Radiological study of Neural Tube Defects

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Abstract

Neural tube defects (NTDs) are a group of severe congenital abnormalities result from the failure of closure of anterior neuropore or neural fold .The pattern of inheritance of these complex defects is multifactorial, making it difficult to identify the underlying causes.

Recent studies have shown that the addition of folic acid (Vitamin B9) to the diet of child-bearing age women may significantly reduce although not eliminate, the incidence of NTDs.

Imaging tests may be used to help in detection of defects in the developing fetuses. These may include: Ultrasonography, MRI and CT scan.

During the period of the work, routine antenatal trans-abdominal ultrasound examination was made for 6720 outpatients' women with missed period of 12-36 weeks in the private clinic during the period from september 2014 to october 2016 in Baghdad city.All patients are followed post deleivry. Thirty two patients were diagnosed as NTDs sonographically. Twenty nine cases were terminated according to the parent decision. Post-termination, MRI and CT scan was performed on 25 cases with anencephaly and encephalocele to show the extend of the brain tissue and the defect in the skull vault**.**

Blood sample from 200 pregnant women was aspirated in the laboratory for folic acid estimation. Pregnant woman who taking folic acid preconception were excluded, Among the cases 82.4% of them were with low folic acid level.

The frequency of NTDs in the present work was 0.47%, the majority of cases was anencephaly 17 (53%) followed by encephalocele 8(25%) and the spina bifida 7(22%).

Key words: NTDs; Ultrasound, MRI, CT scan, congenital abnormality.

Introduction

Neural tube defects (NTDs) are a group of severe congenital abnormalities resulting from the failure of closure of neural tube. Identifying the underlying causes are very difficult ,because of the multifactorial complex defect(1).

The main theory behind the origin of this birth defect is that it is caused by a failure of the anterior neuropore or neural fold to close correctly. In addition, decreased blood levels of some vitamins, most notably folic acid, may cause neural tube defect (1).

Maternal nutritional factors seem to contribute substantially to the complex aetiologies of NTDs. The most important factors among these is the periconceptional use of supplements containing folic acid, which is associated with a reduction in the risk of women having NTD-affected pregnancies.

Other studies showed that taking folic acid or multivitamins containing folate during the periconceptional period resulted in a four fold reduction in the risk of recurrence (2, 3).

Diagnosis of NTDs include laboratory and non-laboratory test .Non-laboratory test include .Ultrasonography, MRI and CT scan. Ultrasonography is used antenatally for screening while MRI is the study of choice for imaging neural tissue and for identifying contents of the defect in the newborn. This allows the visualization of associated anomalies, both intraspinal and intracranial (4). CT scan allows direct visualization of the bony defect and anatomy.

Aim and objectives

The aim of the study was to highlight the incidence of NTDs

1-Determine the frequency of NTDs.
2-Compare the gender differences.
3-Determine the associated risk factors to NTDs.
4-Determine the radiological appearance of NTDs and other associated anomalies.
5-Determine the role of folic acid in preventing NTDs.

Patients and methods

In a prospective study 6720 pregnant women consulting a private ultrasonographic clinic were examined ultrasoungraphically.All patients are followed post deleivary.The study was carried out during a peroid of two years duration from september 2014 to october 2016. Inclusion and exlusion criteria was included in the study. The inclusion criteria: was included all women who consulted the clinic with 12- 36 weeks missed period and were subjected to ultrasound examination . While exclusion criteria was all pregnant women with < 12wk or > 36 weeks gestational, women with missed period but were not pregnant were also excluded.

Pregnant women with fetus proved to have well developed skull vault (i.e. hydrocephalus, iniencephaly) were also excluded.

Calculation of the gestational age depends on the history of LMP confirmed by U/S assessment of fetal age by measuring the Biparietal diameter

(BPD). Femoral length (FL). Head circumference (HC). Abdominal circumference (AC) Crown rump length (CRL) .Humerus length (HL). In case of anencephaly measurements was depended on measuring FL, AC and CRL. For assessing the age of fetus because of the absence or incompletely developed skull vault.

