Factors Affecting Maternal Mortality in Pregnant Women With Sickle Cell Disease in Ahvaz, Iran: A 10-Year Epidemiological Study

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Abstract

Background: In sickle cell disease, red blood cells are sickle shaped and consequently lose their ability to carry oxygen, which may cause vessel blockage. Pregnancy in the setting of classic sickle cell disease could be extremely dangerous for both mother and fetus.

Objectives: The aim of this study was to determine the effective factors related to the maternal mortality among pregnant women with sickle cell disease.

Materials and Methods: In this descriptive study conducted with data from 41 hospital records of women with sickle cell disease from 2001 to 2011, various data such as demographic, midwifery, and laboratory test information were recorded in a questionnaire. The relationship between this information and sickle cell disease was assessed. Descriptive statistics, analysis of variance, Fisher exact test, and chi-square test were used in the data analyses.

Results: The mean maternal age was 27.60 ± 6.37 years. The hemoglobin level at hospital admission was 8.9 ± 1.61 g/dL for the survivors and 7.73 ± 1.19 g/dL for the deceased patients ($P < 0.05$). All the patients with the sickle cell trait, 73% of the patients with sickle cell disease, and 50% of the patients with sickle cell-thalassemia disease survived ($P < 0.05$). The gestational age of the deceased patients was lower than that of the survivors (34.12 vs. 35.81 weeks, $P = 0.08$).

Conclusions: Ultimately, we can conclude that the hemoglobin level at the time of admission and before delivery, the type of disease, gestational age, and transfusion could be effective factors of patient mortality.

Keywords: Anemia, Sickle Cell Trait, Mortality, Risk Factors, Pregnancy

1. Background

Sickle cell disease (SCD) is the most common inherited hemoglobinopathy and is a group of autosomal recessive red cell disorders resulting from hemoglobin S (HbS) (1). The most common type of sickle cell genotype is the sickle cell trait, which is a carrier of both defective HbS and some quantities of normal HbA genes. Patients with sickle cell-hemoglobin C disease inherit both HbS and HbC genes simultaneously. Sickle cell-hemoglobin E disease is similar to sickle cell C disease, except that one element of the hemoglobin molecule is replaced. Hemoglobin S-beta thalassemia and sickle cell gene inheritance occurs simultaneously (2, 3). The disease manifestation in patients with HbSS is mostly more severe than in patients with the HbSC type (4).

Based on recent research studies, 3.2% of Iranians (5), 4.2% of Saudi Arabians (6), 1 - 40% of Indian tribal populations (7), and 10.1% of the Sub-Saharan African (8) population have SCD. Anemia is the most common sign of SCD. Red blood cells are sickle shaped, consequently losing their ability to carry oxygen. After releasing their oxygen in the tissues, they become insoluble and result in red blood cells with abnormal shape. Sickling causes the red blood cells to lose their elasticity and these cells can cause blood vessel blockage, pain, and stroke (9). In addition, the reduction in red blood cells leads to anemia. Severe anemia makes the patient tired and pale. Meanwhile, the ability of red blood cells to carry oxygen to the tissues would be deteriorated. Sickle or pain crisis occurs when the sickle cells block blood vessels, interrupting blood flow accordingly.

Some complications such as high blood pressure and premature labor are exacerbated in the context of SCD in pregnancy, causing an exacerbation of the symptoms of the disease. In addition, vitamin D deficiency is prevalent in pregnant women with SCD (10).

Pregnancy in classic SCD is a high-risk situation (11) and could be extremely dangerous and accompanied with many severe complications for mothers and the newborns (12-16), particularly in the case of hemoglobin

SS and SC, both of which confer the same risk of death or severe complications for mothers (17). According to general opinion, the incidence of pregnancy complications in SCD is higher than that in normal pregnancy (18). However, a cohort study with a large sample size showed that only one-third of these pregnant women had miscarriage and 4.8% died (among 104 pregnancies). Moreover, women with hemoglobin SS and hemoglobin S/β0 had a higher percentage of preterm deliveries, more frequent episodes of vaso-occlusive crises, and more transfusions in the antepartum and postpartum than women who had hemoglobin SC and hemoglobin S/β+ thalassemia (17).

The adjusted odds of fetal death in deliveries in African women with SCD are 2.2-fold greater than that in women without SCD (19). In addition, the maternal mortality risk of mothers with SCD is 5.98 times higher than that of healthy women (20).

Cesarean delivery is more likely in SCD, and women who undergo cesarean delivery are likely to experience pregnancy-related complications such as gestational hypertension/preeclampsia, eclampsia, placenta abruption, antepartum bleeding, preterm labor, fetal growth restriction, cardiomyopathy, or pulmonary hypertension at the time of delivery (2).

