Bahrain Medical Bulletin, Vol. 36, No. 4, December 2014

Maternal Mortality in Women with Sickle Cell Disease

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Background: Sickle cell disease (SCD) is a major health problem encountered in the Kingdom of Bahrain; it is associated with high maternal morbidity and mortality.

Objective: To determine the immediate cause/s of maternal mortality.

Design: A Retrospective Study.

Setting: Health Information Directory, Ministry of Health.

Method: All reported maternal deaths in Bahrain from 1977 to 2012 were included in the study. Personal characteristics, pregnancy outcome and the main cause of death were compared between women with and without SCD.

Result: Hundred twenty-two maternal deaths were reported in Bahrain between 1977 to 2012; 37 (30%) had SCD. The study showed a significant decline in overall Maternal Mortality Rate (MMR). The OR of maternal mortality by SCD was 117. The most important causes of maternal mortality in SCD were embolism 13 (35%), sepsis 9 (24%), hemorrhage 6 (16%) and acute chest syndrome 5 (13.5%). In the non-SCD group, the leading cause of death was embolism 18 (21%), hypertensive disorders 18 (21%), followed by infection 14 (16.5%), hemorrhage 14 (16.5%) and heart disease 10 (11.8%).

Conclusion: Sickle cell disease is the leading cause of maternal death in Bahrain. A significant decline in MMR in Bahrain over the years has been revealed, but unfortunately there was no substantial reduction amongst SCD mothers.

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Sickle cell disease is a major health problem encountered in Bahrain. Malaria was endemic in Bahrain until 1970; therefore, malaria-associated genetic defects of red cells, such as SCD, thalassemia and G6PD were found to be common[1]. In a study of the hospital population covering 56,198 Bahrainis, 2% of newborns have SCD and 18% have sickle-cell trait, while 24% are carriers of the thalassemia gene[2]. Recent studies showed that SCD incidence had declined to 0.4% after the implementation of national prevention program[3].

The incidence of SCD amongst pregnant women in Bahrain was reported to be 0.7%-0.8% while the reported incidence of SCD in other studies varied from 0.1-1.3%[4-7]. SCD is associated with

high maternal morbidity and mortality[4-8]. The first major review of SCD in pregnancy was published in 1941, which reported 50% fetal wastage and 33% maternal death[9,10]. The maternal mortality in pregnant women with SCD had declined to 0.4%-5% after improving the medical care[6,7,11,12]. SCD is the leading cause of maternal death in Bahrain, responsible for one-quarter to one-third of all maternal deaths[13,14].

SCD is not only associated with high maternal mortality but also with high maternal morbidity, such as thrombo-embolism, stroke, pulmonary hypertension, infection and acute chest syndrome. This disease is also associated with high perinatal morbidity and mortality[4,6,15].

The aim of this study is to determine the immediate cause/s of maternal mortality.

METHOD

This study included all reported maternal deaths, which occurred during pregnancy, delivery and up to 42 days postpartum in all the hospitals in Bahrain from 1 January 1977 to 31 December 2012.

All maternal deaths which were reported to the Health Information Directory at the Ministry of Health were recorded. The following data were recorded: date of admission, expiry date, nationality, gravidity, parity, number of living children, gestational age, pregnancy outcome, mode of delivery and direct cause of death.

To compare the two study groups, Chi square test or Fischer's exact test was used. Data was analyzed using SPSS version 18.

RESULT

The number of sickle cell diseased women who deliver in the Ministry of Health hospitals ranged from 84 to 112 per annum. The incidence of SCD in parturient mothers between 2007 to 2012 was found to be 0.55% (582/104677). The annual maternal deaths amongst sickle cell disease women in the Ministry of Health Hospitals ranged from 0-4 in 2007- 2012, the incidence is 1.5%, see table 1.