After the diagnosis of NTDs, the woman referred to obstetrician for the termination of pregnancy .Then the fetus after termination were examined clinically to determine the type of anomaly then a picture was taken for the case .(after taking the permission)

MRI and CT were performed for 25 cases with anencephaly and encephalocele to show the extend of the brain tissue and the defect in the skull vault.

Folic acid estimation: A sample of blood from 200 pregnant women was aspirated in the laboratory for folic acid estimation. Any women with history of preconception folic acid therapy were excluded.

A Human folic acid (FA) ELISA kit, CSB-E17109h from CUSABIO Company, was used. The procedure followed according to what is mentioned in the user manual (5). A range of 12.5-200pg/ml is considered as normal range.

Results

The frequency of NTDs was 0.47%, of the total: Thirty two patients were diagnosed as NTDs sonographically . The majority of cases was anencephaly (17 cases 53%) followed by encephalocele

(8 cases 25 %) while spina bifida cystica was (7 cases 22 %) out of which 5/7 cases were myelomeningocele and 2/7 cases were meningocele.

NTDs were, generally, more common among female than male fetuses with a ratio of 3:1; 24 cases (75%) were female while 8 cases (25%) were males. As shown in (Table 1). Moreover the ratio was highest in case of anencephaly to reach about 5:1.

Table 1: Type of NTDs related to gender

NTDs	Male %	Female %	Total
Anencephaly	3 (9.3%)	14 (43.7%)	17(53.1%)
Encephalocele	2 (6.2%)	6 (18.7%)	8(25%)
Spina bifida	3 (9.3%)	4 (12.5%)	7(21.9%)
Total	8(25%)	24(75%)	32(100)

P-value =0.432

Table 2: Risk factors in NTDs.

Risk Factors	No.	%*
Consanguinity	27	84.4
Low socioeconomic status	24	75
previous NTD	6	18.7
Poorly controlled diabetes	5	15.6
Treatment with antiepileptics or trimethoprim drug	3	9.3
Obesity	2	6.2
No obvious risk	5	15.6

*Note: the percent is calculated out of the total number = 32.

19 patients have more than one risk factor.

Residency and risk factors

The frequency was higher in rural area than urban 21(65.6%) and 11(34.4%) respectively among the risk factors consanguinity, low socioeconomic status previous NTDs, poorly controlled diabetes and other were the most pronounced. Table (2) show the risk factors in the present study.

NTDs and termination

Twenty one cases were terminated after 20 weeks of gestation. (Table 3) shows the type of NTDs related to time of termination. All anencephalic cases were terminated, 7(87.5%) of encephalocele cases were terminated except one case refused and continued to term when born alive and died after 2 months, 5(71.4%) of spina bifida were terminated because of its association with severe hydrocephalus and very thin or absence of brain tissue, while 2(28.6%) cases continue to terms because they were only meningocele without hydrocephalus and were surgically correctable.

Table 3: Type of NTDs related to time of termination.

NTDS	No.	Percentage	Early termination < 20 weeks	Late termination > 20 week
Anencephaly	17	53.1	5	12
encephalocele	8	25	3	4*
Spina bifida	7	21.9	-	5**
Total	32	100	8	21

- **P-value=0.253** *One case refuse termination.

** two cases correctable so continued to term

Table 4: Folic acid level estimation in relation to NTD

Folic acid level(pg/ml)	Women without NTD. No (%)		Women with NTD No. (%)		Total No. (%)
Normal (12.5-200)	165	90.2%	18	9.8%	183(100%)
Low(5- 12.5)	3	17.6%	14	82.4%	17(100%)
Total	168	84%	32	16%	200(100%)

- P-value <0.000

Folic acid level

The study also clarifies the relation of folic acid level to the frequency of NTDs. Fourteen patients out of thirty two have low serum folic acid Table 4 show these results.

