Study of Neural Tube Defects at Al-Diwaniyah Province / Iraq

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Abstract

Background: The Neural tube defects NTDs refers to defect occurr at birth resulting from defect in closure of the neural tube during early intra uterine life after conception; these anomalies are usually divided into cephalic and spinal forms. They include three main type , anencephaly, spina bifida and encephalocele , These NTDs are considered important causes of morbidity and mortality in infancy, childhood, and even young adulthood.

Objective: The aim of study is to study the type and incidence of the neural tube defect and it is it is risk factors and other associated variable.

Methods : This descriptive prospective study was carried on 120000 lived newborns from December 2013 to December 2015 in al diwaniya teaching hospital , neurosurgical department and pediatrics hospital in al diwaniya province in south west Iraq ,the questionnaire include all the information's case were defined as women residing in the al diwaniya government , delivered live or still born with neural Tube defect . important feature related to the neonates and their parents like gender , date of birth , type of neural tube defect ,father and mother age ,consanguineous marriage, drug take during pregnancy ,maternal diseases ,previous history of neural tube defect .

RESULTS : During a period of three years 2013-2015, there were (120,768 total ) birth ; the number of total births registered during the 3 years was 41761 in 2013, 39353 in 2014, and 39652 in 2015 . Among this sample population,112 women had fetus or newborn with NTD ( 1.078 per 1000birth ). An encephaly {3 (2.7%)} , spina bifida {103(92%)} , Encephalocele{6(5.3%)} Meningocele {20(17.9%)} ,Meningomyelocele {76 (67.9%)} , myeloschiasis {7 (6.2%)}. The age of 112 women that her babies affected NTDs , 30(26.8%) had 16-25 years , 55 (49.1%) had 26-35 years while 27 (24.1%) had above 35 years .

Conclusion: This study showed that folate deficiency are very important in reducing the NTDs occurrences consanguineous marriage is not important risk factor for NTDs.

Key word: Neural tube defect, risk factor, Iraq

Introduction: 

The term “Neural tube defects” NTDs means a collection of birth defects resulting from defective development of the neural tube during early fetal life after conception [1]This defect can occur at different levels of spinal cord , from cephalic to the caudal end, and to a variable degree. This results in abnormalities of the meninges, the vertebrae or skull, with a variable impact on the nervous tissue [2]. There are two main malformations of NTDs cephalic and spinal forms and they include firstly anencephaly and spina bifida and lastly encephalocele [3]. These diseases are considered an important causes of morbidity and
mortality in infancy & childhood & in young adulthood also.[4] Each year
in the US , the spina bifida and anencephaly are the two most common
form of NTDs, occurring in 1/4000 pregnancies.[5]. The NTDs range
from a very simple and often subclinical small opening in the
posterior vertebral canal, to a loss of closure of the whole tube, producing
the most severe type of neural defect, the craniorachischisis. Spina bifida
is classified into spina bifida cystica, aperta, and occulta. The incidence
of NTDs ranges from ten to one hundred per 10,000 births with similar
frequencies of spina bifida and anencephaly [6]. Incidence of NTDs
has been reported as slightly more than nine to 14.6/10 000 births in the US,
twelve in Ireland [7] , more than seventeen in England, fifteen in
Turkey [8]& about thirty in Iran [9] .
NTDs occur more frequently in the white color population and female sex
affected commonly than male. In more than eighty percent of NTDs the
lumbo-sacral region is site of defect .
With myelomeningocele, the external
sac is filled with cerebrospinal fluid
(CSF)&spinal cord& nerves roots that have
pulging through a defect . With
meningocele, the defect contains
meninges and cerebro- spinal fluid, and
may or may not lead to symptoms.
When the defect is opened & exposed
called spina bifida aperta, while
anencephaly involves the absence
of the skull bone, and the cerebral
hemispheres are completely lossed or
malformed or reduced.[10] Anencephaly is a
common CNS anomalies in the
Western countries, and seen in more
than thirty five times more frequently
to certain drugs like chemotherapy,
anticonvulsant, maternal diabetes,
fever, low economic state, and folate
deficiency have been shown to
increase the risk of NTDs .[12,13,14,
15,16,17,18,19,20,21] Hereditary
causes are believed to be important.[12] The prevalence of NTD
at birth varies considerably by
countries, family descent and ranges
of incidence is variable , as high as 1
/100 births in certain area of China ,
to approximately 1/5000 or less in
some Scandinavian regions .
important related factors for NTDs
have been reported as past history of
NTDs; age of the mother less than
twenty or more than thirty five ;
multipara; poor nutritional status and
poor both maternal and father
educational levels; low maternal folic
acid; low B12 and serum zinic ; high
copper; racial differences; higher levels
of benzene; radiation; maternal
hyperthermia & infection and use of
medications before and during
pregnancy ; and poor antenatal care
[22,23,24,25,26,27,28,29 ] . during
pregnancy the NTDs could be
diagnosed by serum alphafetoprotein
level between the 15th and 18th week
of gestation. Confirmation requires
amniotic fluid analysis and ultrasonic
study. Without treatment, only up to
thirty percent of myelomeningocele
patients survive infancy but with
treatment, eighty five percent of infants
survive.Degree of disability in treated
NTDs children varies highly from very
simple to sever neurological disability
with different system disability. 1/3 of
the live cases are mentally deficient or
learning disability . Studies have
shown that very severely affected child
who are not treated during the neonatal
period ;die in the first few months after
birth[30].
Objective: The aim of study is to
study the type and incidence of the
neural tube defect and it is it is risk
factors and other associated variable.
Patients and method
this descriptive study was carried on
120000 lived newborns from
December 2013 to December 2015 in al diwaniya teaching hospital, neurosurgical department and pediatrics hospital in al diwaniya province in south west Iraq, the questionnaire include all the information's case were defined as women residing in the aldiwaniya government, delivered live or still born with neural Tube defect. Demographic characteristic of the neonates, and their parents such as sex, date of birth, type of neural tube defect, site of lesion and any associated abnormalities, father and mother age, consanguineous marriage, rural or urban, folate intake & other like drug take during pregnancy, maternal diseases, previous history of neural tube defect. The data was analyzed use SSPS program.

