

Short communication

Incidence of neural tube defects among neonates at King Hussein Medical Centre, Jordan

H.E. Aqrabawi¹

معدّل وقوع عيوب الأنبوب العصبي لدى الولدان، في مركز الملك حسين الطبي، في الأردن
هاشم عقرباوي

الخلاصة: على الرغم من أن عيوب الأنبوب العصبي هي من العوامل المهمة في حدوث وفيات الأجنة والرُضّع، إلا أنه لم تجر دراسات حول معدل وقوع عيوب الأنبوب العصبي في الأردن. ولذلك، أجرى الباحث دراسة استطلاعية مدتها عام في المدة من نيسان/أبريل 2002 إلى نيسان/أبريل 2003 في وحدة المواليد بمركز الملك حسين الطبي لتحديد معدل وقوع عيوب الأنبوب العصبي بين الولدان في الأردن. وتم تحري وجود عيوب الأنبوب العصبي في جميع المواليد الأحياء، سواء من أتموا مدة الحمل أم من وُلدوا قبل تمام مدة الحمل. وتمت مقابلة أمهات الأطفال المصابين بهذه العيوب، بعد الولادة، لسؤالهن عن الرعاية التي تلقينها قبل الولادة وعن سوابق وقوعات عيوب الأنبوب العصبي في الأسرة. ومن بين المواليد المشتركين في الدراسة والبالغ عددهم 5088 ولِيدا، كان 33 منهم مصابا بعيوب الأنبوب العصبي، أي بنسبة 6.5 حالة لكل ألف ولادة حية. ولم يكن لدى أي من الأمهات اللاتي وُلدن أطفالاً مصابين بهذه العيوب سوابق من الإصابة بهذا الداء، وحصلت جميعهن على الرعاية السابقة للولادة، ولكن لم تحصل أي منهن على الفولات (أملاح حمض الفوليك) كمكمل غذائي، بل لم يعرفن أهمية الفولات. ولم يتم تشخيص وجود هذا العيب قبل الولادة، على الرغم من إجراء التفريغ بالموجات الفائقة الصوت طوال مدة الحمل.

ABSTRACT Neural tube defects (NTDs) are important factors in fetal and infant mortality. There have been no studies on the incidence of NTDs in Jordan. A one-year prospective study was therefore conducted in King Hussein Medical Centre neonatal unit (April 2002–April 2003) to determine the incidence of NTDs among Jordanian neonates. All liveborn babies, both term and preterm, were assessed for NTDs. Mothers of babies with NTDs were interviewed postnatally regarding antenatal care and family history of NTDs. Of 5088 live births, 33 had NTDs, giving an incidence of 6.5/1000 live births. None of the women with affected babies had a history of NTDs and all had received antenatal care, but none had taken folate supplementation. The majority of the women had not had a diagnosis before the birth, despite having had ultrasound scans throughout their pregnancies.

Incidence des anomalies du tube neural chez les nouveau-nés au Centre médical Roi Hussein (Jordanie)

RÉSUMÉ Les anomalies de fermeture du tube neural représentent un facteur important dans la mortalité fœto-infantile. Il n'y a pas eu d'études sur l'incidence des anomalies du tube neural en Jordanie. Une étude prospective d'un an (avril 2002-avril 2003) a donc été réalisée au service de néonatalogie du Centre médical Roi Hussein pour déterminer l'incidence des anomalies du tube neural chez les nouveau-nés jordaniens. Tous les bébés nés vivants à terme et prématurés ont été examinés à la recherche d'une anomalie du tube neural. Les mères d'enfants présentant cette anomalie ont été interrogées après la naissance pour ce qui concerne la surveillance prénatale et les antécédents familiaux d'anomalies du tube neural. Sur les 5088 naissances vivantes, 33 présentaient une anomalie du tube neural, ce qui donne une incidence de 6,5 pour 1000 naissances vivantes. Aucune des femmes ayant un bébé avec anomalie du tube neural n'avait d'antécédents de cette anomalie et toutes avaient bénéficié d'une surveillance prénatale, mais aucune n'avait pris de suppléments en folates. Pour la majorité des femmes, il n'y a pas eu de diagnostic porté avant la naissance, bien qu'elles aient eu un suivi échographique de leur grossesse.