In present study the pregnant women with low serum folic acid level were treated with folic acid supplementation in
4 mg/day , 2 months before conception and continued up to second trimester , their follow up U/S is normal and some of them gave birth to normal infants including the 3 with history of recurrences.

Ultrasound, MRI and CT finding

Thirty two cases were detected by U/S examination. (figure 1) shows a thirty four week gestational age fetus with anencephaly was diagnosed using ultrasound by measurements of FL = 68 mm, HL = 53 mm, AC = 345 mm. Absence of cranial vault above the orbit with bulging of the eye (frog eye appearance) .The case was associated with Polyhydramnios (red arrow) excessive amount of liquor mostly due to

defect in swallowing due to absent brain Post termination the following physical finding are detected: flat nose, absent skull vault above the orbit, very short or absent neck, Bulging eyes, enlarged tongue and lips, distended abdomen with kyphotic change (figure 2). MRI post termination (figure 3 and 4) shows tissue .
absent cranial vault above the orbit. With small cervical vertebra and kyphotic change in thoracic vertebra. Figure 5 shows: CT of anencephaly absent vault.
The defect may extend to the thoracic or lumber region (figure 6).

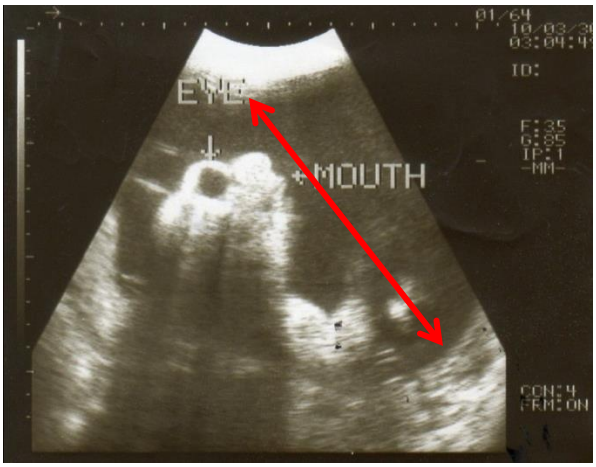

Figure 1: Coronal ultrasound shows frog eye appearance.

Figure 2: Thirty four week fetus with anencephaly.

Figure 3: MRI coronal view (T2 weighted) shows absence of the cranial vault of fetus of 34 weeks of gestation after termination.

Figure 4: MRI saggital veiw shows kyphosis in fetus with anencephaly .

Figure 5: CT of anencephaly absent vault

Figure 6: NTD extends to the lumber region

NTDs may be associated with other congenital abnormality such as omphalocele. In present study two of the cases the NTDs is associated with omphalocele.

figure (7) shows ultrasound of fetus of 13 week diagnosed as anencephaly (red arrow) with protrusion of liver outside the abdominal cavity (blue arrow) and herniation of bowel from abdominal cavity (green arrow). Post termination figure (8) shows the same fetus above with protrusion of both lungs (blue arrow) and heart (green arrow) outside the chest cavity, with herniation of bowel (yellow arrow) and liver (red arrow) due to absence of anterior abdominal and chest wall.

Encephalocele usually diagnosed by U/S antenatally; Brain matter herniate through a defect in skull. A cranial meningocele contains only meninges, encephalocele contain brain tissue; a ventriculocele contains part of the ventricle within the herniated part of the brain.

