Factors Associated with Neural Tube Defects of Neonates in Al-Najaf Government.

العوامل المؤثرة في تكوين تشوه الأنبوب العصبي لدى الأطفال حديثي الولادة في محافظة النجف الاشرف

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الخلاصة:

الهدف: تحديد علاقة تشوه الأنبوب العصبي مع بعض عوامل الخطر المرتبطة به.

المنهجية: دراسة الحالات والشواهد، أجريت في اثنين من المستشفيات الكبرى في مركز مدينة النجف الاشرف (مستشفى الزهراء التعليمي للولادة والأطفال و مستشفى الحكيم العام) خلال المدة من الأول من شباط إلى نهاية أيار من عام 2014 . تم ادخال جميع الحالات (التشوه)التي أدخلت في المستشفيين في الدراسة واختيرت الشواهد بصورة عشوائية بطريقة الأعتيان العشوائي المنظم ،حيث كانت مجموعة المرضى (50) حالة تشوه مقارنة ب(100) رضيع سليم من التشوهات من الشواهد لنفس الجنس و العمر من الأطفال حديثي الولادة تم تشخيص الجميع من قبل أخصائيي الأطفال . جمعت المعلومات بواسطة أسئلة منظمة في ورقة استبانة اعدت لهذا الغرض وطرحت بمقابلة مباشرة مع أمهات الأطفال الرضع قام بها الباحث نفسه .تم حساب نسبة الارجحية لتحديد العوامل وقوة تأثيرها في تكوين تشوه خلل الأنبوب العصبي .

النتائج: أظهرت النتائج ثلاث أنواع من خلل تشوه الأنبوب العصبي وكانت نسبها كالأتي : شق الحبل الشوكي (52%)، الهيضة الدماغية (36%) ، عدم تكون الدماغ (12%) . وأظهرت الدراسة إن قوة العوامل المؤثرة (نسبة الأرجحية Odd Ratio) من طرف الأم في تكوين تشوه خلل الأنبوب العصبي كانت: عدم اخذ حمض الفوليك بداية وقبل فترة الحمل هي (12,55)مرة أكثر عرضة لإصابة رضيعها بتشوه خلقي من الأمهات الآتي تناولن حمض الفوليك بشكل منتظم من بداية فترة الحمل، وكان عامل عدد زيارات الرعاية الصحية الأولية القليلة(اقل من ثلاث زيارات) هي(3,6) مرة تشوه من عدد زيارات الرعاية الصحية الأولية الجيدة (أكثر من ثلاث زيارات)والأم التي لديها إسقاطات سابقة هي (5,52) مرة من ألام بدون إسقاطات و الأم التي تدخن السكائر هي(2,25)مرة من اللائي لا يدخن و عمر الأم الأكثر من 35 سنة هي(1,95)مرة لديها تشوه من عمر الأم الأقل من 35 سنة وتاريخ الأم العائلي الايجابي للتشوه الخلقي هي (1,36) مرة من التي ليس لها تاريخ عائلي للتشوه الخلقي و الأم الغير متعلمة (4,86) مرة عرضة للتشوه من الأم المتعلمة .أما قوة العوامل المؤثرة من جهة الأب في تكوين التشوه الخلقي كانت : التاريخ العائلي الايجابي (21,7) مرة من ليس له تاريخ العائلي في تشوه الأنبوب العصبي والأب المدخن للسكائر (3,8) مرة من الأب الغير مدخن و عمر الأب 40 سنة أو أكثر هو (4) مرة عرضة لتشوه الأبناء من الآباء الأصغر من 40 سنة .بينما كانت قوة تأثير السكن في الريف هي3,7 مرة من السكن في المدينة ونسبة زواج الأقارب(3,8) مرة من الزواج بالأغراب في ظهور تشوه الأنبوب العصبي. وأظهرت الدراسة إن عمر الوليد الأقل من 37 أسبوع من الحمل عند الولادة هم الأكثر عرضة إصابة من عمر المولود 37 أسبوع أو أكثر ب(2) مرة.