Table 1: Risk of Maternal Death Associated with SCD (2007-2012)

	2007	2008	2009	2010	2011	2012	Total
Deliveries with SCD	84	97	85	112	105	99	582
Maternal death associated with SCD	2	1	0	2	0	4	9
Risk of death associated with SCD	1:42	1:97	0	1:56	0	1:25	1: 65

There were 122 reported maternal deaths in Bahrain from 1977 to 2012. Thirty-seven women with SCD had died during the study period, which account for 30% of maternal deaths. There was a significant decline in maternal mortality in Bahrain as it had dropped from 34/100,000 in 1977 to 1986 to 19/100,000 in 2005 to 2012 (P value 0.0026, OR 2.46, 95% CI 1.3-4.4), see table 2. The OR of maternal mortality due to SCD from 2007 to 2012 was found to be significantly high (OR: 117; 95% CI [50.5 to 271.9] P<0.0001).

Table 2: Maternal Mortality in Bahrain (1977- 2012)

	1977- 1986	1987- 2004	2005- 2012	1977-2012
Maternal deaths	37	60	25	122
Total births	109,221	243,232	135,037	48,7490
MMR/100,000 Total births	33.88	24.66	19	25

The personal characteristics and pregnancy outcome of maternal deaths were compared between mothers with SCD and without SCD, see table 3. SCD group were younger, of low parity and less gestational age but the difference was not statistically significant. All deceased SCD group were Bahraini while 24 (28.2%) of non SCD were non-Bahrain and the difference was very significant. Thirty-four (92%) of the SCD deaths were at Salmaniya Medical Complex (SMC) compared to 67 (78.8%) in the other group. Though there was no significant difference in the pregnancy outcome of both groups, the fetal loss was high as it was 62% amongst SCD group and 48% among non SCD. Most maternal deaths occurred in the postnatal period, with no significant difference between the two groups.

Table 3: Personal Characteristics and Pregnancy Outcome of Maternal Deaths in Bahrain: 1977- 2012 According to Sickle Cell Disease Status

Variable	SCD maternal deaths (n=37)	Other maternal deaths (n=85)	P-value
Age in years (mean ±SD)	29.25±6.2	32.4±6.4	0.01
Gravidity, (mean ±SD)	3.9 ±2.7	4.7±3.0	0.5
Parity (mean ±SD)	2.3±2.2	3.7±3.1	0.02
Living children (mean ±SD)	2.0±2.2	3.3±2.8	0.02
Nationality: Bahraini	37 (100%)	61 (71.8%)	0.0001
Nationality: Non Bahraini	0 (0%)	24 (28.2%)	
Gestational age (mean ±SD)	31.6±9.15	31.8±6.8	**0.87**
Place of death: SMC	34 (91.9%)	67 (78.8%)	0.011
Place of death: Other hospitals	2 (5.4%)	14 (16.5%)	
Place of death: Home	1 (2.7%)	4 (4.7%)	
Early fetal loss	3 (8.1%)	9 (10.6%)	
Stillbirth	20 (54.1%)	32 (37.6%)	
Live birth	14 (37.8%)	39 [a] (45.9%)	0.4
Time of death: Antenatal	14 (37.8%)	19 (22.4%)	
Time of death: Postnatal	22 (59.5%)	59 (69.4%)	
Time of death Post abortion	1 (2.7%)	6 [b] (7.1%)	0.19
Vaginal delivery	15 (40.5%)	31 (36.5%)	
Cesarean section	6 (16.2%)	26 (30.6%)	
Undelivered	16 (43.2%)	28 (32.9%)	0.23

[a]5 missing data; [b]1 missing data, SMC

Table 4 shows the difference in personal characteristics over two 18-year periods: 1977 to 1994 and 1995 to 2012. Sixty-one deaths in each period was found and the MMR dropped from 28 in the first period to 23 per 100,000 total births in the second period but the difference was not significant (OR=1.25; 95 % CI 0.88 to 1.78; P=0.22). During the first period, 18 mothers with SCD died while 19 patients died in the second period, the difference was not significant. The

first group had a significantly higher parity and number of living children. However, there was no significant difference between both groups regarding the age, gravidity, nationality and gestational age. During the second period, there were more deaths in other hospitals compared to the first period. There was no significant difference in pregnancy outcome in the two groups. Most maternal deaths occurred in the postnatal period but there was no significant difference between the two periods. No significant difference in the mode of delivery between the two periods was found.

