

## Awareness of spina bifida among family of affected child. *A cross sectional questionnaire*

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### ABSTRACT

**Objectives:** To evaluate the awareness of spina bifida (SB), risk factors and possible preventive measures among mothers who had been following in our clinic with a spina bifida affected child.

**Methods:** A cross-sectional questionnaire-based study with 38 mothers of SB patients who are following at SB and hydrocephalus clinic at King Fahad University Hospital, Khobar, Eastern Province, Saudi Arabia.

**Results:** Thirty-eight mother were included in this questionnaire. Most of the participants were Saudi (94.7%). Ten out of 38 women (26.3%) had used medications during pregnancy (pain medications and herbal drugs), 4 out of 38 (10.5%) had been exposed to imaging radiation, while 9 (23.7%) had experienced moderate to high grade fever (39-41°C) during pregnancy. Moreover, the majority (86.8%) of these women did not receive folic acid (FA) before pregnancy, and 42.1% of them did not have FA during their first trimester. Only one (2.6%) gave positive family history of SB while, 6 (15.8%) reported having other SB children.

**Conclusion:** There is a considerably low level of awareness in mothers of SB patients despite prevalence of this anomaly in the Eastern province. This necessitates an effort from health care providers to educate the community about this birth defect entity. Furthermore, genetic counseling should be encouraged especially in those who have a positive familial history for better understanding. Also, larger sample size with randomized controlled trials and larger epidemiological studies should be implemented.

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Spina bifida (SB) is a type of neural tube defect (NTD) associated with significant mortality and morbidity worldwide.<sup>1</sup> Approximately 3,000 cases of NTDs are diagnosed every year in the United States of America, and more than 300,000 cases are diagnosed annually worldwide.<sup>2,3</sup>

Several risk factors including genetic and environmental factors are associated with NTDs. These include a family history of NTDs, intake of anti-seizure medications, diabetes, obesity, fever at the onset of pregnancy, and low folic acid (FA) intake.<sup>1</sup> Unfortunately, referral center registries for NTDs cases are unavailable in Saudi Arabia.<sup>1</sup> A study performed at the Security Forces Hospital (SFH) in Riyadh, Saudi Arabia showed that the prevalence of NTDs was 1.2 per 1,000 live births. After excluding syndromic and genetic causes and the pre-fortification of flour with FA, the prevalence of NTDs was 1.46 per 1000 live births, whereas the post-fortification prevalence was 1.05.<sup>4</sup> Syndromic causes constitute 20% of all NTDs. Notably, genetic disorders with an autosomal recessive inheritance pattern and the high rate of consanguineous marriages in Saudi Arabia are considered important contributors to NTDs in this country.<sup>4</sup>

Food fortification and the intake of adequate quantities of FA before conception and throughout the first month of pregnancy are important for the prevention of NTDs. However, this strategy is ineffective to treat hereditary types of myelomeningocele (MMC).<sup>4</sup> Several studies have revealed that adequate FA intake periconceptional can prevent approximately 70% of NTDs. The United States Public Health Service has recommended that all women of childbearing age should be administered 0.4 mg of FA/day. Women who have borne a prior infant with NTDs are at a higher risk of a subsequent NTD-affected pregnancy. Such women need to seek consultation with their physician prior to planning a pregnancy.<sup>5</sup>

A randomized controlled trial study published by the British Medical Research Council showed that women who have previously borne an infant with NTDs can reduce the risk of a subsequent NTD-affected pregnancy by 70% with the intake of 4 mg/day of FA. Women with a prior NTD-affected pregnancy, those with a personal or a family history of NTDs, those with a history of alcohol abuse, diabetes or obesity, and women using anti-seizure medications constitute the high-risk group. When these women plan to get pregnant, they are prescribed 5 mg of FA with close monitoring over at least 3 months pre-conceptionally

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to 12 weeks post-conception in addition to increased dietary intake of folate-rich foods.<sup>6</sup>

Unfortunately, a low level of awareness prevails among women of childbearing age in Saudi Arabia regarding the importance of FA in preventing NTDs.<sup>7</sup> This study aimed to evaluate the incidence of SB in the Pediatric Neurosurgery Clinic at King Fahad Hospital of the University, Al Khobar, Saudi Arabia and also aimed to establish preventive strategies for SB to improve patients' quality of life. Additionally, this study investigated the following: i) the role of FA in preventing SB, ii) the possible contributors to failure of therapy, and iii) the levels of awareness regarding SB among mothers with infants affected by this condition. We are looking for implementing a referral center registry for NTD cases at King Fahad Hospital of the University, Al Khobar, Saudi Arabia.