الاستنتاجات: أظهرت هذه الدراسة وجود علاقة ايجابية قوية ومهمة بين تشوه الأنبوب العصبي لحديثي الولادة والعوامل التالية من بين عوامل أخرى(التاريخ الأب العائلي الايجابي لتشوه الأنبوب العصبي، قلة أو عدم استعمال الفولك أسد قبل و أثناء بداية الحمل ،زواج الأقارب، أمهات أمية التعليم) بينما أظهرت الدراسة إن الأمهات ذوات التعليم العالي محمية أبنائهن من الإصابة بهذا التشوه وانه لايوجد علاقة بين عدد الإنجاب و تشوه الأنبوب العصبي

التوصيات:التأكيد على تجنب التزاوج الداخلي وخصوصا للعوائل التي لديها تشوهات خلقية والتأكيد على اخذ حب حمض الفوليك قبل و أثناء فترة الحمل بجرعة(400-500 مايكروغرام) للنساء اللواتي لديهن أطفال مشوهين سابقا او إسقاطات متكررة او اللاتي تاخذ علاج مضاد للفوليك، تجنب التدخين من جهة الأبوين والحث على تكملة مستوى التعليم العلمي بما فيه زيادة الوعي الصحي لديهن في تجنب جميع العوامل للمسببة في تشوه الأنبوب العصبي.

Abstract

Objective: To identify the association of neural tube defects with some possible risk factors in Iraqi neonates.

Methodology: This is a hospital based case control study carried out in two major hospitals in AL Najaf province during the period (first of February through the end of May 2014). All the available fifty responded cases of neonates with gross Neural Tube Defects (NTDs) who were diagnosed and confirmed as neural tubes defects by specialist pediatrician were studied as cases and compared with (100) randomly selected sex and age matched control group neonates (Free from neural tube defects). Data collection were done through a structured questionnaire by interviewing mothers of both groups single handy by the researcher ,Odds Ratios (OR)were calculated to identify the probable risk factors of neural tube defects.

Results: The proportions of types of neural tubes defects in this study were; spina bifida (52%), encephalocele (36%) and anencephaly (12%). the factors that significantly associated with increased risk for NTDs were a lack of folic acid supplementation (OR=12.55,(95% confidence interval CI 5.59-28.17); poor ante natal care OR=3.67(95%CI 1.80-7.48),abortions OR=5.52(95% 2.64-11-54) ,previous still birth OR=2.02(CI 95% 0.79-5.14),number of parity OR=1.10(CI 95%0.48-2.30),

maternal smoking OR=2.25(CI 95% 0.87-5.83) maternal age 0R=1.95 (0.88-4.31), maternal family history OR=1.36(0.37-5.1), maternal educational level [low educational level] was OR=4.86[2.2-10.9], while paternal factors were father family history of neural tube defect OR=21.7[2.67-53.42] ,father smoking OR=3.8 [1.77-8.34] father age OR=4.04 [1.55-10.55]. Residence OR=3.78[1.85-7.72], consanguinity OR=3.84[1.77-8.34] ,while the association between neonates factors and anomalies were age of neonates OR=2.125[1.10-4.30] , birth weight OR=1.52[0.72-3.30].

Conclusion: The main factors that associated positively with neural tube defectsamong others factors were (father family history of neural tube defects, lack of folic acid supplementations ,mothers with low education and consanguinity marriages)which highly significant and strongly effects in neural tubes defects among others factors ,while mothers with higher education was protected them siblings from this anomaly and found the number of parity had no relation on neural tube defects formation.

Recommendation: Confirmation to avoid internal marriages and especially for families that have birth defects and an emphasis on taking the tab of folic acid before and during pregnancy in dose (400-500 micrograms) for women with children deformed previously or frequent abortion or who take drugs interferon Folic acid, parents should avoid smoking and urge the supplement level of science education due to increasing awareness of the health help them avoid all the factors causing neural tube defects.

Keyward: Neural tube defects, risk factors, AL-Najaf Governorate.