Results:
During a period of three years 2013-2015, there were (120,768 total) birth; the number of total births registered during the 3 years was 41761 in 2013, 39353 in 2014, and 39652 in 2015. Among this sample population, 112 women had fetus or newborn with NTD (1.078 per 1000birth), Anencephalus {3 (2.7%)}, spina bifida {103(92%)}, Encephalocele {6(5.3%)}, Meningocele {20(17.9%)}, Meningomyelocele {76 (67.9%)}, myeloschisis {7 (6.2%)}, as shows below by Table-1 -Types of NTD.

Regarding the gender among 112 affected NTDS 64 (57.2%) were female and 48 (42.8%) were male, this difference is statically significant (p<0.05). Figure-1 shows the sex distribution of NTDS.

Table-1 -Types of NTD

<table>
<thead>
<tr>
<th>Type</th>
<th>Total no &amp;%</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spinabifida :</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-meningomylocele</td>
<td>103 (92)</td>
<td>76</td>
<td>27</td>
</tr>
<tr>
<td>2-Meningocele</td>
<td>76 (67.9)</td>
<td>34</td>
<td>42</td>
</tr>
<tr>
<td>3-myeloschisis</td>
<td>20 (17.9)</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>Anencephalus</td>
<td>3 (2.7)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Encephalocele</td>
<td>6 (5.3)</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>total</td>
<td>112 (100)</td>
<td>48</td>
<td>64</td>
</tr>
</tbody>
</table>

The site of the spina bifida depend on the level of the spinal cord involvement at which neural tube closure was incomplete. The lesion is location in our study the lumbosacral & dorsolumbar region represent nearly the most common site of the cases 27.2%, 49.5% while the cervical and
dorsal regions are the least common sites 3.9% & 4.9% respectively; other few cases in all the cases of anencephaly and encephaly were excluded. Table-2 NTD According To Site

**Figure- 2 sex distribution of NTD**

![Sex distribution of NTD](image)

<table>
<thead>
<tr>
<th>site</th>
<th>Total no&amp;%</th>
<th>male</th>
<th>female</th>
</tr>
</thead>
<tbody>
<tr>
<td>cervical</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>dorsolumbar</td>
<td>51</td>
<td>21</td>
<td>30</td>
</tr>
<tr>
<td>lumbosacral</td>
<td>28</td>
<td>13</td>
<td>16</td>
</tr>
<tr>
<td>dorsal</td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>lumber</td>
<td>15</td>
<td>7</td>
<td>8</td>
</tr>
</tbody>
</table>

Regarding the associated anomalies with NTDs, in our study the Hydrocephalus is the common associated congenital malformations of the brain represent 61 (59.2 %) in patients with spina bifida and 4 (66.6%) in patients with encephalocele. The orthopedic anomalies like club foot 28 (27 %), congenital hip dislocation 14 (13.6%) commonly occur in the patients with spina bifida and not reported with anencephaly and encephalocele in current study.