Self-management interventions are effective in promoting self-efficacy in patients with SCD. Thus, the use of self-management programs is advisable to change behaviors and promote self-efficacy in such patients. Self-efficacy and enhanced health status can be promoted in patients with SCD through self-management programs (21).

Even with new treatments, SCD can cause serious or life-threatening complications. Severe infections such as acute chest syndrome usually begin a few days after painful sickle crisis and confer serious consequences for mother. This condition is common in pregnancy and the postpartum period (7).

Although the advances in medical care have improved the obstetric outcomes in pregnant women with SCD, morbidity and mortality are still higher than in normal pregnancy. The geographic distribution of sickle cell anemia in Iran has a scattered pattern, and numerous reports indicate the probable high prevalence of the disease in the southern area of Iran. The reduction in maternal mortality rate is an important index among the national health indexes. In addition, information about the outcome of pregnancy and effective factors of maternal mortality is lacking among women with SCD.

2. Objectives

Therefore, the primary aim of present study was to assess the risk factors of maternal mortality in pregnant women with SCD in educational hospitals of Ahvaz between 2001 and 2011.

3. Materials and Methods

This was a descriptive study performed by using data from 41 hospital records of women with SCD who were admitted to Imam Khomeini and Razi hospitals of Ahvaz between 2001 and 2011. These two hospitals are educational hospitals affiliated to Ahvaz Jundishapur University of Medical Sciences. The study design was approved by Ahvaz Jundishapur University of Medical Sciences. All available medical data were searched. The inclusion criteria were pregnant women at more than 24 weeks of gestation and women with SCD confirmed by using laboratory tests.

The management protocols for SCD in both hospitals were similar. Gestational age was determined based on the sonographic results during the first trimester of pregnancy. All demographic and laboratory data, including complete blood count, urine analysis results, urine culture results, and liver enzyme levels, were obtained from medical records and transferred to the questionnaire, which was prepared for data collection. The validity of this questionnaire was assessed by using content validity, and the content of the questionnaire was examined by five experts from medical schools. The anonymity of the patients in all the study procedures was preserved.

3.1. Statistical Analyses

The obtained data were analyzed by using SPSS version 20. Descriptive statistics, analysis of variance, Fisher exact test, and chi-square test were applied for statistical purposes. A P value of < 0.05 was considered significant.

4. Results

The mean age of the women was 27.60 ± 6.37 years. Most (17, 41.5%) of them did not have any live birth. Most women (15, 36.6%) had a history of one pregnancy, and the mean number of pregnancies was 2.31 ± 1.45. Nineteen patients (48.7%) had blood transfusion, 13 (32.5%) had normal vaginal delivery, and 28 (67.5%) had cesarean delivery. Of the 41 patients in this study, 33 (80.5%) survived and 8 (19.5%) died (Table 1).

The survivors were older (28 vs. 25.2 years) and had more pregnancies (2.39 vs. 2) than those who died. However, these differences were not significant. The survivors also had higher gestational age and higher hemoglobin level at the time of admission (8.9 vs. 7.7, P = 0.03) and before delivery (9.4 vs. 8.8 g, P = 0.04; Table 2).

Eleven patients survived (84.6%) and 2 patients (15.4%) died after normal vaginal delivery, whereas 21 (75%) patients survived and 7 (25%) died after cesarean delivery (P = 0.47 by Fisher test). Fourteen patients (73.7%) survived after transfusion, but 5 (26.3%) of them died. The number of patients who survived without transfusion was 18 (90%), but 2 (10%) of them died (P > 0.05).

Nine patients (100%) with sickle cell trait and 22 patients (73%) with SCD survived, whereas 8 patients (27%) died. One patient with thalassemia survived, while the other one died (P = 0.35 by Pearson test).

Table 1. Personal, Midwifery, and Laboratory Characteristics of the Participants[a]

Variables	Total Number of Patients (n = 41)
Gestational age, wk	35.48 ± 3
Type of disease	
Sickle cell trait	9 (22.5)
Sickle cell anemia	29 (72.5)
Thalassemia	2 (5)
Number of live births	
Zero	17 (41.46)
One	7 (17.07)
≥ 2	17 (41.46)
History of abortion	
Yes	38 (92.68)
No	3 (7.31)

[a]Data are presented as mean ± SD or No. (%).

Table 2. Comparison of Some Personal, Midwifery, and Laboratory Variables in the Survivors and Deceased Patients[a]

Variable	Survived Patients (n = 3)	Dead Patients (n = 8)	P Value
Age, y	28.18 ± 6.91	25.25 ± 2.37	0.24
Number of pregnancies	2.39 ± 1.57	2 ± 0.75	0.50
Number of abortion	0.66 ± 0.36	0.53 ± 0.50	0.60
Gestational age	35.81 ± 3.27	34.12 ± 1.7	0.08
Hb at the admission, g	8.9 ± 1.61	7.73 ± 1.19	0.03
Hb before delivery, g	9.45 ± 1.7	8.83 ± 0.99	0.04

[a]Data are presented as mean ± SD.