INTRODUCTION

Neural tube defects (NTDs)are congenital structural abnormalities of the brain and vertebral column that occurs either as an isolated malformation alone or with other malformation [(1)]. NTD is the second most common major congenital anomaly after cardiac malformation [(2)] It's the most serious and common birth defects affecting more than 300,000 fetuses or infants in the world each year .[(3)] The etiology of most causes is still unknown[(4)]. It is believed that there is a genetic-environmental intervention in the causation of NTDs because NTDs its multi factorial in origin which occur when there is a genetic predisposition to malformation triggered by environmental risk factors [(2)] including poor maternal nutritional status and folic acid deficiency early antenatal clinical visit is an important steps in prevention of congenital malformations by folic acid supply Parity has shown either a U-shaped pattern of NTDs risk,[(5)] . NTD risk seems to be greater if a woman has had a previous fetal or infant death, even if the previous infant or fetus did not have an NTDs, maternal age risk for NTDs to be U-shaped, i.e., highest among youngest and oldest women, advanced paternal age is associated with genetic changes in the sperm; this could lead to an increased risk for congenital anomalies in offspring[(6).] With respect to consanguinity, NTD rates have been found to be higher when the parents are related, In the Middle East where consanguineous marriage is common,[(6)] the other environmental factor effect on NTD; maternal cigarette smoking and maternal exposure to second hand smoke increased the risk for neural tube defects in offspring[(6)], previous family history of NTD, and maternal educational level which have been shown to play a very powerful role in the occurrence of these defects[(7)] .Rural areas reporting higher rates, suggesting that environmental exposure may affect NTDs rates It has been suggested that the regional difference in NTDs rates may be explained by differential dietary consumption of foliate[(7)]Neural tube defects may lead to spontaneous abortion, still birth, and early infant death from ascending CNS infections, or to long life crippling disabilities, ranging from lower paralysis and loss of sensation, to stool and urine incontinence, hydrocephalus, mental, and physical retardation. Still, such morbid and mortal anomalies compose an important part of congenital anomalies noticed in Al-Najaf Governorate in Iraq, NTDs .

It has been estimated that one out of four affected fetuses will be stillborn, one of two will result in spontaneous abortion, and the remaining one will probably survive [(8)] Neural Tube Defects are among the few birth defects for which primary prevention is possible, prenatal screening and diagnosis are widely available, and prenatal therapy is being investigated[(9,10])]In view of the significant healthy costs

specially in developing countries [10]. This study was done to evaluate some probable risk factors that may be attributed to causing NTDs affected neonates in AL Najaf governorate .

METHODOLOGY:

This is a hospital based case control study conducted in two major referral hospitals in Al- Najaf Governorate. This province is situated in the south central part of Iraq, about 180 kilometers from the capital Baghdad and populated about one million and three hundred thousand persons. The duration of the study started from the first of February through the end of May 2014, all live neonates (mature and premature) were included in this study. This study excluded aborted fetus and neonates who were delivered and died soon after delivery (stillbirth) before being examined by the principle investigator /pediatrics resident/pediatrician, and dead neonates were excluded from the study, neonates with the signs of occult spinal bifida were not included. The study was carried out in AL-Najaf city (AL-Zahra maternity and children teaching hospital), and (AL-Hakeem general hospital), these two hospitals are referral hospitals that cover Al-Najaf province. After getting the approval of health ethical committee in Al Najaf health directorate and the similar committee in the family and community department in Babylon Medical College, mothers informed concepts were taken. Fifty cases of confirmed, grossly NTDs were studied compared to the same age and sex matched randomly selected (100) healthy neonates confirmed by pediatricians the selection was done by a simple randomization from the same wards of the same hospital in the same period, both general and local physical examinations were done for all neonates thoroughly by specialist pediatrician, the weight of each neonate was measured, and their medical files and papers were checked to prove the diagnosis and collecting needed data**.**

Data collection were performed at the labor room and neonatal intensive care units and neonatal care units through a structured questionnaire filled single handy by the researcher himself who directly interviewed the mothers ,the questions included: age of mother, educational level of the mother, mother smoking, mother family history of NTDs, parity, numbers of abortions and still births, ante natal care, peri conception folic acid supplementation, father age, father smoking, father family history of NTDs, consanguinity of marriage and residence in addition questions about the neonates(age, gender, birth weight). The data were entered into the computer, and analyzed using the SPSS version (20). p value was considered significant if it was less than 0.05. Chi-sequare and Odds Ratio were calculated.

RESULTS:

Table (1).Distribution of types of NTDs according to sex of neonate

Sex of neonate	Types of NTDs						
	Spia Bifida		Encephalocele		Anencephaly		Total NTDs
	No.	%	No.	%	No.	%	
Male	17	54.8	12	38.7	2	6.5	31
Female	9	47.4	6	31.6	4	21.1	19
Total	26	52.0	18	36.0	6	12.0	50
Chi square = 2.23, P.value = 0.30							

This table revealed the distribution of NTDs according to sex, shows that out of the 50 NTDs cases, males were 31represented (62%) and females were 19 represented (38%), male to female ratio 1.6:1 .

