NEURAL TUBE DEFECTS IN SULAIMANIYAH, IRAQI KURDISTAN: A DESCRIPTIVE STUDY OF 50 CASES

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ABSTRACT

Background

Very little is known about neural tube defects (NTDs) in Iraqi Kurdistan. This study was undertaken in Sulaymaniyah province in order to describe these defects in the area and report on the outcome of patients.

Methods

This descriptive study involved a case series of 50 patients admitted with NTD to the department of neurosurgery at Sulaimaniyah Teaching Hospital during 2006-2010.

Results

Ninety eight patients were admitted to the centre of whom 50 patients were included in the study. The estimated incidence at birth was 3.5 per 10,000, 56% of the patients were females and 44% were males with a female to male ratio of 1.27. The median age at first visit was 9 days (Interquartile range 1, 36). The maternal age ranged from 17-42 years with a mean age of 28 years (SD 6 years). Eight percent of the children had siblings with NTDs, 6% had other anomalies and 12% of their parents were relatives in blood. The majority of lesions (76%) were myelomeningocele, 14% were meningocele and 10% were myeloschisis. Only half of the patients were diagnosed during pregnancy and 30% of all patients had hydrocephalus at time of diagnosis. There was no significant association between sex and site of lesion (P=0.3) and between sex and type of the lesion (P=0.5).

Conclusion

Establishment of prenatal screening is essential in order to help parents to be prepared and make an informed decision about pregnancy. Antenatal care must be strengthened for all pregnant women and folic acid supplementation should be emphasized.

Keywords: Neural tube defect, spina bifida. Sulaimaniyah, Iraqi Kurdistan, case series.

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INTRODUCTION

Neural tube defects (NTDs) are common and serious malformations that originate in the early weeks of pregnancy affecting the developing brain and spinal cord [1, 2]. NTDs include two major categories of spina bifida (meningoceles, myeloceles, and myelomeningoceles) and encephalocele in addition to the two less common forms of iniencephaly and anencephaly [1]. The worldwide incidence of NTDs ranges from 10 to 100 per 10,000 births with similar frequencies of spina bifida and anencephaly [2]. Incidence of NTDs has been reported as 9.3 to 14.6 per 10 000 births in the USA, 12 in Ireland [3], 17.9 in England, 15 in Turkey [4] and 28 to 32 in Iran [5]. NTDs occur more frequently in the white population and females are affected more than males. In 80-90% of the cases of NTDs the lumbosacral region is affected.

These defects are often associated with malformations of the brainstem and the early potential for developing hydrocephalus. Hydrocephalus develops in 65-85% of patients with myelomeningoceles, and 5-10% of these patients have clinically overt hydrocephalus at birth. Over 80% of myelomeningocele patients who will develop hydrocephalus do so before 6 months of age [6]. In meningocele, neurological function below the level of the lesion is usually normal and there is rarely any evidence of hydrocephalus [7].

Potential risk factors for NTDs have been reported as past history of NTDs; maternal age of less than 20 or more than 35; low or high parity; low socioeconomic status with poor nutritional status and poor parental education levels; low maternal folic acid; low vitamin B12 and zinc levels; high copper level; racial differences; higher levels of ambient benzene; radiation; maternal infections, hyperthermia and use of medications; and poor antenatal care [4, 8-15].

Prenatally NTDs could be detected by serum alpha-fetoprotein screening between the 15th and 18th week of gestation. Confirmation requires amniocentesis and ultrasonographic imaging. Without treatment, only 14-30% of myelomeningocele patients survive infancy but with modern treatment, 85% of infants survive. Degree of disability in treated NTDs children varies highly from little to crippling multisystem disability. One-third of the survivors are mentally retarded. Studies have shown that severely affected babies who are not operated on during the neonatal period; die in the first few months of life [7]. NTDs cause 89 deaths per 100 000 live births in Poland, 8 deaths in the UK and 25 deaths in Hungary [16]. Very little is published about NTDs in Iraqi Kurdistan and Sulaimaniyah in particular, therefore this study was undertaken on NTDs in this province to provide an estimate of incidence and describe main characteristics of the condition through analysis of 50 cases.