¹Neonatal Unit, Paediatric Department, King Hussein Medical Centre, Amman, Jordan (Correspondence to H.E. Aqrabawi: h_aqrabawi@hotmail.com).

Introduction

Abnormalities of the brain can be classified as malformations (a developmental defect in which the brain was never normal) and deformations, where an external insult has affected normal brain development causing an abnormality in subsequent structure [1].

Malformations of the central nervous system apparent at birth result from abnormalities in central nervous system development. These can be divided into two groups: disorders of dorsal induction and disorders of ventral induction.

Dorsal induction refers to the formation and migration of the neural tube, with subsequent development of the anterior tube into the primitive brain structures. These processes occur during the third and fourth weeks of gestation. Disorders occurring at this time include anencephaly, encephalocele, meningomyelocele and meningocele. These are collectively known as neural tube defects (NTDs), and the incidence of babies born with these disorders has fallen markedly over the last 10 years [2]. Ventral induction refers to development at the ventral end of the neural tube, particularly cleavage into bilateral hemispheres and ventricles, with thalamic and hypothalamic growth. These processes occur mainly in the fifth and sixth weeks of gestation. The commonest disorder occurring at this time is holoprosencephaly, which may be associated with abnormalities in facial development [3].

Worldwide the incidence of NTDs is declining, although it is still high in some parts of the world, particularly in developing countries. In the United Kingdom, it has fallen more than 10 fold in the last 30 years and in 1996 it was less than 0.5 per 1000 live births [4]. NTDs are important factors in fetal and infant mortality. In the United States, approximately 4000 fetuses are af-

ected annually, at least one-third of which are lost because of spontaneous or elective abortion [1,5]. The risk of early death among infants with open spina bifida varies considerably and depends on both the severity of the lesion and other factors such as the availability, use and acceptance of medical and surgical intervention. For example, the estimated rate of death among affected infants in rural areas of northern China is almost 100% [6], in Netherlands it is 35% and in United States it is 19% [7].

There is little information on the incidence of NTDs in Jordan as no previous studies have been conducted. We therefore undertook a prospective study in the King Hussein Medical Centre to estimate the incidence of NTDs among Jordanian neonates.

Methods

King Hussein Medical Centre is a large public hospital that serves the capital city of Amman and its suburbs. The estimated population of this area is about one million (the total population of Jordan is about 4 million). The maternity care unit receives about 400–500 deliveries monthly.

All liveborn babies, both term and pre-term, over the 1-year period from April 2002 to April 2003 were included in the study and were assessed for the presence of NTDs. Stillborn babies were excluded (17 babies). The number of babies with anencephaly, encephalocele, meningocele and meningomyelocele was recorded. All mothers of affected babies were interviewed postnatally by the paediatrician in the neonatal unit; none refused to participate. Detailed antenatal history (including previous medical illnesses, drug exposure, antenatal visits, vitamins supplements taken, ultrasound scans and time of antenatal

diagnosis of NTD, if such a diagnosis was made) was taken from all of the mothers. Family history was also reviewed. The medical records of those who were booked in our hospital were reviewed to assess: number of visits, vitamin supplementation, ultrasound diagnosis, time of diagnosis and mother's awareness of the problem of NTDs in general and whether her baby was affected.

Results

The total number of live births over the period of the study was 5088 babies. Of these, 33 had NTDs giving an incidence of 6.5/1000 live births.

The NTDs fell into the following categories:

- 30 cases (91%) of spina bifida cystica
- 28 cases (85%) of meningocele
- 2 cases (6%) of meningocele
- 2 cases (6%) of occipital encephalocele
- 1 case (3%) of Meckel–Gruber syndrome.