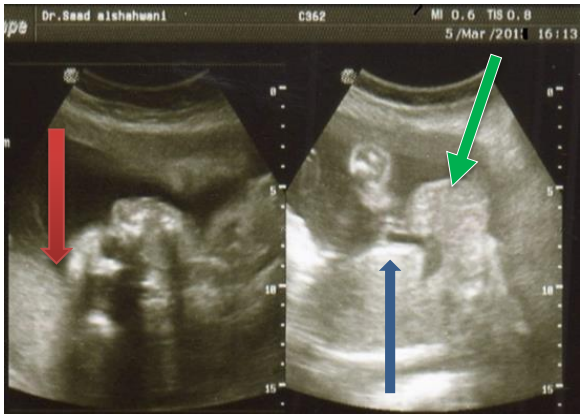

Figure 7: U/S of fetus with anencephaly and omphalocele

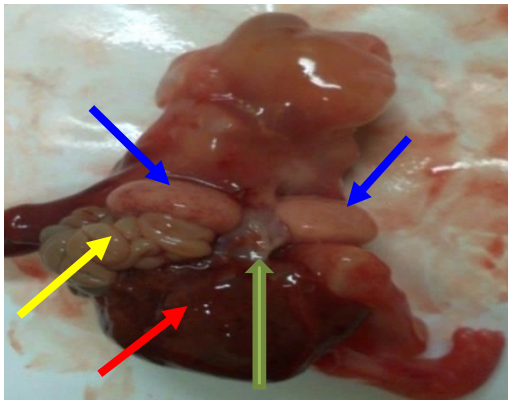

Figure 8: anencephaly and omphalocele

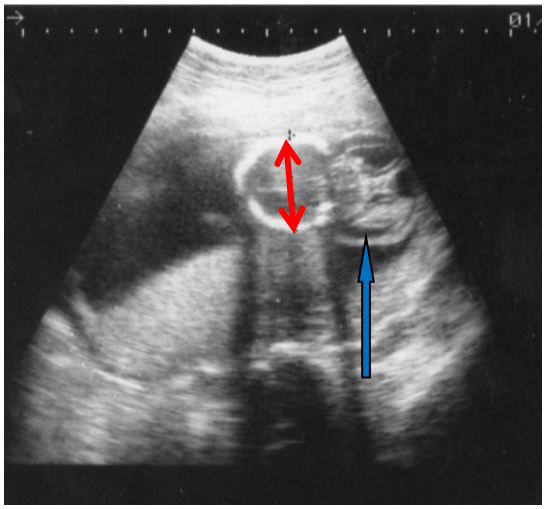

Figure 9:U/S of fetus with occipital encephalocele.

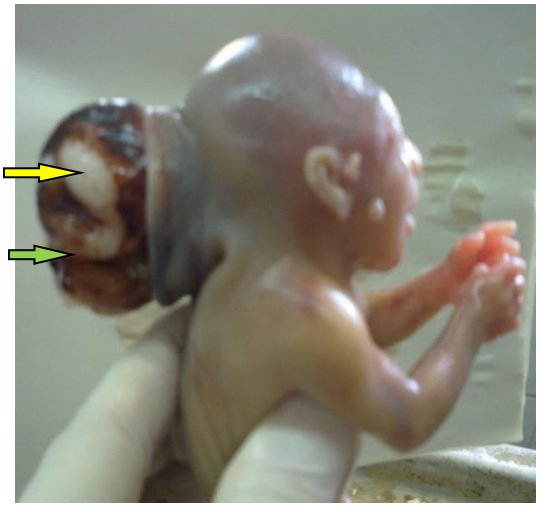

Figure 10: Occipital encephalocele

Figure (9); reveals U/S of 16 week gestational age fetus according to the BPD =3.59 mm (red arrow), FL=22 mm. HL = 17 mm. HC=132 mm and AC = 106 mm. An encephalocele shows the protrusion of the brain through the defect in the occipital region (blue arrow).post termination figure (10) shows encephalocele after termination of the same fetus with gyri (yellow arrow) and sulci (green arrow).

Figure (11) Shows MRI of occipital encephalocele post termination; herniation of the brain is seen clearly from a defect in the occipital region (red arrow head) otherwise the skull vault is well developed.

Figure 11: MRI of encephalocele shows herniation of brain through a defect in the skull.

Figure (12) reveals CT of the same fetus in figure (10) with defect in the bone in the occipital region (Red arrow) herniation of brain tissue is seen through the defects (Yellow arrow).