MATERIAL AND METHODS

This descriptive case series study was conducted in Sulaimaniyah province of Iraq with a population of 1.7 million. Patients admitted with open NTDs to the department of neurosurgery at Sulaymaniyah Teaching Hospital during 2006-2010 and treated by the research team were included in the study. These patients were referred to the neurosurgery department from other hospitals and clinics throughout the province. Patients were recruited during their first visit to the centre. After obtaining informed consent from parents, information was collected in relation to the disease, the family and pregnancy. Diagnosis of NTD was done by clinical examination and confirmed by ultrasound. Computerized tomography (CT) scan was performed for all children. Further investigations were done to the child as needed.

Data were entered into an excel sheet and analysis was performed using Stata version 10 [17]. Associations between categorical variables were tested using Chi-Squared test with a significance level of 5%. Operations were planned for patients after obtaining written consent from parents. The initial operations aimed to preserve all neural tissue, reduce it into the intervertebral canal, untether the spinal cord and cover the defect with muscle, fascia and skin. Subsequent decisions concerning treatment of hydrocephalus and other associated malformations were taken as necessary.

RESULTS

Patient characteristics

During the 5 years of the study, 98 patients with open NTD were admitted to the centre of whom 50 patients were included in the study since their data were available to the research team. Forty seven patients (94%) belonged to Sulaimaniyah city and various districts of Sulaimaniyah province and 3 of them (6%) were from other provinces. Estimating from the total number of patients who visited the centre, and a crude birth rate of 33 per 1000 in Iraq according to World Bank data [18], the rough

incidence at birth for the population of Sulaimaniyah province (1.7 million) will be around 3.5 per 10,000. Table 1 shows characteristics of the patients. There were 22 males and 28 females with a female to male ratio of 1.27. The age at first visit was not normally distributed and ranged from 0-241 days. The median age at first visit was 9 days (IQR 1, 36) and there were no significant differences between males and females in relation to first visit. Maternal age was normally distributed and ranged from 17-42 years with a mean age of 28 years (SD 6 years). Majority of the children (34%) were the first child of the family. Eight percent of the children had siblings with NTD, 6% had other anomalies (all of which were club foot) and 12% of their parents were relatives in blood.

Table 1. characteristics of patients with spina bifida.

Patient characteristics	Number (%)
Total	50 (100)
Sex	
Male	22 (44)
Female	28 (56)
Age at first visit	
0-7 days	25 (50)
8-30 days	9 (18)
1 month and over	16 (32)
Child order in family	
First child	17 (34)
Second child	11 (22)
Third child	12 (24)
Fourth and more	10 (20)
Mother's age at first visit	
17-25 years	21 (42)
26-35 years	21 (42)
36 and over	8 (16)
Father's age at first visit	
17-25 years	9 (18)
26-35 years	22 (44)
36 and over	19 (38)
Siblings with NTD	4 (8%)
Consanguinity	6 (12)
Other anomalies (all club foot)	3 (6)
Use of folic acid in first trimester	6 (12)

Lesion characteristics

Table 2 shows characteristics of the lesion in all patients. In majority of cases (46%) the lesion was in the dorsolumbar region and only 2% were cervical. In relation to the type of the lesion, the majority (76%) were myelomeningcele (figure 1); 14% were meningocle (figure 2) and 10% were myeloschisis (figure 3). Half of the patients were diagnosed during pregnancy and 30% of them had hydrocephalus at the time of diagnosis.

All patients underwent operation except 3 whose parents refused operation. Disability was associated with the type and level of the lesion. None of the children with meningocele had neurological deficit or hydrocephalus before operation or at follow-up during the postoperative period. But cases of myelomeningocele and myeloschisis had variable degrees of lower limb weakness and incontinence of faeces and urine with some transient deterioration after operation due to manipulation of the neural tissue.

In relation to sex differences as shown in table 3, there were no significant association between sex and site of lesion ($\chi 2$ =4.4, P=0.3), sex and type of the lesion ($\chi 2$ =1.3, P=0.5) and sex and presence of hydrocephalus at diagnosis ($\chi 2$ =3.5, P=0.06).