The other associated problems with NTDs like bladder and bowel control problems, including incontinence, and abnormal eye movement and seizure present in few percent mainly in spine bifida cases 11.6%. Table-3 common associated anomalies and problems with NTDs.
Regarding the Mother variable associated with NTDs in this study, 62.5% and 37.5% of parents with affected newborns lived in rural and urban areas, respectively, and our results also shows that there is no significant relation between consanguineous marriage of parents and NTDs in which conseguinity available in 40.2% and not present in 59.8%.

This study show that no folic acid supplementation during pregnancy in 82 (73.2%) of cases of NTDs and no intake in about 30 (26.8%) statistically significant result.

The age of 112 women that her babies affected NTDs, 30(26.8%) had 16-25 years, 55 (49.1%) had 26-35 years while 27 (24.1%) had above 35 years. Table-4 shows the Mother variable associated with NTDs.

### Table-3- Associated anomalies

<table>
<thead>
<tr>
<th>Associated anomaly</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
<th>Spina bifida NTDs(N=103)</th>
<th>Anencephaly NTDs(N=3)</th>
<th>Encephalocele NTDs(N=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>hydrocephalus</td>
<td>65</td>
<td>30</td>
<td>35</td>
<td>61 59.2 %</td>
<td>4 66.6%</td>
<td></td>
</tr>
<tr>
<td>Club foot</td>
<td>28</td>
<td>12</td>
<td>16</td>
<td>28 27%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DDH</td>
<td>14</td>
<td>5</td>
<td>9</td>
<td>14 13.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>others</td>
<td>14</td>
<td>7</td>
<td>7</td>
<td>12 11.6%</td>
<td>2 66.6%</td>
<td></td>
</tr>
</tbody>
</table>

Figure-2: relation of parental age with ntd

[Bar chart showing the percentage of mothers and fathers across different age ranges (16-25, 26-35, Above 35) with NTD cases.]
### Table 4- Mother variable associated with NTD

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>NO</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Residency:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>70</td>
<td>(62.5)</td>
</tr>
<tr>
<td>Urban</td>
<td>42</td>
<td>(37.5)</td>
</tr>
<tr>
<td><strong>Consanguinity:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>45</td>
<td>(40.2)</td>
</tr>
<tr>
<td>No</td>
<td>67</td>
<td>(59.8)</td>
</tr>
<tr>
<td><strong>Parity:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primi gravida</td>
<td>30</td>
<td>(26.8)</td>
</tr>
<tr>
<td>Multipara</td>
<td>82</td>
<td>(73.2)</td>
</tr>
<tr>
<td><strong>Antenatal care:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Booked</td>
<td>50</td>
<td>(44.6)</td>
</tr>
<tr>
<td>Unbooked</td>
<td>62</td>
<td>(55.4)</td>
</tr>
<tr>
<td><strong>Folic acid:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taken</td>
<td>82</td>
<td>(73.2)</td>
</tr>
<tr>
<td>Not taken</td>
<td>30</td>
<td>(26.8)</td>
</tr>
<tr>
<td><strong>Previous sibling:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>8</td>
<td>(7.2)</td>
</tr>
<tr>
<td>no</td>
<td>104</td>
<td>(92.8)</td>
</tr>
<tr>
<td><strong>maternal disease during 1st trimester:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>5</td>
<td>(4.5)</td>
</tr>
<tr>
<td>no</td>
<td>107</td>
<td>(95.5)</td>
</tr>
</tbody>
</table>

**Discussion:**

In the current study prevalence equal to 1.078 per 1000 which is differ from that and in the United States, before 1980 the prevalence of myelomeningocele in the united states was 11.02 per 1000 live birth more recently, prevalence has declined to 0.44 per 1000 live birth 20% to 30% of the declined this may be return to pregnancy termination after prenatal diagnosis and prenatal folate supplementation (31) the termination of pregnancy is prohibited in our society belong to religious causes.
In other region there are small difference between our study in the occurrence of NTDs in different region ; The united kingdom practically Ireland , has a higher prevalence of NTDs than to continentals Europe , U K 1.1 per 1000(36 ) , Canada 1.41 per 1000 (37 ) , study in France 1.4 per 1000(36),study in turkey 1.5 per 1000(38), data in Saudi Arabia shows 1.3 per 1000 (39). In our study from 2013 to 2015 , the prevalence 1.078 per 1000 birth unlike other previous study in AL –Ramadi/Iraq ,3.3 per 1000. ( 32), and other study in Sulaimaniyah 2006-2010, incidence 3.5per 10000 (33).

