Risk Factors and Spine Abnormalities in Children with Spina Bifida in Central Sudan

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ABSTRACT

Spina bifida is a common cause of disability in infancy and childhood. Up to 70% of spina bifida cases can be prevented by maternal periconceptional folic acid supplementation. The aim of this prospective research was to study the risk factors and spine abnormalities in children with spina bifida in Central Sudan. Between June 2009 and May 2011, 105 Sudanese children with spina bifida, 55 females and 50 males, aged between the first day of life to 9 years were recruited in this study. Data were collected through a structured questionnaire and radiographs. Statistical package for social science (SPSS) was used to perform data analysis. First born child had increased risk for the disease and incidence was more common in winter. Thirty nine percent of mothers were in the age group (26-35) and no mother had used folic acid before pregnancy. The neural arch defect involved three vertebrae in 23.5% of myelomeningocele cases and one vertebra in 40.9% of meningocele cases. Complete absence of laminae was seen in 66.3% of cases. In 55.8% of patients the defect was less than one centimeter in width. None of mothers used folic acid before getting pregnant and about half of mothers used it after they detected their pregnancy.

Keywords: Folic acid, Radiograph, Deformities, Vertebra, Defect

INTRODUCTION

Spina bifida (SB) is the most common central nervous system birth anomaly. It is recognized as the most complex developmental defect of the neural tube, notochord, ectoderm, mesoderm and very rarely endoderm (Pang et al., 1992). The general term spina bifida refers to those spinal anomalies that have incomplete midline closure of mesenchyme, osseous and neural tissue (Barkovich & Naidich, 1990). Maternal folic acid deficiency is an environmental factor strongly associated with neural tube defects (Berry et al., 1999). Spina bifida ranges from minor types (spina bifida occulta) to severe, clinically significant types (spina bifida cystica). Spina bifida occulta is the mildest form of spina bifida, resulting from a gap in one or more vertebral arches,

but the spinal cord and meninges remain entirely within the vertebral canal (Moore et al., 2003; O'Rahilly & Müller 1996). Severe types of spina bifida involve protrusion of the spinal cord and/or meninges through a defect in the vertebral arch and are referred to as spina bifida cystica (meningocele and myelomeningocele).

Spina bifida varies across gender, ethnicity, and geographic location. The prevalence rate is between 1 and 5 per 1000 live births. Up to 70% of spina bifida cases can be prevented by maternal, periconceptional folic acid supplementation (Laura et al., 2004; Bolander, 2009).

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In Africa, the reported incidence of spina bifida (SB) is variable, e.g. in Malawi it was 0.47/1000; in Tunisia, was 1.05/1000; in Cape Town the prevalence of neural tube defects (NTDs) was 1.74/1000 and it was higher in the whites than the blacks (Soumaya et al., 2001). In Sudan the reported incidence was 3.48/1000 in Omdurman Maternity Hospital (Ghada and Salah, 2001).

Little work has been done in spina bifida in Sudan and detailed descriptions about the anatomical abnormalities of the spine and the vertebral defects are hardly found in literature. This research aims at studying the risk factors and spine abnormalities in children with spina bifida in Central Sudan.

MATERIAL AND METHODS

Materials

In this study, 105 Sudanese children with spina bifida aged between the first day of life to nine years were recruited at the Gezira National Centre for Pediatric Surgery in Central Sudan over a 24 month period. All were examined on admission and assessed with regard to their general condition.

Methods

A cross-sectional observational prospective study conducted between June 2009 and March 2011. Ethical approval was given by Review Committee in the Gezira University and the director of Gezira National Centre of Pediatric Surgery. Data collection tools of this study included:

1. A developed interview questionnaire prepared and designed by the researchers. It was filled in an interview with the mothers or patient care taker. The questionnaire included; (i) patient demographic data; (ii) maternal history including maternal age, consanguineous marriage, history of previous birth of baby with spina bifida and folic acid supplementation; (iii) x-ray findings included; number of vertebrae involved in the lesion, complete and partial absence of vertebral arches, sites and size of vertebral arch defect.
2. Radiograph: Of 105 children with spina bifida, x-rays of the spine (posterior-anterior and lateral) were done in 104 patients to determine and to diagnose the vertebral deformities. The radiographs were saved electronically on a computer for analysis.
3. Magnetic resonance imaging (MRI): Spine MRI was done for one patient who was admitted with occult spina bifida.