**Methods.** This is a cross-sectional questionnaire-based study. Mothers who had borne infants with SB responded to the questionnaire and consented to participate in the study. Data confidentiality and participants' privacy were assured, and the data were used only for research purposes. Data were obtained between 2017 and 2018. This study included 38 women with infants diagnosed with SB. The study was not associated with any physical, psychological, social, legal, economic or any other anticipated risk to participants. It was performed at the SB and hydrocephalus clinic at King Fahad University Hospital, Al Khobar, Saudi Arabia. The ethical approval for this study was obtained from the Institutional Review Board of Imam Abdulrahman bin Faisal University, Dammam, Saudi Arabia.

The exclusion criteria of the study are as follows: 1) any other type of congenital anomalies; and 2) any child present to the clinic for follow up without his or her mother, since most of the questions can be answered by the mother only.

All women completed a questionnaire consisting of 22 questions that evaluated the risk factors of SB in the parents such as: diabetes mellitus, obesity, receiving medication, exposure to radiation, high grade fever in the first 3 months of pregnancy, the antenatal period, and the infant itself (diagnosis and interventions performed in each affected infant). The questionnaire responses were analyzed by the Statistical Package for the Social Sciences version 21 (SPSS Inc. Chicago, IL, USA). Categorical variables were expressed as frequencies and percentages. Descriptive analysis was performed using the Fisher exact test to determine the significance of the association between categorical variables. The level of significance was set at  $p < 0.05$ .

**Results.** In this study, 38 mothers of infants with SB completed the questionnaire. Most women were Saudi (94.7%), had completed secondary education (81.6%), and were unemployed (97.4%). Only one mother reported a history of diabetes mellitus, and no other medical condition was reported in any parent of infants with SB investigated in this study. More than 50% (57.9%) of the investigated women were aged 25-35 years, and their mean weight was  $71.1 \pm 18.14$  kg at the time of their pregnancy. We observed that 10 women (26.3%) had received medications, 4 (10.5%) had received radiation exposure, and 9 (23.7%) had developed high fever during their pregnancy. Additionally, approximately 50% (47.4%) of these women reported unhealthy nutrition during pregnancy. Moreover, most women (86.8%) did not receive FA before pregnancy and 42.1% did not receive FA during their first trimester. Only one woman (2.6%) reported a positive family history of SB, and 6 women (15.8%) reported having previously borne an infant with SB. Most women (73.7%) had received education in this regard for their subsequent pregnancies (Table 1).

Notably, 65.8% of all infants with SB were females. All infants were mature and most (73.7%) were delivered by cesarean section. Myelomeningocele was diagnosed in 50%, SB occulta in 42.1%, and meningocele in 7.9% of these infants. More than 50% (57.9%) of these infants were diagnosed during intrauterine life and 36.8% were diagnosed with the defect post partum (Table 1). Social issues associated with this condition led to a divorce in one woman. As shown in Table 2, no statistically significant association was observed between the type of NTD diagnosed and radiation exposure in the mother or occurrence of high-grade fever during pregnancy. Additionally, the administration of FA before or during pregnancy was not significantly associated with the type of NTD ( $p > 0.05$ ). As shown in Table 3, no statistically significant association was observed between a family history of SB, having another infant with SB or awareness regarding SB, and the administration of FA before pregnancy ( $p > 0.05$ ).

**Discussion.** Spina bifida is a challenging and partially preventable congenital disease. A growing body of evidence has shown female preponderance in susceptibility to NTDs, which was proved in this study, wherein approximately 66% of the affected infants were females. A similar observation (remarkable female preponderance with respect to NTDs) was reported in Saudi Arabia by Al Shail et al<sup>1</sup> and in Turkey by Kanit et al.<sup>8</sup>