Birth defects are the leading cause of infant mortality in developed countries and in current study the main cause of death associated with anencephalus and encephalocele which represent 8% of cases of NTDs in which differ to other study (34 ,35). The Midwest had the highest rate of NTD-specific infant deaths among US regions (36).

In the current study anencephaly represent 2.7% from all NTDs , while in the united states anencephaly occurs in about 1 out of every 10,000 births.(37) the average rate are high among Africans populations with like Nigeria estimated about 3/10,000 in 1990 & in Ghana estimated at eight per / 10,000 in 1992 .(38) data from China are estimated at five per /10,000 (38) in general average of the incidence of anencephaly in the US during previous century have change from 0.3 to 7 per 1000 births.(35)

Encephalocele present in 5.3 % in our study , but the control of disease centre report 1/ 12,200 babies born in the United States each year will have encephalocele. This means that more than three hundred U.S. babies are born with this disease every year.(39)

Regarding the site of spinal lesion , the cervical and thoracic regions are the least sites to be involved , and lumbar and lumbosacral regions commonest area for these lesions. The manifestations of the spina bifida depend on the level of the spinal cord involvement at which neural tube closure was defected. The lesion is located in lumbosacral area in more than eighty percent of the cases(40) while in our study the lumbosacral and dorsiolumbar region represent the most common of the cases 27.2,49.5 % respectively while the cervical and thoracic regions are the least common sites 3.9% & 4.9% respectively.

Regarding the associated anomalies with NTDs, in our study the Hydrocephalus is the common associated congenital malformations of the brain represent 59.2 % in patients with spina bifida and 66.6% in patients with encephalocele also these not in line with other study in the US in which hydrocephalus present at birth in 85-95% of cases as shown by ultrasonography (40,41)

The Orthopedic anomalies like club foot 27 %, hip dislocation 13.6% commonly occur in the patients with spina bifida and not reported with anencephaly and encephalocele in current study ,also differ from other study (42)

The other associated problems with NTDs like Bladder and bowel control(sphinictors) problems, including incontinence, urinary tract infections(UTI), and abnormal eye movement and seizure present inform of 11.6% in spina bifida and 66.6% in anencephalus unlike other study( 43,44). Seizures may occurred in up to seventeen percentof the children with meningomyelocele and commonly occur in hydrocephalus (45).
Abnormalities of the central nervous system (CNS) are the most common birth anomalies and NTDs represent the commonest part of it (40). In our work, malformations of the nervous system are the most frequent and the first neural tube defects. Only nutritional factors are related factors on which it is possible to prevent (41).

This study shows that no folic acid supplementation in 73.2% of cases of NTDs and no intake in about 26.8%, so the folic acid may decrease the disease and similar to the study current and should be used for women before and during pregnancy (46).

In this study, 62.5% and 37.5% of parents with affected newborns found in rural and urban areas. The mother reside in urban that showed a higher incidence in rural localities. This result was similar to a study was reported from Texas (47).

Regarding our results, there was no clear relation between consanguinity and NTDs. Various reports considered consanguineous marriage have attributed to higher incidence of NTDs to consanguinity (48-49). A study in India reported that NTDs was statistically significantly higher between babies born to parents of consanguineous marriages (P < 0.01) (50).

This study showed that there was significant difference between mothers’ ages and NTDs, the higher incidence occur between the age (26 – 35) years in which reach 49.1% whereas maternal age of more than 40 years in a study at Texas (51) and maternal age of over 30 years in Russia (52) were associated with NTDs. In Turkey (53), so a significant association between mothers’ ages and NTDs was found.

Mothers of nineteen years old or less have a higher risk for having a child with spina bifida in other study (54).

We observed a significant female predominance in our NTD cases. 57.2% female with 42.8% a male, which similar to the sex difference consistent in many studies. This female predominance in Canada study in both still & live births (55), and differs from other studies in Iran (56) and not in line with China study (57).

**Conclusion:**

This study showed that Folate deficiency are very important in reducing the occurrences of NTDs, considered that the consanguineous marriage is not important predisposing factor for NTDs, the disease is common in rural area, multipara womens with poor antenatal care. In our opinion, folate supplements are appropriate to prevent recurrence of NTD in infants of high-risk women but this required specific isolated study. Further studies should be carried out with large sample size to verify the cause-effect relationship of paternal factors, other nutritional factors and vitamins deficiency with NTDs.

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