On the spine radiograph,; the number of the vertebrae involved in the lesion, the pattern of the absence of the vertebral arches, the size and site of vertebral defects; and scoliosis and kyphosis were determined. The vertebrae involved in the lesions were counted in all patients. For the purpose of describing the vertebral defect, the patients were divided into three groups; (i) patients with complete absence of vertebral arch; (ii) patients with partial absence of vertebral arch; (iii) patients with both complete and partial absence of the vertebral arches. The site on the vertebra where the defect was located was detected by analyzing the postero-anterior radiographs. The patients were divided into three groups, patients with central neural arch defects, patients with right laminar defect and patients with left laminar defect. The defect site was obtained by drawing a vertical line between the spinous processes proximal and distal to the defective laminar arches.

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The associated deformities of the vertebral column; scoliosis and kyphosis that result from vertebral anomalies were studied. We also obtained the length of the vertebral arch defect in centimeter by measuring the transverse distance between the margins of the defective laminar arches. Data obtained from images were analyzed and recorded.

Data Analysis

The data were coded, processed and transferred to a computer. The descriptive analysis was adopted; this included percentage, frequency distributions, tables and figures. Software Program: Statistical Package for Social Science (SPSS) version 13 (SPSS, Inc., 2004) was applied. Results were considered statistically significant at $p < 0.05$.

FINDINGS

Eighty two (78.1%) of patients had myelomeningocele, twenty two (22%) had a meningocele and one patients (0.9%) presented with occult spina bifida. Forty seven percent (47.6%) of the cases were males, 25.7% of the cases presented on the first day of life [Table I]. Twenty seven percent of the patients were the first born child, (12.4%) were the second and 17.1% third [Figure 1].

Table 1. Distribution of study population according to baseline characteristics and type of the defect

Baseline characteristic	*Number (n)*	*Percentage*
Age		
1 day	27	25.7
2-7 days	28	26.7
1-4 wks	28	26.7
1-6 month	16	15.2
> 6 month	6	5.7
Total	105	100
Sex		
Male	50	47.6
Female	55	52.4
Total	105	100.0
Type of Spina Bifida		
Occult	1	0.95
Meningocele	22	20.9
Meylomeningocele	82	78.15
Total	105	100.0

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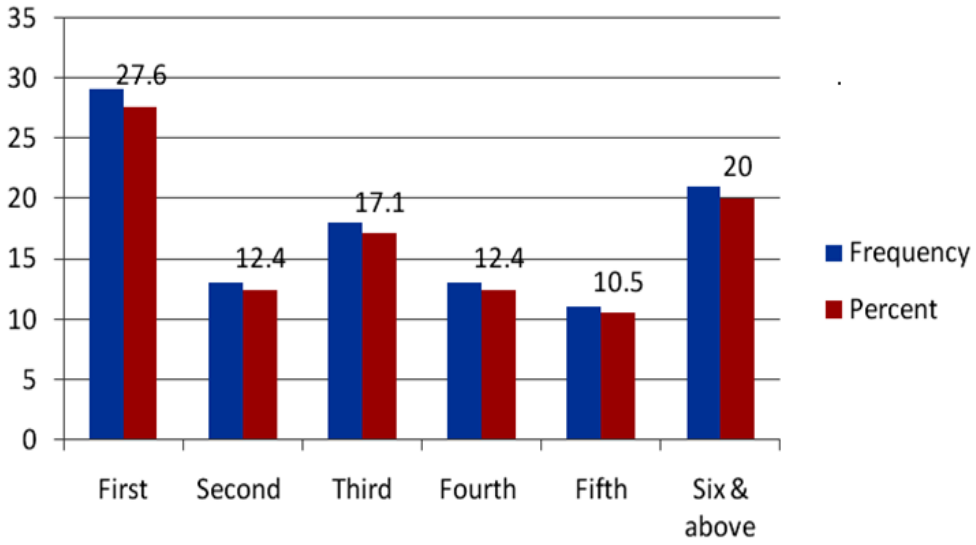

Figure1. Distribution of the patients according to the birth order

The highest frequency occurred in the winter, December (15.5%) and November (11.4%), whereas the lowest frequency (2.9%) occurred in July at the beginning of autumn [Figure 2].