**Table 1** - Ante-natal, perinatal, post-natal history of mothers with spina bifida child (N=38).

History variables	n (%)
<i>Age at pregnancy</i>	
15-25	10 (26.3)
25-35	22 (57.9)
35-45	6 (15.8)
<i>Over the counter medications during pregnancy</i>	
Yes	10 (26.3)
No	28 (73.7)
<i>Nutrition of the mother during pregnancy</i>	
Healthy	20 (52.6)
Unhealthy	18 (47.4)
<i>Exposure to radiation during pregnancy</i>	
Yes	4 (10.5)
No	34 (89.5)
<i>Moderate/high grade fever during pregnancy</i>	
Yes	9 (23.7)
No	29 (76.3)
<i>Receiving folic acid during the first 3 months</i>	
Yes	22 (57.9)
No	16 (42.1)
<i>Receiving folic acid before pregnancy</i>	
Yes	5 (13.2)
No	33 (86.8)
<i>Family history of spina bifida child</i>	
Yes	1 (2.6)
No	37 (97.4)
<i>Another spina bifida child</i>	
Yes	6 (15.8)
No	32 (84.2)
<i>Gender of the child</i>	
Boy	13 (34.2)
Girl	25 (65.8)
<i>Full term baby</i>	
Yes	38 (100)
No	0
<i>Type of defect</i>	
Spina bifida occulta	16 (42.1)
Meningocele	3 (7.9)
Myelomeningocele	19 (50.0)
<i>Method of delivery</i>	
Normal	10 (26.3)
Cesarean section	28 (73.7)
<i>Time of diagnosis</i>	
Intrauterine	22 (57.9)
At delivery	2 (5.3)
After delivery	14 (36.8)

In this study, more than 50% of the women investigated were aged 25-35 years. Reportedly, an increased risk of SB was observed in mothers aged >40 years or <19 years.<sup>9</sup> In this study, MMC was diagnosed in 50%, SB occulta in 42.1%, and meningocele in 7.9% of the infants diagnosed with SB. Based on analysis of the NTD registry maintained at the King Faisal Specialist Hospital & Research Center, Dammam,

Saudi Arabia since it was established in October 2000 until December 2012, it was observed that most infants with SB presented with MMC.<sup>1</sup>

Prenatal ultrasonography shows 98% sensitivity and 100% specificity for the detection of NTDs. Moreover, owing to advances in prenatal diagnostic technology, detection of SB is possible as early as the first trimester.<sup>10</sup> However, intrauterine diagnosis was accurately established in only approximately 50% of the studied infants, and the remaining infants were diagnosed either at or after delivery. This is most likely attributable to the fact that not all women undergo a detailed anomaly scan and undergo only a social scan to ascertain only the presentation and viability of the pregnancy.<sup>1</sup> It is important to create awareness among health care providers regarding the need to perform detailed ultrasonographic evaluation or refer women to centers that can provide such services.

The pattern of occurrence of NTDs in humans suggests a multifactorial etiology. This emphasizes the importance of gene-gene and gene-environment interactions as etiological contributors to these defects.<sup>11</sup> Mutations in >200 genes are known to cause NTDs in mice.<sup>12</sup> Among all the surveyed mothers, 6 women (15.8%) reported having borne another infant with SB, and one woman (2.6%) reported a family history of SB. In contrast to this finding, a study reported by Al Shail et al<sup>1</sup> observed that an NTD-affected pregnancy did not occur in any of the women who had previously borne an infant with SB. Moreover, they observed that most women did not report a history of NTDs in a first-degree relative.

Several environmental factors are known to be associated with NTDs; however, limited data exist regarding the etiopathogenic mechanisms in this context.<sup>12</sup> Evidence-based studies show that women diagnosed with obesity, those with poorly controlled diabetes, those using certain types of anti-seizure medications, or those with high fever during the first 4-6 weeks of pregnancy are at a greater risk of delivering an infant with SB.<sup>13</sup> These risk factors were identified in a number of participants in this study as follows: 10 women (26.3%) had received medications, 4 (10.5%) had history of radiation exposure, and 9 (23.7%) had experienced high fever during their pregnancy. The association between radiation exposure during pregnancy and the development of SB has shown inconsistent results.<sup>12</sup> It is unclear whether the type or the cumulative dose of radiation could play a role in the development of this condition, and this factor needs further investigation. Moreover, this study explored a non-significant association between radiation exposure,

**Table 2** - Association between type of neural tube defect to fever, folic acid supplement before or during pregnancy, and radiation exposure.

