Neural Tube Defects : A Different Pattern in Northern Thai Population

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Abstract

The objective of this descriptive study was to describe the demographic and sonographic patterns of fetal neural tube defects (NTDs) in Thai pregnant women. The study was conducted at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University. The subjects included all pregnancies with diagnosis of fetal neural tube defects. Basic clinical data of the subjects was prospectively collected at the time of diagnosis for NTDs and followed-up until delivery. Antenatal diagnosis was based on sonographic criteria. The results showed that the incidence of NTDs was 0.66/1,000 births, however, spina bifida was very rare, found in only 0.06/1,000 births, similar to encephalocele. All anencephalic fetuses had no concurrent spina bifida, and only a few cases had other associated anomalies. Ultrasound was able to diagnose NTDs with very high accuracy. All cases of antenatal diagnosis were electively terminated. In conclusion, NTDs in the Thai population were rather rare when compared to that of the Europeans and spina bifida was extremely rare. The accuracy of antenatal diagnosis of NTDs with ultrasound was highly reliable.

Key word : Neural Tube Defect, Ultrasound, Antenatal Diagnosis

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Neural-tube defects (NTDs) result from failure of tubal closure by day 26 to 28 after conception(1). This produces a spectrum of cranial and spinal canal defects that range from anencephaly to very slight vertebral defect. Its incidence in the USA has been estimated at 1/1,000 deliveries, anencephaly (0.6-0.8/1,000) and open spina bifida (0.5-0.8/1,000)(2). Anencephaly is much more common in the UK, however, with an incidence as high as 6.7/1,000 in Belfast(3). The three major types of NTDs

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are anencephaly, cephalocele and spina bifida. Less common types of NTDs include exencephaly and iniencephaly. Anencephaly is characterized by absence of the cranium along with cerebral hemispheres that are either rudimentary or absent. A cephalocele is a protrusion of the meninges and, frequently, brain tissue through a defect in the cranium. Spina bifida refers to a defect in the spine resulting from failure of the two halves of the vertebral arch to fuse. These lesions usually occur in the lumbosacral and cervical regions. If the meninges protrude through this defect, the lesion is designated a meningocele; if neural tissue is included, it is a meningomyelocele. The vast majority of NTDs are sporadic and believed to be multifactorial in origin[4]. For a long time, it seems that the pattern of NTDs in our experience has been so different from that mentioned elsewhere, since spina bifida has been found very rarely. Furthermore, the prevalence of NTDs is highly variable, and depending on an individual's geographical location. Therefore, we have prospectively accumulated the data of a ten-year experience to describe the pattern of NTDs in our population.

MATERIAL AND METHOD

This descriptive study was undertaken at the Department of Obstetrics and Gynecology, Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University, Thailand. The subjects were pregnant women giving birth at Maharaj Nakorn Chiang Mai Hospital during June 1989-May 2000. The data was prospectively collected at the time of diagnosis for NTDs. We divided the subjects into two groups. The first group (42 out of 46) was pregnancies with fetal NTDs prenatally diagnosed with ultrasound. Ultrasound examinations were selectively performed with indication, using Aloka model 650, 680 or 1700 with transabdominal probe of 3.5 MHz and all were done by the authors. Once NTDs were diagnosed, the pregnancies would be followed until delivery. The second group was pregnancies with NTDs fetuses, who were diagnosed at the time of delivery. Antenatal sonographic diagnosis of NTDs was based on the standard criteria described elsewhere[5]. Demographic data of the patients were taken and recorded. Pregnancies suspected of NTDs, referred from other hospitals for ultrasound examination, were not included into the study.

RESULTS

During the study period, a total of 66 cases of NTDs were diagnosed at Maharaj Nakorn Chiang Mai Hospital. Twenty were referred from other hospitals and diagnosed by ultrasound. The remaining 46 cases, attending and delivering at Maharaj Nakorn Chiang Mai Hospital, were analyzed. The basic data of the patients is shown in Table 1. The mean maternal age (±SD) was 25.9±6.1 years, range 16-41 years. The mean gestational age (±SD) was 23.7±6.7 weeks, range 11-43 weeks. Most of them had a normal delivery, 2 cases not examined by ultrasound were delivered by caesarean section, due to placenta previa in one case and misunderstood breech presentation in the other. Two cases of anencephaly, one case of exencephaly and one case of spina bifida could not be detected before delivery. Six were diagnosed for NTDs in the intrapartum period and ultrasound examination was requested due to clinical suspicion. Thirty-six were antenatally diagnosed. The subgroups of neural tube defects are shown in Table 2. The incidence

Table 1. Basic clinical data of the pregnant women.

Birthweight	Means	1,292	grams
	SD	1,231	grams
	Range	50-3,400	grams
Gestational age	Means	23.7	weeks
	SD	6.7	weeks
	Range	11-43	weeks
Delivery	Normal	39	(84.8%)
	Forceps	1	(2.2%)
	Caesarean	2	(4.3%)
	Evacuation	4	(8.7%)

Table 2. Subgroups of neural tube defects (NTDs).