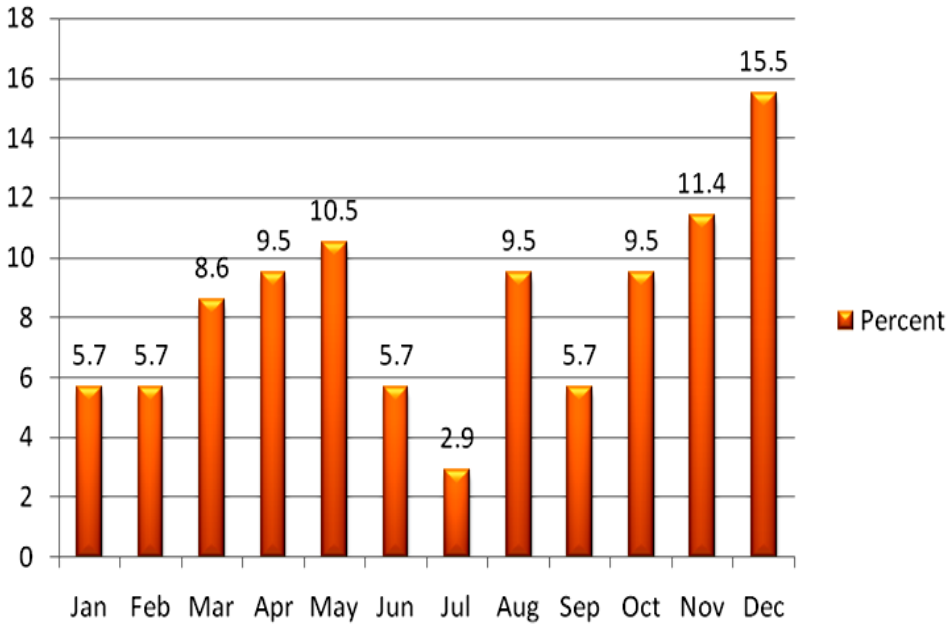

Figure 2. Distribution of spina bifida according to the seasons of the year

Thirty nine percent of mothers were in the age group (26-35), whereas mothers more than 36 years old were 28.6% [Figure 3]. Table 2 reveals that, of total of 105 mothers, (39%) had consanguineous marriage. More than half of mothers (54%) had folic acid supplementation during pregnancy, while none of the mothers used folic acid before getting pregnant. Six mothers had the history of a previous birth of a baby with spina bifida.

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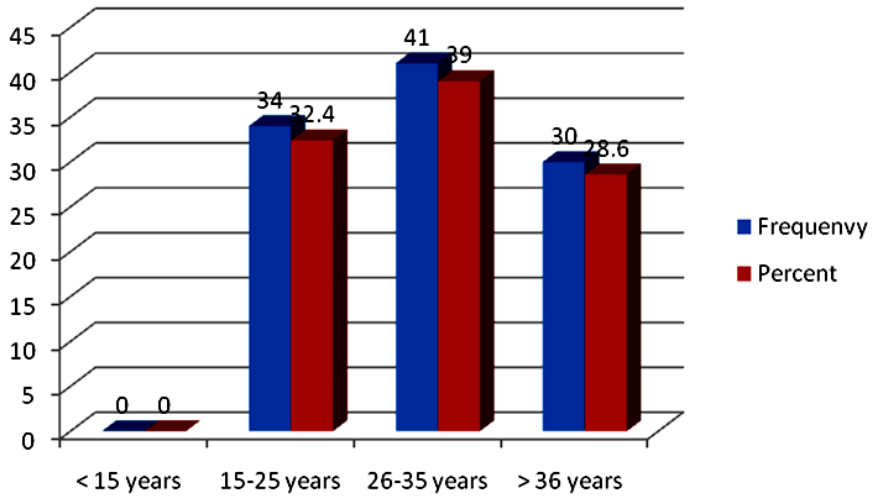