Meckel–Gruber syndrome is an autosomal recessive syndrome of encephalocele, polydactyly, polycystic kidney disease, cleft lip and palate and other craniofacial abnormalities. These babies usually die early in life due to central nervous system or renal defects. The baby with Meckel–Gruber syndrome and one with a large encephalocele died in their first few days. One baby with a small encephalocele and the two with meningocele were operated on early and survived with some disability (e.g. ventriculoperitoneal shunt, lower limb weakness, neurogenic bladder). Of the 28 babies with meningocele, 16 (57%) had lumbosacral lesions and 12 (43%) had large thoracolumbar lesions. All of them had hydrocephalus as confirmed by post-

natal ultrasound examination, total paralysis of both lower limbs and anal atony. In addition, 20 (71%) had associated skeletal deformities such as scoliosis, kyphoscoliosis and lower limb deformities. In all 28 cases, the families refused surgical intervention and took their babies home of their own choice after joint discussion with the neurosurgeon. All died within 3 months of birth.

When reviewing the maternal history of the women with affected babies we found the following.

- 31 mothers were multigravida (age range 25–35 years); 2 mothers were primigravida (age: 23 and 25 years).
- 23 mother were in consanguineous marriage (70%).
- None had been affected previously.
- All mothers were booked antenatally to deliver at our hospital.
- 29 women were followed antenatally by private doctors, mainly general practitioners. They had had monthly visits and ultrasound scans since early pregnancy, but the NTDs had not been diagnosed antenatally in any of them. Four women were booked and followed up monthly in our hospital's antenatal clinic but for all of them the NTD was only discovered late in the third trimester. All 4 were examined by ultrasound at every antenatal visit.
- None had received or was aware of the importance of periconceptual folate supplementation.
- None had any medical illness or received medications.
- None smoked.
- None had any family history of NTDs.
- All answered that they would opt to terminate of their pregnancies if they knew early on.

Discussion

NTDs in general, and spina bifida in particular, have become much less common than they were previously. There are 2 main reasons for this decline: periconceptual folate intake and antenatal fetal screening. In this study, neither of these measures were used with the mothers.

In our study, the incidence of NTDs was 6.5 per 1000 live births, which is high compared to other countries such as the United States (1 per 2000 live births), United Kingdom (0.5 per 1000 live births) and Australia (1.2 per 1000 live births) [8].

It is now known that folic acid is an important substrate for normal early neural tube development, and periconceptual supplementation of at-risk women with folic acid reduces the incidence of this condition by approximately 75% [9]. As it is not possible to know which women are at increased risk until their first baby is born with spina bifida, it is now recommended that all women intending to become pregnant take regular folate for 3 months prior to conception [10,11]. In our study, none of the women had received folate and they were not aware of the importance of folate supplementation to mothers intending to become pregnant. This may suggest that the women were not receiving appropriate and thorough antenatal care from their doctors.

The second factor in the falling incidence of NTDs is early fetal ultrasound to detect congenital spine or brain abnormalities. Various abnormalities can be assessed, including careful examination of the spine for a skin defect and examination of the skull base for the "banana" sign, which is a feature of Arnold-Chiari malformation. In many industrialized countries virtually all pregnant women are screened at about 18 weeks of gestation for fetal abnormalities.

The detection of a seriously abnormal fetus offers the opportunity for the parents to consider terminating the pregnancy [12]. In our study, most of the women had undergone ultrasound scans but the NTDs had not been detected, which may indicate a misuse of antenatal ultrasound scanning by inexperienced practitioners.

Another screening test for NTDs is blood α -fetoprotein; blood is taken from the mother at 14–18 weeks' gestation and α -fetoprotein measured. Those women with high serum levels should have repeat samples taken 1 week later. It has been found that α -fetoprotein is elevated in 90% of cases of anencephaly and in most cases of open meningomyelocele [13]. This screening test was not done in any of the affected mothers in our study although it is available in most of our medical centres.

Given the high incidence of NTDs found in this study, measures are needed to reduce this rate in our country. Folate should be given to all mothers intending to become pregnant and efforts should be directed to educate them about its importance. In addition, medical practitioners delivering antenatal care should take steps to minimize the occurrence of NTDs and at the same time increase early diagnosis to allow parents other options.

Currently in Jordan, anencephaly is the only accepted grounds for termination of pregnancy. Since all the women indicated that they would have sought to terminate the pregnancy had they known the outcome at an early stage, there may be a need to re-assess the criteria for termination in Jordan.

As data on NTDs in Jordan are limited, further studies are warranted to build a more detailed picture of these conditions in our country and work towards their reduction.

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