5. Discussion

The aim of this study was to determine the risk factors of maternal mortality from SCD. The results of this study showed that when women had higher hemoglobin levels at the time of admission and before labor, they had less mortality.

The maternal mortality was 19.5% in this study. It was reported to be 4.8% in Brazil and 30% in Bahrain in the period 1977 - 2012 (17, 22), 1.6 per 1000 deliveries in women with SCD in the study of Alayed et al. (23) and 41% between 1998 and 2007 in Jamaica (6), indicating a higher maternal mortality in our research than in those in other developed countries.

Based on a cohort study conducted by Serjeant et al. who evaluated the outcome of 157 gestations in 68 patients with homozygous sickle cell anemia (SS), the mortality rate was 2.2%. Moreover, the increased maternal mortality in women with homozygous sickle cell anemia was confirmed in this survey (13).

In a study by Asnani et al. (2011), demographic, service delivery, and cause-specific mortality rates were compared between women with (n = 42) and without SCD (n = 376), and between SCD women who died in 1998 - 2002 and 2003 - 2007. Results showed that those with SCD had significantly fewer viable pregnancies. Cause-specific

mortality was higher for cardiovascular complications, gestational hypertension, and hemorrhage. The main immediate cause of death was respiratory failure (24).

The type of the disease differs according to the area, management approaches, and type of health facilities in Iran. On the other hand, cultural differences and the level of knowledge of women with SCD could contribute to the decrease in maternal mortality.

In a retrospective study that included all reported maternal deaths in Bahrain during the period 1977 - 2012, a significant decline in maternal deaths was evident. The main direct causes of maternal mortality among SCD women were pulmonary embolism (35%), sepsis (24%), postpartum hemorrhage (16%), and acute chest syndrome (13.5%; 35% were preventable) (22).

A systematic review and meta-analysis of observational studies by Oteng-Ntim et al. (4) (21 eligible studies until 2014) indicated that, compared with women without SCD, pregnant women with the HbSS genotype had increased risk of maternal mortality (relative risk [RR], 5.98; 95% confidence interval [CI], 1.94 - 18.44), preterm delivery (RR, 2.21; 95% CI, 1.47 - 3.31), preeclampsia (RR, 2.43; 95% CI,

1.75 - 3.39), stillbirth (RR, 3.94; 965% CI, 2.60 - 5.96), and infants who were small for their gestational age (RR, 3.72; 95% CI, 2.32 - 5.98). In this study, genotype (HbSS vs. HbSC) and low gross national income were associated with increased relative risks (4). In our study, the abortion rate was 31.6%, which had been reported to be 12.2% in Bahrain (22) and 2.1% in another survey in Africa (19), indicating a variation between various studies in different countries. The number of abortions in Iran is higher than that in other countries. This may be due to the insufficient follow-up during pregnancy among sickle cell patients.

In the present study, a significant relationship was observed between the type of disease and maternal mortality, so that in the SS homozygous type, the number of deaths was higher than that in other genotypes. Other studies showed similar results. Serjeant et al. (13) showed that the number of abortions in the SC type of the disease was less than that in the SS type. Cardoso et al. (17) reported that mothers with SS-type SCD was significantly at higher risk of painful crises during pregnancy, transfusion during pregnancy, and hospital admission (17). No significant difference was found between the types of the disease in terms of side effects and maternal mortality, based on the study by Ngo et al. (25). This might be due to variations in the type of the disease and the level of health care in the other countries in comparison with Iran.

Despite the fact that the mean gestational age showed no significant statistical difference between the survivors and the deceased patients, considering the value of P = 0.08, gestational age seems to be an effective factor in the occurrence of the side effects of pregnancy. Lack of or low significant statistics might be attributed to the sample size in this study. Gestational age was obviously lower in the patients with sickle cell anemia than in the healthy individuals, based on the research performed by Serjeant et al. (13). Gestational age had been reported to be 31.2, 32.1, and 32.4 weeks in different studies (22, 24).

No significant relationship was found between transfusion and maternal mortality in our study. However, the p value of 0.09 was close to a significant level. Transfusion had been reported as an effective factor of decreasing the incidence of side effects; however, transfusion was only recommended in case of emergency, based on the research of Ngo et al. (25).

We recruited all the patients with SCD who referred to the two educational hospitals during the 10-year period. Some relationships need larger sample sizes to be evident. Further studies that aim to better understand the level of knowledge of patients, the satisfaction of health services, the problems, and complications related to the disease, and finally, to codify preventive and comprehensive protocols based on the present study in the national level are recommended.

Ultimately, it can be concluded that the hemoglobin level at the time of admission and before parturition, type of disease, and probably, gestational age, as well as transfusion, could be effective factors in patient mortality.

Acknowledgments

Footnotes

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