Figure 3. Distribution of cases according to the maternal age

Table 2. Maternal risk factors associated with spina bifida

Risk factors	*Yes*		*No*	
	Frequency	*Percent*	*Frequency*	*Percent*
Consanguinity	41	39.0	64	61.0
Folic acid supplementation during pregnancy	54	51.4	51	48.6
Folic acid supplementation before pregnancy	0	0.0	105	100
Family history of spina bifida	6	5.7	99	94.3

The neural arch defect involved three vertebrae in 23.5% of myelomeningocele cases, one vertebra in 40.9% of meningocele cases and six vertebrae in the occult spina bifida case [Table 3] and [Figure 4].

Table 3. Distribution of the number of vertebrae involved in the lesion according to the different types of spina bifida in 104 patients

Number of vertebrae	*Myelomeninocele N (%)*	*Meningocele N (%)*	*Occulta N (%)*	*Total N*
One	11(13.6)	9 (40.9)	0 (0)	20
Two	17 (21)	4 (18.2)	0 (0)	21
Three	19 (23.5)	4 (18.2)	0 (0)	23
Four	13 (16)	0 (0)	0 (0)	13
Five	8 (9.9)	2 (9.1)	0 (0)	10
Six	5 (6.1)	1 (4.5)	1 (100)	7
More than six	8 (9.9)	2 (9.1)	0	10
Total	81 (100)	22 (100)	1 (100)	104

[Table 4] shows that (66.3%) of the children with spina bifida had complete absence of the vertebral arch, whilst 26% of sample showed both complete and partial absence of vertebral arch in the radiographs and only 7.7% of patients had partial absence of vertebral arch. In most cases (88.5%) the vertebral arch defect was nearly centrally placed. The defect was right laminar in 7.7% of cases and left laminar in 4.8% of cases. The width of the vertebral arch defect was less than one centimeter in 55.8% of cases and more than one centimeter in 44.2% of patients [Table 4].

Table 4. Subject distribution according to the pattern of absence of vertebral arch, site and width of laminar defect.

Laminar defect site and width	*Number (n)*	*Percent*
Absence of vertebral arch		
Complete	69	66.3
Partial	8	7.7
Complete and partial	27	26
Total	104	100
Site of laminar defect		
Central	92	88.5
Right laminar	8	7.7
Left laminar	4	3.8
Total	104	100.0
Width of the defect		
Less than one centimeter	58	55.8
More than one centimeter	46	44.2
Total	104	100.0

In 104 cases of spina bifida who had radiographs done, scoliosis and/ or kyphosis were seen in (36.5%) patients; scoliosis was seen in (17.3%), kyphosis in (11.5%) and scoliosis together with kyphosis was seen in (7.7%) of patients [Figure 5] and [Figure 6].

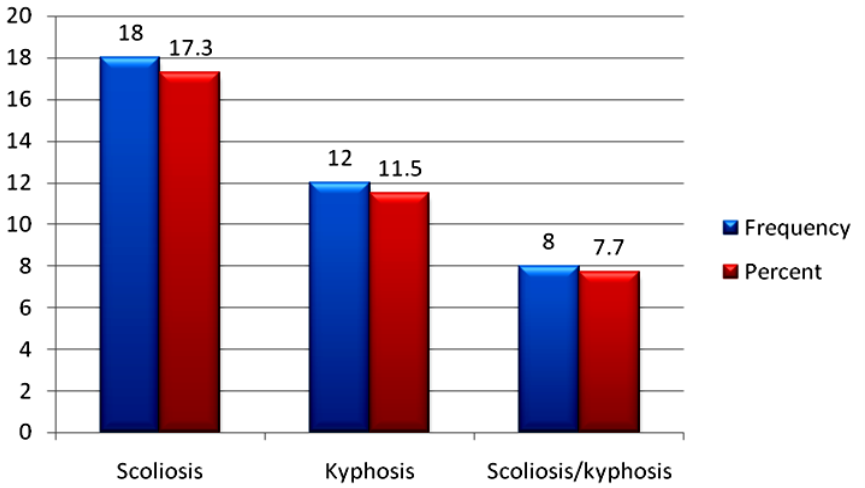

Figure 5. Scoliosis and kyphosis as neuro-orthopedic deformities in 104 patients with spina bifida