Table 4: Personal Characteristics and Pregnancy Outcome of Maternal Deaths in Bahrain: 1977-1994 and 1995-2012 (n=61)

Variable	Maternal deaths (1977-1994)	Maternal deaths (1995- 2012)	P-value
SCD	18 (29.5%)	19 (31.1%)	
Age in years (mean ±SD)	30.6±6.7	32.2 ±6.3	0.2
Gravidity(mean ±SD)	4.8±2.9	4.16±2.9	0.26
Parity (mean ±SD)	3.9±3.2	2.7±2.5	0.02
No. living children	3.5±2.8	2.3±2.3	0.027
Nationality : Bahraini	48 (78.7%)	50 (82%)	1.0
Nationality :Non Bahraini	13 (21.3%)	11 (18%)	
Gestational age (mean ±SD)	32.1±8.2	31.2±8.8	**0.6**
Place of death : SMC	56 (91.8%)	44 (72.1%)	0.015
Place of death: Other hospitals	3 (4.9%)	13 (21.3%)	
Place of death: Home	2 (3.3%)	3 (4.9%)	
Early fetal loss	5 (8.2%)	7 (11.5%)	
Stillbirth	26 (42.6%)	26 (42.6%)	
Live birth	27 **a** (44.3%)	25 **b** (41%)	0.8
Time of death : Antenatal	16 (26.2%)	17 (27.9%)	
Time of death : Postnatal	41 (67.2%)	40 (65.6%)	
Time of death :Post abortion	4 (6.5%)	2 **c** (3.3%)	0.8
Vaginal delivery	20 (32.8%)	17 (27.9%)	
Cesarean section	11 (18%)	20 (32.8%)	
Undelivered	20 (32.8%)	24 (39.3%)	0.3

a (missing data3), b (missing 3), c (missing 1)

Table 5 shows the immediate causes of death amongst SCD compared to non SCD. Embolism is the leading cause of death in SCD women as well as non SCD. Embolism includes both pulmonary and amniotic fluid embolism. Hypertensive disorders were also the leading cause of death amongst non SCD group but none of SCD patients died as a result of hypertension. The most important direct causes of maternal mortality amongst SCD were pulmonary embolism 13 (35%), sepsis 9 (24%), postpartum hemorrhage 6 (16%), and acute chest syndrome 5 (13.5%). However, the leading causes of death in non SCD group were embolism 18 (21%), hypertensive disorders 18 (21%), followed by infection 14 (16.5%), hemorrhage 14 (16.5%) and heart disease 10 (11.8%).

Table 5: Immediate Cause of Death among SCD Women as Compared with Non-SCD (1977-2012)

Immediate Cause of Death	SCD Maternal Deaths (N=37)	Other Maternal Deaths (N= 85)	Odds Ratio (95% CI)	P-value

Embolism	13 (35%)	18 (21%)	1.86 (0.8 - 4.3)	0.15
Hypertension	0	18 (21%)	0.05 (.003- 0.83)	0.0368
Hemorrhage	6 (16%)	14 (16.5%)	0.98 (0.34-2.79)	0.97
Heart disease	1 (3%)	10 (12%)	0.2 (0.025-1.69)	0.14
Infection	9 (24%)	14 (16.5%)	1.6(0.63-4.19)	0.3
Acute chest syndrome	5 (14 %)	0	28.9 (1.6-538.2)	0.024

N.B: Other causes in SCD group: 3 (8%) and non SCD group: 11(13%)

Forty-three (35%) maternal deaths were avoidable; 20 (46.5%) were due to negligence by the patient and 23 (53.5%) were due to substandard care and lack of ICU bed. On the other hand, 18 (48.6%) maternal deaths were avoidable amongst SCD group. Fifteen (83%) deaths were due to substandard care and lack of ICU bed and 3 (17%) were attributed to patients failure to seek or to comply with medical advice.