Variable	SB occulta	Meningocele	MMC	P-value
<i>Moderate/high grade fever during pregnancy</i>				
Yes	3 (18.8)	0	6 (31.6)	0.52
No	13 (81.3)	3 (100)	13 (68.4)	
<i>Receiving folic acid during the first 3 months</i>				
Yes	11 (68.8)	1 (33.3)	10 (52.6)	0.54
No	5 (31.3)	2 (66.7)	9 (47.4)	
<i>Receiving folic acid before pregnancy</i>				
Yes	1 (6.3)	1 (33.3)	3 (15.8)	0.33
No	15 (93.8)	2 (66.7)	16 (84.2)	
<i>Exposure to radiation during pregnancy</i>				
Yes	2 (12.5)	0	2 (10.5)	0.99
No	14 (87.5)	3 (100)	17 (89.5)	

Data is presented as number and percentage (%). SB - Spina bifida, MMC - myelomeningocele

**Table 3** - Effects of level of education, positive family history, and having another spina bifida child on folic acid supplementation before pregnancy.

Variable	Receiving FA before pregnancy		P-value
	Yes	No	
<i>Previous education</i>			
Yes	4 (80.0)	24 (72.7)	1.0
No	1 (20.0)	9 (27.3)	
<i>Family history of SB child</i>			
Yes	0	1 (3.0)	1.0
No	5 (100)	32 (97.0)	
<i>Another SB child</i>			
Yes	2 (40.0)	4 (12.1)	0.17
No	3 (60.0)	29 (87.9)	

Data is presented as number and percentage (%). FA - folic acid, SB - spina bifida

the occurrence of high fever or folate supplementation and the specific type of SB.

Several randomized controlled trials and observational epidemiological studies have provided evidence that FA supplementation can reduce the risk of NTD-affected pregnancies.<sup>12</sup> The underlying mechanisms by which FA supplementation reduces the risk of NTDs remain unclear.<sup>14</sup> The current study showed that most mothers did not use FA before pregnancy. Furthermore, no significant association was observed between a positive family history of SB or having an infant with SB and FA intake before the subsequent pregnancy. This could be attributed to inadequate patient education regarding the importance of such supplementation or a lack of appropriate planning by a woman for the pregnancy. In a study performed between 1998-2010, Kelly et al<sup>15</sup> reported that knowledge regarding the benefits of FA was relatively low among young women of childbearing age.

In contrast, the use of FA during the first trimester was reported by more than 50% of the women. This could indicate that health caregivers tend to emphasize the importance of FA supplementation during pregnancy to all pregnant woman they encounter in clinical practice in keeping with the policy adopted by the Ministry of Health, Saudi Arabia whereby all women receive FA during pregnancy. However, previous studies have shown that the delayed intake of FA after conception appears to be inadequate to reduce the incidence of the disorder.<sup>12</sup> Moreover, an important drawback in this context is that women receive FA after the most critical period (4-8 weeks of pregnancy), during which neural tube formation occurs.<sup>7</sup> Several studies have shown that despite the implementation of the aforementioned policy (administration of FA during pregnancy), only 4%-8.3% of Saudi women actually receive FA during pregnancy. This finding is mainly observed among young women.<sup>4,16</sup> Folic acid fortification of flour has been implemented in Saudi Arabia and has been associated with a significant reduction in the incidence of NTDs.<sup>17</sup> Additional efforts are required to increase the level of awareness and these should be supported by the concomitant implementation of highly specialized health education programs among young women of childbearing age. These programs should include information regarding preconception care, particularly in terms of development of NTDs and the associated morbidity and mortality burden. Additionally, the importance of planned pregnancies should be emphasized.

However, there are some limitation in this study. We could not conduct this study with a sufficient sample size, as some of the mothers refused to participate in the questionnaire and some children were following up in the clinic without their mothers. This resulted in

difficulty to identify significant relationships from this data.

In conclusion, despite NTD being a multifactorial pathogenetic disorder, there is a considerably low level of awareness in mothers of Spina bifida patients despite prevalence of this anomaly in eastern province. This necessitates an effort from health care providers to educate the community about such a birth defect entity, possible risk factors and preventable measures during pregnancy in addition to the folic acid supplement ahead of pregnancy planning and during the first 3 months of pregnancy. Furthermore, genetic counseling should be encouraged especially in those who have a positive familial history for better understanding.

Furthermore, due to some limitation of this study, a larger sample size with randomized controlled trials and larger epidemiological studies should be implemented.

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