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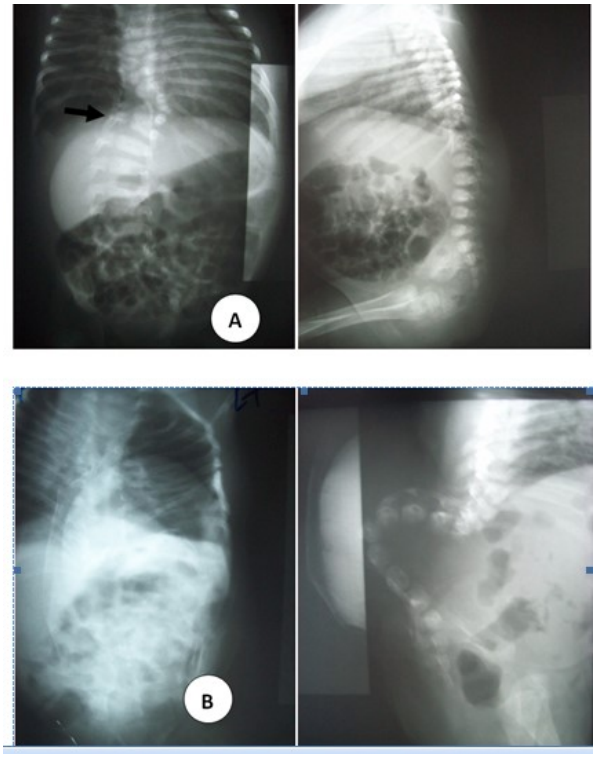

Figure 6: A: anteroposterior and lateral radiographs of 22 days aged female with lumbo- sacral spina bifida showing a segmented hemivertebra in T12 (*black arrow*). Scoliosis is already developed. B: Anteroposterior and lateral radiographs of spine for 28 days age infant with large lumbar myelomeningocele, associated with kyphosis and scoliosis.

DISCUSSION

Spina bifida is one of the congenital anomalies with complex etiology. Both genetic and environmental factors are implicated (Norman et al., 2008). Maternal folic acid deficiency is an environmental factor strongly associated with neural tube defects (Berry and Erikson, 1999; Botto et al., 1999).

The incidence of spina bifida was almost equal in males and females as sex ratio (male to female) was found to be 1: 1.1; in contradiction with previous studies conducted in United States in which incidence was higher in females than males (Mitchell et al., 2004, King Sing Au et al., 2008). The incidence of spina bifida was found to be higher in the beginning of winter, and the highest frequency occurred in December (15.5%) followed by November (11.4%), consistent to the findings of a previous study conducted at Gezira, Sudan (Nugud et al., 2003).

Maternal History and Possible Risk Factors

The role of maternal age in the etiology of spina bifida and other neural tube defects was poorly understood. Multiple studies had examined maternal age in this defect. Several studies had shown an increased risk with an increased maternal age. Strassburg et al noted a general pattern of increasing risk with increasing maternal age for spina bifida in a study in Los Angeles County (Strassburg et al., 1983). From this study it was found that women between 26 and 35 years old had increased risk to the disease. This may be due to the fact that, age, 26- 35 is age of pregnancy and delivery, hence the number of babies with the defect was higher at this age. Our finding is inconsistent with study conducted in Omdurman

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Maternity Hospital; in which women less than 25 years old had increased risk to the disease (Ghada and Salah, 2009). Studies in Oman and Palestine reported that the incidence of spina bifida increased with maternal age (Rajab et al., 1998; Duin, 1997). In contrast, other studies found no relationship between neural tube defects and maternal age (Canfield et al., 1996; Brender et al., 1990). Because of these conflicting reports, the importance of maternal age in risk for spina bifida occurrence is unclear.

There was evidence that late birth order was associated with some complex disorders. For spina bifida and other neural tube defects there is no consensus as to whether first or increased birth order is associated or not (Vieira, 2004). In this study the results revealed that first born children were more likely to be affected with spina bifida. This finding is in agreement with the finding of a previous studies conducted in central Sudan (Nugud et al., 2003) and Nigeria (Maboguje, 1990) and contrast with the finding of Rajab et al who reported that later born was more likely to be affected.