Total cases of NTDs	66	cases
Antenatal care at Maharaj Nakorn Chiang Mai Hospital	46	cases
Undiagnosed	4	cases
Intrapartum diagnosis	6	cases
Antenatal diagnosis	36	cases
Classification of NTDs	**Number**	**%**
Anencephaly	37	80.4
Encephalocele	3	6.5
Spina bifida	4	8.7
Exencephaly	2	4.3

Table 3. Sonographic data of NTDs.

Ultrasound before delivery	42 cases
Accuracy	100%
Indications for ultrasound	
Large-for-date	16
Small-for-date	7
Premature labor	7
Intrapartum suspected	7
Uncertain date	5
Anencephaly	35
Isolated	30
Cleft lip/palate	3
Omphalocele	3
Club foot	3
Limb-body-wall complex	1
Cephalocele*	3
Meningocele	2
Encephalocele	1
Multiple malformations	1
Spina bifida*	3
Splaying of spines	3
Lemon sign	3
Cerebellar sign	3
Multiple malformations	2
Excencephaly	1

* Multiple lesions in one cases

of NTDs was 46/69,207 (0.66/1,000) births. The incidence of anencephaly was 37/69,207 (0.53/1,000) births, female:male ratio of 2:1 (25:12), whereas, spina bifida occurred in only 4/69,207 (0.06/1,000) births, similar to that of cephalocele. The most common type of NTDs was anencephaly, and accounted for 80.4 per cent of cases. Only 42 cases of 46 deliveries were examined with ultrasound and all of them were correctly diagnosed before delivery. Of 35 fetuses with anencephaly, ultrasound demonstrated the absence of a skull with rudimentary brains in all cases. Polyhydramnios was visualized in 57.1 per cent (20/35) of anencephaly but none of the other types. Most anencephalic fetuses had no other malformations and none of them had spina bifida. However, the minority (6/37) had associated anomalies. Of 4 cases with spina bifida, 3 had lesions at the lumbosacrum whereas the defect of the other one was located at the cervical spines. Splaying of dorsal posterior ossifications, banana sign and lemon sign were demonstrated in all cases. All skull defects in cases of cephalocele were located at the occipital regions. Chromosome study was successfully done in only 29 cases, and all were normal except for one fetus with trisomy 18. All NTDs with antenatal diagnosis were electively terminated and confirmed by postnatal autopsies.

DISCUSSION

In general, anencephaly and open spina bifida occur with nearly equal frequency of 1/1,000 births, with some variation, depending upon geographic location and socioeconomic factors[6]. Encephalocele occurs less often with a frequency of about 1/4,000 pregnancies. Nevertheless, not only was the incidence of spina bifida in this study very low, when compared to that of the West, but the overall incidence of NTDs was also rather rare.

Unlike anencephaly in the Western world which had associated anomalies in 33 per cent of the cases[7], especially spina bifida (27%), we found only 5/37 had associated anomalies. Furthermore, there was no spina bifida among them. However, since anencephaly itself is uniformly fatal, further search for associated anomalies is not of clinical importance.

Anencephaly is virtually 100 per cent detectable with ultrasound[8]. Furthermore, the likelihood of open NTDs associated with abnormal serum values is decreased by 95 per cent or more if the ultrasound examination is normal and is performed in a specialized center[9,10]. A woman with an elevated maternal serum alpha-fetoprotein (MSAFP) should be counseled that the risk is reduced by 95 per cent or more if high resolution ultrasound is normal[11-13]. Nearly 100 per cent accuracy of detection of NTDs with ultrasound. Thus, measurement of amniotic fluid alpha-fetoprotein (AF-AFP) was probably not neccessary or cost effective if high-resolution ultrasonography was normal[12,14,15].

Although MSAFP screening is widely recommended now[16], it is probably not justified or cost-effective for NTDs identification in our population. This is due to the fact that the incidence of NTDs in our population is rather low and especially, the pattern of NTDs in Thai pregnancies is so different from that of the Western world. Nearly all NTDs are anencephaly, much easier to detect by ultrasound than spina bifida. Even in cases of elevated MSAFP, there is no justification for analysis of amniotic fluid if the targeted ultrasonic examination was normal.

Sonographic diagnosis of anencephaly is based on absence of the skull. After 14 weeks, it is abnormal for the bony structures of the skull above the orbits not to be seen. Of course, the head must be accessible to ultrasound examination (i.e. not hidden in the pelvis of the mother) for these structures to be adequately visualized. When the area cerebrovasculosa prominent, an ill-defined mass of heterogeneous density may be seen by ultrasound. In addition, many of these pregnancies are complicated by hydramnios, presumably due to impaired fetal swallowing(5). Anenecephaly is commonly associated with other anomalies, especially spina bifida, found in 27 per cent of cases (17). Surprisingly, we did not find a single case associated with spina bifida. This is, presumably, due to the racial factor.