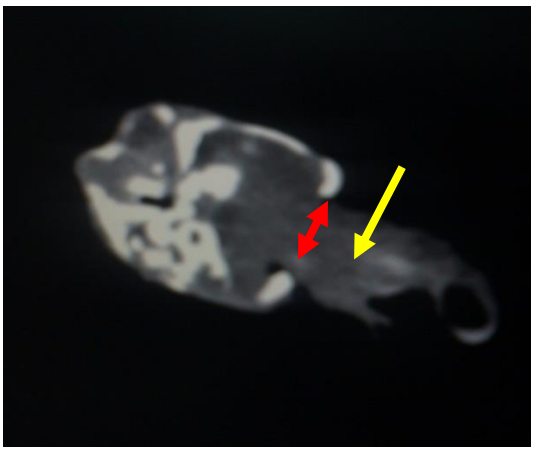

Figure 12: CT of fetus with encephalocele.

Discussion

The incidence of NTDs in present study was 0.47% which is approximately similar to other studies performed in other countries; annually worldwide an estimated 300,000 or more babies are born with spinal bifida and anencephaly. In the United States reported birth prevalence rates vary from 4 to 10 per 10,000 live births. Some studies in countries such Ireland, United Kingdom, China, Hungary, Mexico and India (3.9 to 9 per1000) has reported higher rate (6) Myelomeningocele, anencephaly , and encephalocele are the most common type of NTDs (7)so as the present study revealed that anencephaly was the most common type among the NTDs (53%), while it comprised 60% in another study, its incidence in USA was approximately 1/1000 deliveries the risk of having another affected child is increased compared to the risk in the general population (8) .The incidence of both anencephaly and spina bifida accounted for up to 95% of all NTDs with equal prevalence (9).

With respect to consanguinity, NTD rates have been found to be higher when the parents are related (10) although not all studies identified this association (11) .The present study showed that, 27(84%) of parents with affected newborns had consanguineous marriage (first-cousin). The relatively high proportion of first cousin marriages among parents of individuals with neural tube defects suggests that some of these cases are due to monogenic disorders. The possibility

that consanguinity could be a risk factor for .NTD in a population requires further research (12).

Women had low folic acid level formed 82.4% in the result of the present study in pregnant women who had NTDs. Folic Acid might weaken the effects of certain medicines prescribed against epilepsy. Some medicines cause the level of Folic Acid to fall , hence increasing the risk to NTDs (13)

About 300,000 children are born each year with severe birth defects due to maternal folate deficiency; adequate intake can prevent 225,000 cases (75%).Food folate is broken down and converted to the active form in the small intestine before absorption (14).

The NTDs, in present study, were more common among females than males fetuses with a ratio of 3:1, and nearly 5:1 in anencephalic fetuses, 3:1 for encephalocele and nearly 1.3: 1 for spina bifida.compering with other study The female sex ratio was significantly higher for anencephalic and spina bifida and anencephalic compared with spina bifida while in another study the Girls are three times more likely than boys to have anencephaly (15).

The sonographic diagnosis of anencephaly is based upon the absence of brain and calvaria superior to the orbits on coronal views of the fetal head. The sonographic diagnosis of this condition is highly accurate and should not be missed on any routine second- or third-trimester ultrasound examination. In the present study U/S appearance is characteristic and pathognomonic in cases of anencephaly, encephalocele It has accuracy of 100% Two cases of small meningocele was missed diagnosed as normal in U/S because the lesion was very small The sensitivity of U/S in NTDs was 94.2%.

Conclusions

Ultrasound is the method of choice in diagnosis of NTDs antenatally.

1- NTDs is a common condition in our community (0.47%).

2- The commonest type of NTDs was anencephaly.

3- NTD may be associated with other congenital abnormality such as omphalocele.

4- Women with low socioeconomic status are at highest risk.

5- In 6 cases the neural tube defects extend below the cervical region and extend to the lumber region while the distal part of the neural tube is closed so the fusion of neural tube extend from distal or caudal neuropore toward cranial neuropore in such cases

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