A family history of spina bifida was a weak risk factors for this disorder. The findings of the present study showed that 5.7% of children had family history of spina bifida and hydrocephalus, in contradiction with study conducted in United Arab Emirates (Al Talabani et al., 1998) and the finding of Demenais (1982). Consanguinity was one of the risk factors which raise the possibility of the genetic factors in spina bifida and other congenital anomalies. From this study it was observed that 39% of mothers had consanguineous marriage. In contrast with the finding of Ghada et al who stated that consanguinity was not a significant risk factor (Ghada and Salah, 2009). In Oman, it was observed that there was a much higher consanguinity rates in families with neural tube defect and congenital hydrocephalus than in general population (Rajab et al., 1998).

Periconceptional supplementation with folic acid alone or with multivitamins containing folic acid can reduce the risk of spina bifida by up to 70% (Bell and Oakley, 2009; Oakley, 2009;

Cotter and Daly, 2005). In this study, it was evidence that folic acid supplementation was not taken in the first month of pregnancy, although 51.4% of mothers used it after they detected their pregnancy. It was also found that, no mother received periconceptional folic acid. These results confirmed the finding obtained by Elsheikh et al (2004) and, Ghada and Salah (2009) who conducted studies in Omdurman Maternity Hospital in Sudan. Ghada and Salah reported that poor parental education and lack of antenatal care were factors that may partly explain the reason that none of the mothers of the cases received folic acid before or during pregnancy.

Radiological Findings

Specific studies about the number of vertebrae affected in spina bifida are rarely found in the literature. In this study accurate number of the affected vertebrae was obtained in one hundred and four cases of spina bifida. In myelomeningocele group, the neural arch defect involved three vertebrae in 19 of 81(23.5%) patients with this type of spina bifida. In patients with meningoceles, most of them (40.9%) showed involvement of only one vertebra. In the only case of occult spina bifida, that patient demonstrated involvement of six vertebrae in contrast with a previous study conducted by Musrard (1979).

Result of this study showed that, the majority of children with spina bifida (66.3%) had complete absence of the vertebral arch (both laminae were completely absent). Twenty seven children (26%) showed both complete and partial absence of vertebral arch in the radiographs. Only 8 patients (7.7%) with spina bifida had partial absence of vertebral arch.

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From this study it was found that in 92 (88.5%) of cases the vertebral arch defect was nearly centrally placed. The defect was right laminar in 7.7% of cases and left laminar in 3.8% of cases. The size of the defect was also an important factor in surgery beside the lesion size. In the present study, it was less than one centimeter in fifty eight patients (55.8%), while in forty eight patients (44.2%) it was more than one centimeter. Scoliosis with or without kyphosis was an extremely important issue in spina bifida. It was one of the most common neuro-orthopedic syndromes in this series. Scoliosis and/ kyphosis were seen in 46.9% of babies with myelomeningocele (36.5% of patients with spina bifida). Scoliosis was seen in 18 patients, while kyphosis was seen in 12. Eight patients had both kyphosis and scoliosis. It was evidenced that 36.5% of patient with spin bifida had scoliosis and or kyphosis. This finding was lower than that obtained by Kumar et al (2003) and Brenzer (1999) , they found that 60% and 77% were affected respectively. Sandler (2004) reported that improvement of scoliosis was likely to occur in more than 50 percent of children with spina bifida with low lumbar myelomeningocele. [31] Scoliosis was seen in 17.3% of babies with spina bifida. It is much similar to the finding of Sandler Anderian who reported 15-25% for the congenital scoliosis in newborn babies with spina bifida.

CONCLUSIONS

This research studied a series of 105 consecutive cases of spina bifida together with their mothers; cases were seen during a 24-month period. In the light of the findings, it can be argue that first born child was more affected and the highest frequency of birth child with spina bifida occurred in winter. Sudanese women did not used folic acid before pregnancy and about half of the mothers used it after they detected their pregnancy. Family history was a weak factor associated with the disorder. Three vertebrae were often affected in myelomeningocele cases and one vertebra was affected in nearly half of meningocele cases.

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