia |
|------|------|-------------------|
| 1992 | 2    |                   |
| 1993 | 1    |                   |
| 1994 | 1    |                   |
| 1995 | 1    |                   |
| 1996 | 1    |                   |
| 1997 | 1    |                   |
| 1998 | 2    |                   |
| 1999 | 2    |                   |
| 2000 | 4    |                   |
| 2001 | 1    |                   |
| 2002 | 1    |                   |
| 2003 | 1    |                   |
| 2004 | 1    |                   |
| 2007 | 2    |                   |
| 2010 | 1    |                   |
| 2012 |      | 1                 |
| 2013 |      | 1                 |

Graph:

Delivery cases according to the following years

10 women diagnosed with sickle cell disease SS gave birth naturally and for other 12 cesarean section was performed.
Indications reasoning C-section births are listed below:

- Fetal suffering and preeclampsia - 4 (30.9%)
- Status post c section - 2 (15.4%)
- Distaco Placenta - 1 (7.7%)

As seen above, fetal suffering was the main indication for cesarean section; many authors have concluded that such indication, in these type of cases, is common due to fetal hypoxia (5,13).

The number of premature, hypotrophic births as well as preeclampsia was higher in the group of women with hemoglobinopathy, as noticed in the table below:

**Frequency of premature deliveries and preeclampsia**

| Pregnant women          | Number of deliveries | Hypotrophic deliveries | Premature deliveries | Preeclampsia |
|-------------------------|----------------------|------------------------|----------------------|--------------|
| Homozygous hemoglobinopathies | 24                  | 7 (29%)                | 12 (50%)             | 9 (37%)      |
| Control group           | 47                   | 3 (6.33%)              | 5 (10.63%)           | 1 (2.12%)    |
| P values                | <0.001               | <0.001                 | <0.0001              |

As noticed in the table above, the results are statistically significant: The frequency of premature births, hypotrophy and preeclampsia is higher in the group of pregnant women with hemoglobinopathy.

Babies born from mothers with homozygous sickle cell SS had an average weight at birth of $2425\pm 69$gr compared with babies born from mothers with normal electrophoresis with an average weight at birth of $3309\pm 59.74$gr. The results are statistically significant ($P<0.01$).

The average weight of babies born from mothers with homozygous drepanocytosis and thalassemia major is smaller than the average weight of babies born from mothers with normal electrophoresis.

Thalassemia major patients have received hemotransfusion every three weeks during the pregnancy and every 2 weeks during the last month. It is noticeable that both cases have had a full term pregnancy (39 weeks) and with infant weight at birth 3000g and 3100g respectively.

Regarding women with homozygous drepanocytosis the frequency of hemotransfusion was unpredictable. There were cases that required few hemotransfusion and other cases that received hemotransfusion more often, due to hemolytic and vaso-occlusive crisis. For those that received transfusion monthly starting fourth month of the pregnancy, at the eighth and ninth month of the pregnancy there was an increased need for hemotransfusion every two weeks.

**Conclusions:** Due to contemporary multidisciplinary treatment pregnant women with homozygous hemoglobinopathy can successfully give birth, but there is still a high risk of complications for both, mother and the fetus.
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