Sonographically, cephalocele appear as sac-like protrusions about the head not covered by bone. The diagnosis can be made with certainty only if a defect in the skull is detected. Such a defect may be small, however, and may be difficult to visualize. Like other reports, we found that the occipital region was the most common site. Sonographically, spina bifida is seen as a dysrhaphic spinal defect, soft tissue findings (myelomeningocele sac and/or disruption of the overlying integument), and associated cranial findings (hydrocephaly, banana sign or lemon sign) with highly predictive value(5). We could not make any conclusion for the sonographic findings in this series because of the small number of cases, however, we found that all four cases had both signs of spinal defect and cranial signs.

It is essential to realize that most NTDs had no risk factor. Thus, any clinical clue, especially polyhydramnios, might warrant an ultrasound examination. Anencephaly is probably the most common cause of gross hydramnios, which occasionally may be sufficiently massive to require therapeutic amniocentesis. The prevalence of polyhydramnios in the study presented here was rather high (57.1%). This might be due to delayed diagnosis as more prevalence is found in advanced gestational age(18). Without routine ultrasound, we found that antenatal diagnosis might be delayed, or impossible in some cases. Clinical suspicion alone may not be sensitive for early detection.

Among anencephalic fetuses, females are affected more frequently than males, with a frequency of 2:1. However, this sex difference may be not as much as in Western reports, the ratio of 4:1(17). For other forms of NTDs, the sample size was too small to evaluate.

The vast majority of NTDs are sporadic and believed to be multifactorial in origin(4). The gene responsible for many cases of NTDs has been identified(19) and may invlove a defect in the production of an enzyme neccessary for folate use. Recently, a gene possibly responsible for some cases of NTDs was detected(20). This abnormal gene represents a variation in the gene that produces the enzyme, 5,10-methylenetetrahydrofolate reductase, which is crucial for folate use, specifically in homocysteine metabolism. Preconceptional folic acid supplementation may decrease recurrences of NTDs. For women with a prior affected infant, supplementation is currently recommended with folic acid, 4 mg daily. Women without a history of NTDs should receive 400 ug of folic acid prior to attempting pregnancy and during the first trimester(21).

In conclusion, the incidence of NTDs was 0.66/1,000 births, however, spina bifida was very rare, found in only 0.06/1,000 births, similar to encephalocele. All anencephalic fetuses had no concurrent spina bifida. These findings indicate the different spectrum of NTDs in our population. Finally, antenatal diagnosis of NTDs with ultrasound was highly reliable.

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ท่อประสาทไม่ปิด : รูปแบบที่แตกต่างในประชากรไทย

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การศึกษาเชิงพรรณาเพื่อวิเคราะห์ลักษณะทางประชากรศาสตร์และคลื่นเสียงความถี่สูงก่อนคลอดของทารกที่ท่อประสาทไม่ปิด (neural tube defects; NTDs) ในสตรีไทยที่ตั้งครรภ์ กลุ่มศึกษาได้แก่สตรีตั้งครรภ์ทุกรายที่ได้รับการวินิจฉัย (NTDs) และคลอดในโรงพยาบาลมหาราชนครเชียงใหม่ ในช่วงระหว่างมิถุนายน พ.ศ. 2532 ถึง พฤษภาคม พ.ศ. 2543 โดยทำการทบทวนข้อมูลพื้นฐานทางคลินิกและข้อมูลทางคลื่นเสียงความถี่สูงของผู้ป่วยทุกรายที่ได้รับการ พิสูจน์ว่าทารกเป็น NTDs การวินิจฉัยก่อนคลอดถือตามเกณฑ์ของคลื่นเสียงความถี่สูง ผลการศึกษาพบว่าอุบัติการณ์ของ NTDs 0.66/1,000 การคลอด และ spina bifida พบน้อยมาก คือพบเพียง 0.06/1,000 การคลอด encephalocele ก็พบน้อยในทำนองเดียวกัน ทารกไร้กระโหลกทุกรายไม่มี spina bifida ร่วมด้วย แต่มีความพิการอื่นร่วมด้วยในจำนวนน้อยราย คลื่นเสียงความถี่สูงสามารถให้การวินิจฉัย NTDs ถูกต้องทุกราย (ร้อยละ 100) ทุกรายที่ได้รับการวินิจฉัยก่อนคลอดได้เลือกยุติการตั้งครรภ์ โดยสรุป NTDs ในโรงพยาบาลมหาราชนครเชียงใหม่พบได้ค่อนข้างน้อย เมื่อเปรียบเทียบกับประเทศทางตะวันตก โดยเฉพาะอย่างยิ่งชนิด spina bifida การวินิจฉัยก่อนคลอดด้วยคลื่นเสียงความถี่สูงมีความเชื่อมั่นได้สูง

คำสำคัญ : ท่อประสาทไม่ปิด, คลื่นเสียงความถี่สูง, การวินิจฉัยก่อนคลอด

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