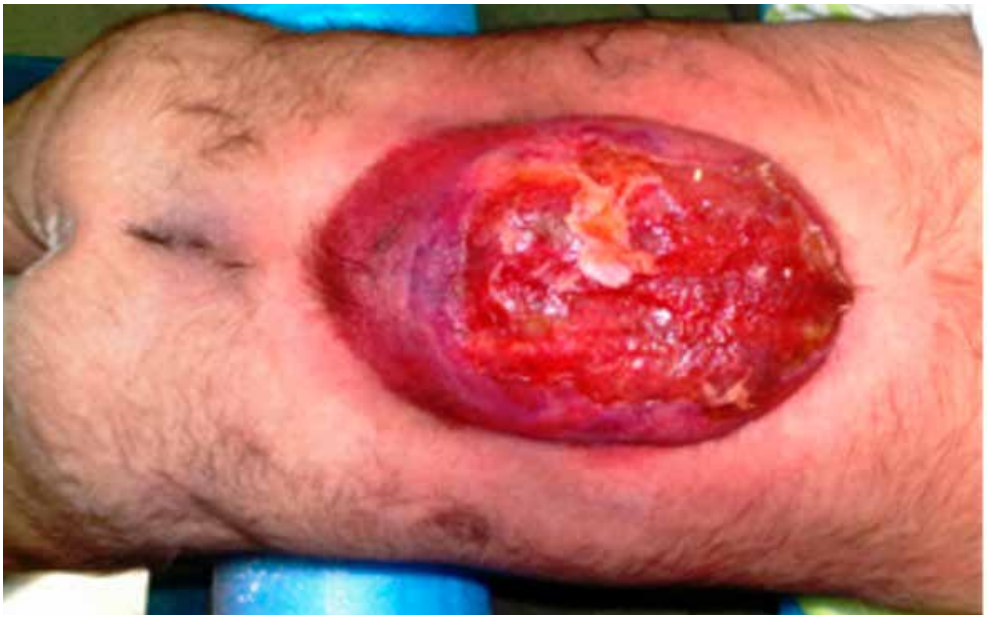

Figure 1. A case of myelomeningocele

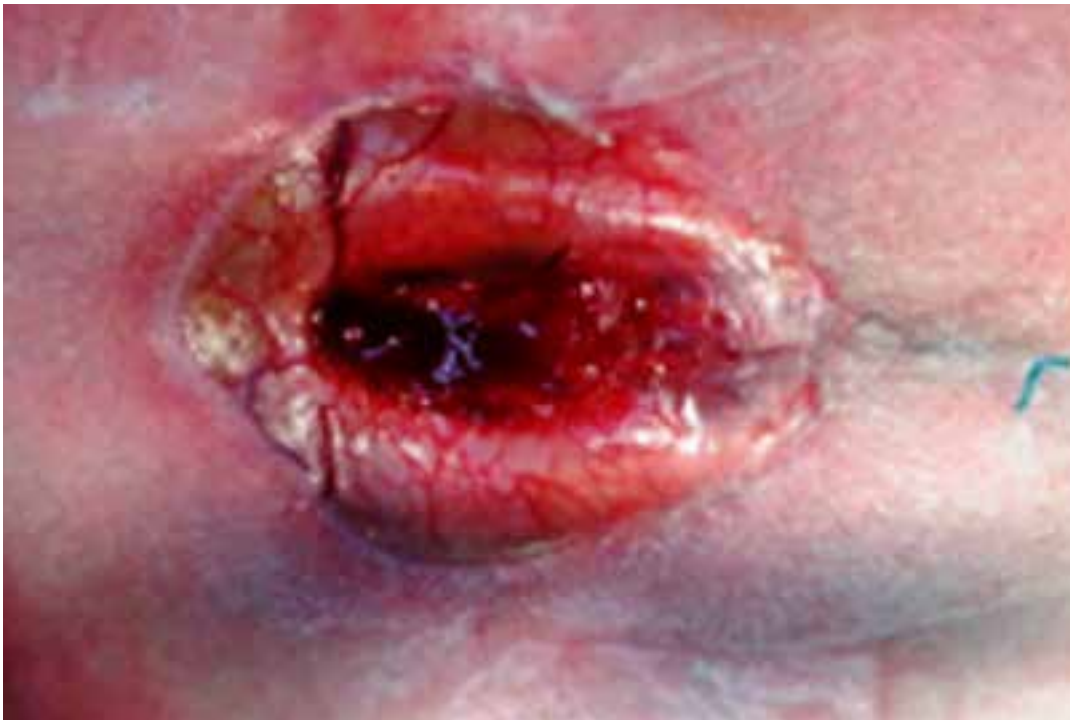

Figure 2. A case of myeloschisis.