DISCUSSION

The incidence of SCD in parturient mothers in Bahrain had declined to reach 0.55% in recent years compared to 0.8% and 0.7% in previous studies[4,5]. This could be attributed to the success of national SCD prevention programs, which include premarital counseling and health education of the public. However, this study showed that SCD is still the leading cause of maternal death in Bahrain which account for 30%. The result of this study is similar to previous national reports which showed that SCD account for one-quarter and one-third of all maternal deaths in Bahrain[13,14]. Other international studies showed that MMR for women with SCD was 6 to 11 times higher than general population[6,8].

In this study, SCD group were younger, with low parity and gestational age, see table 3. In a study by Villers et al, women with SCD were significantly older[6]. However, in a study by Asnani et al, women with SCD had significant lower parity and fewer viable pregnancies[8]. All deceased SCD women were Bahraini while 24 of non SCD were non-Bahraini and the difference was very significant.

Though there was no significant difference in the pregnancy outcome of both groups, yet the fetal loss was high. The fetal loss amongst SCD was 62% compared with 48% amongst non SCD. These findings were similar to previous studies[6,7,11,12,17]. SCD is associated with 2-10 folds increase in perinatal mortality[4,18].

It was found that there was no significant decline in MMR amongst SCD women in the two periods. The first period had significant higher parity and number of living children compared with the second period, see table 4. However, there was no significant difference between both groups regarding age, gravidity, nationality and gestational age, which is similar to a study by Asnani et al[8]. In this study, there were more deaths in other hospitals during the second period as compared with the first period.

It was found that pulmonary embolism was the leading cause of death accounting for 35%, followed by infection, obstetric hemorrhage and acute chest syndrome. In a study by Villers et al, thrombo-embolic events were the most important direct cause of maternal death amongst SCD

women[6]. Though this group had higher rate of hypertensive disorders of pregnancy, yet none of the SCD group had died from the complications of hypertension in our study[6,8].

Maternal mortality amongst women with sickle cell disease was avoidable in 48.6%; 83% were due to substandard care and lack of ICU beds. A similar study by el-Shafei et al concluded that 38% of maternal mortality was avoidable. The majority were due to failure of the patients to seek medical care or follow medical advice[13]. Sandhu et al showed that 28% of maternal deaths were avoidable. Out of avoidable causes, 47% due to failure in the medical management, 41% were due to non availability of ICU beds and 12% did not seek antenatal care[14]. Studies in United States showed that about 40%-50% of maternal mortality were preventable[19,20].

CONCLUSION

For the last four decades, SCD is the leading cause of maternal death in Bahrain, it accounts for 30% of maternal death. We found a significant decline in the overall Maternal Mortality Rate, which could be attributed to the improved health care and socioeconomic status. However, there was no significant reduction in maternal death amongst SCD women. Embolism was the leading cause of death in both groups. Other important causes of maternal mortality in women with SCD were sepsis, hemorrhage and acute chest syndrome.

All efforts should be focused on managing SCD group to reduce maternal mortality. Proper thrombo-prophylaxis should be initiated in pregnant women with sickle cell disease. Antenatal care should be provided by a multidisciplinary team. ICU care should be available because SCD patient could deteriorate very fast.

Author Contribution: All authors share equal effort contribution towards (1) substantial contribution to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of manuscript version to be published. Yes.

Potential Conflicts of Interest: None.

Competing Interest: None. **Sponsorship**: None.

Submission Date: 7 September 2014. **Acceptance Date:** 17 November 2014.

Ethical Approval: Approved from secondary care medical research subcommittee at Salmaniya Medical Complex.

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