Table 2. Characteristics of the lesion in patients with spina bifida

Characteristics	Number (%)
Total	50 (100)
Site	
Cervical	1 (2)
Dorsal	2 (4)
Dorsolumbar	20 (40)
Lumbar	18 (36)
Lumbosacral	9 (18)
Type	
Myelomeningocele	38 (76)
Meningocele	7 (14)
Myeloschisis	5 (10)
Diagnosis during pregnancy	25 (50)
Presence of hydrocephalus at diagnosis	30 (60)
Operation undertaken*	47 (94)

*** Three patients refused operation**

Table 3. Comparison of lesion type and lesion site by gender

	Male Number (%)	Female Number (%)	*P value*
Lesion type			
Menigocle	4 (18.2)	3 (10.7)	χ2 = 1.3 P=0.5
Meningomyelocle	15 (68.2)	23 (82.2)	
Myeloschisis	3 (13.6)	2 (7.1)	
Total	22 (100)	28 (100)	
Lesions site			
Cervical	0 (0)	1 (3.6)	χ2 = 4.4 P=0.3
Dorsal	0 (0)	2 (7.1)	
Dorsolumbar	7 (31.8)	13 (46.4)	
Lumbar	10 (45.5)	8 (28.6)	
lumbosacral	5 (22.7)	4 (14.3)	
Total	22 (100)	28 (100)	
Hydrocephalus at diagnosis			
Yes	10 (45.5)	8 (28.6)	χ2 = 3.5 P=0.06
No	12 (54.5)	20 (71.4)	
Total	22 (100)	28 (100)	

Operation and outcome

All patients except three whose parents refused operation were operated. All operations were done under general anaesthesia. We preferred early surgical intervention within the first 48-72 hours to prevent infection of the cerebrospinal fluid (CSF) and further neurological deterioration. To prevent infection, prophylactic antibiotics (ampicillin plus cloxacillin) were used during the preoperative and postoperative period in addition to intra-operative irrigation of the wound with normal saline. Infection was excluded by CSF investigation prior to the surgery. Postoperatively, assessment for hydrocephalus was done by daily postoperative measurement of the head circumference and trans-cranial ultrasound at any time when hydrocephalus was suspected. Baseline brain CT scan was performed before and after shunting. Once the diagnosis of hydrocephalus was confirmed, ventriculoperitoneal shunt insertion was undertaken. However, shunting was delayed as long as possible to prevent secondary infection. Our aim was to postpone shunting for at least 7 to 10 days after NTD repair.

One patient out of the 47 operated on for NTD (a case of myeloschiasis) developed superficial wound infection and two patients operated on for shunting developed upper end shunt obstruction by choroid plexus which were treated by shunt revision. After one year postoperative follow-up, all children operated on were alive of whom 5 (11%) developed epilepsy.

Sixty percent of patients had hydrocephalus at the time of diagnosis and from those who were operated on, 44% developed/continued to have hydrocephalus at one year follow up. In general and in subsequent long-term follow-up, 74% of the patients were finally found to have hydrocephalus.

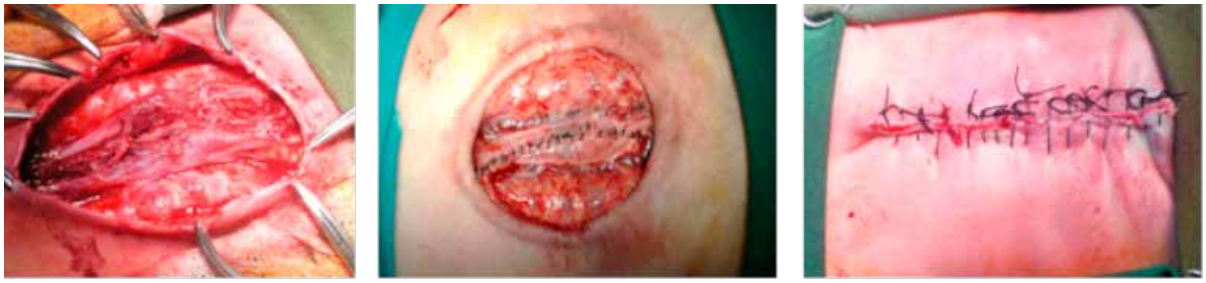

Figure 3. Operation on a case of myelomeningocele.

DISCUSSION

This study reports on 50 cases of open NTD in Iraqi Kurdistan with an estimated incidence of 4 per 10,000 live births. In 94% of cases the lumbar spine was affected alone or in combination with dorsal and sacral spine. Fifty six present of cases were female and, 8% had affected siblings and 12% had consanguinity in their parents. Operation was performed on 94% of cases with one year postoperative follow-up which showed zero mortality rate and 11% incidence of epilepsy.

Limitations

The current study is the first study about NTD in Iraqi Kurdistan and covers main epidemiological features and some important data on the clinical course and outcome of treatment. However, certain limitations have to be mentioned before interpreting findings of this study. Cases included in this study were all spina bifida; other forms of NTD which account for about half of all NTD cases were not included in our study. The sample may not be inclusive of all cases in the province since it is possible that some patients have been treated in other provinces particularly people living farther from the province center. Such a situation leads to underestimation of the incidence. It is also possible that some children may have died before arriving to hospital which is also a possible cause of underestimation.

Comparison with other studies

The incidence of NTDs reported in other parts of the world is variable and generally higher than the result of the current study. For example, 9.3 to 14.6 per 10 000 births in the USA, 12 in Ireland [3], 17.9 in England, and 28 to 32 in Iran [5]. Another study from the USA reported that the incidence of neural tube defects has decreased from 13 per 10, 000 births in 1970 to 6 per 10,000 births in 1989 [19] which is closer to the incidence reported in the current study. However, a much higher incidence of 30 per 10,000 births has been reported 20 by a study from Turkey which could be due to the fact that some forms of NTD were not included in the current study. In our study, females were more affected than males (56% vs. 44%), which is consistent with studies elsewhere. The Turkish study reports exactly similar percentages in females and males(56.1% vs. 43.9% respectively) [20]. An American study reports that spina bifida is less common in males and non-Hispanic black children [21]. However a previous study on NTDs in Sulaimaniyah reports 58% males and 42% females [15] . In our study 42% of the cases were from young mothers aged up to 25 years. This is consistent with a study from Sulaimaniyah which reports the commonest age of mothers as being between 20-29 years15 and with studies from USA [3].

In our study, the percentage of affected siblings were 8%, parental consanguinity was 12%, and 6% had other anomalies indicating a possible role of genetic and familial factors in etiology of NTD as reported by most studies. However, this has to be compared with the percentage of parental consanguinity in the general population in Kurdistan which is not available to the researchers, before making any conclusion about role of consanguinity. A previous study from Sulaimaniyah reported 45% consanguinity but has not found this to be a significant risk factor for NTD [15]. This difference in consanguinity rate could be due to different definitions of consanguinity. Five percent of NTD cases had siblings affected and 22% had additional congenital anomalies in Ireland [3], and 17% in the UK [22]. Other studies have listed several risk factors for NTD including genetic factors, poor socioeconomic status, race and environmental factors [19, 20].

In this study we followed up the children for one year after surgery and they all survived but 11% developed epilepsy. Behavior at pre-school age has been studied amongst children undergoing fetal meningomyelocle surgery and subsequent preterm delivery and no association has been found with increased behavioral problems, impaired social interactions and restricted behavior patterns [23].

In our study, only half of the patients were diagnosed during pregnancy indicating poor prenatal care. Prenatal screening is adopted by many countries to detect and manage NTD. A survey of 18 European countries [24] reported that 88% of cases of NTD were prenatally detected, of which 88% resulted in termination. Establishment of such a policy will is essential in order to help parents be prepared and make an informed decision about the pregnancy. Antenatal care must be strengthened for all pregnant women and folic acid supplementation should be emphasized. Further research is required in Kurdistan to identify all forms of NTD and to investigate the long-term consequences for operated patients in terms of physical, learning and behavioral outcomes.

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