Table (2).Association of anomalies with maternal and paternal demographic factors

Variable		NTDs group		Normal group		OR [95% CI]	P.value
		No.	%	No.	%		
Mother age	≥ 35	15	30.0	18	18.0	1.95 [0.88 – 4.31]	0.14
	< 35	35	70.0	82	82.0		
Father age	≥ 40	13	26.0	8	8.0	**4.04 [1.55 – 10.55]**	**0.006**
	< 40	37	74.0	92	92.0		
Education	Illiterate	21	42.0	13	13.0	**4.86 [2.2-10.9]**	**< 0.001**
	Primary	13	26.0	47	47.0	1.9 [0.39-4.6]	0.42
	Secondary	14	28.0	26	26.0	3.8 [0.75-6.2]	0.11
	Higher education	2	4.0	14	14.0	0.26 [0.1 – 1.2]	0.11
Mother Smoking	Yes	10	20.0	10	10.0	2.25 [0.87 – 5.83]	0.15
	No	40	80.0	90	90.0		
Father smoking	Yes	39	78.0	48	48.0	**3.8 [1.77 – 8.34]**	**< 0.001**
	No	11	22.0	52	52.0		
Residence	Rural	32	64.0	32	32.0	**3.78 [1.85 – 7.72]**	**< 0.001**
	Urban	18	36.0	68	68.0		
Consanguinity	1st.relation	39	78.0	48	48.0	**3.84 [1.77 – 8.34]**	**< 0.001**
	No related	11	22.0	52	52.0		
Mother family history	Yes	4	8.0	6	6.0	1.36 [0.37 – 5.1]	0.92
	No	46	92.0	94	94.0		
Father family history	Yes	9	18.0	1	1.0	**21.7 [2.67 – 53.4]**	**< 0.001**
	No	41	82.0	99	99.0		

This table shows that among the maternal and paternal demographic factors only 6 factors showed significant association with the neonates anomalies these factors included father age, illiterate, father smoking habit, residence, Consanguinity, and father family history.

Table 3. Association between neonate's factors and anomalies.

Variable		Anomaly group		Normal group		Odds ratio (OR) [95% CI]	P.value
		No.	%	No.	%		
Gestational age	< 37	25	50.0	32	32.0	**2.13 [1.10 – 4.30]**	**0.025**
	≥ 37	25	50.0	68	68.0		
	Total	50	100.0	100	100.0		
Sex	Male	31	62.0	62	62	1.000 [0.497-2.10] 2.013]	1.000
	Femal	19	38.0	38	38		
	Total	50	100.0	100	100.0		
Birth weight	< 2.5	15	30.0	22	22.0	1.52 [0.72 – 3.30]	0.28
	≥ 2.5	35	70.0	78	78.0		
	Total	50	100.0	100	100.0		

table 3 shows that, it had been significantly found that neonates with anomalies were about 2 folds more likely to be delivered at < 37 weeks of gestation than those without anomalies (OR=2.13, P=4.30).

Table 4. Association between Maternal obstetrical factors and anomalies

Variable		Anomaly group		Normal group		Odds ratio (OR) [95% CI]	P.value
		No.	%	No.	%		
Parity	Nulliparous	13	26.0	25	25.0	1.10 [0.48-2.30]	0.89
	Multiparous	37	74.0	75	75.0		
Abortion	Yes	33	66.0	26	26.0	**5.52 [2.64– 1.54]**	**< 0.001**
	No	17	34.0	74	74.0		
Stillbirth	Yes	10	20.0	11	11.0	2.02 [0.79 – 5.14]	0.13
	No	40	80.0	89	89.0		
Antenatal Care	≤ 3 visit	30	60.0	29	29.0	**3.67 [1.80 7.48]**	**< 0.001**
	> 3 visit	20	40.0	71	71.0		

Tables 4 shows that there had been significantly found that NTD cases were about 5.5 folds more likely to have history of abortion than normal group. (OR = 5.52, P<0.001), on the other hand, neonates of mothers who had ≤ 3 antenatal visits were 3.67 folds more likely to have anomalies than those whose mothers had > 3 antenatal visits, (OR=3.67, P<0.001). Parity and Stillbirth were not reach the statistical significance, (P>0.05)**.**

Table 5. Association between folic acid administration and NTDs

Folic acid administration	Anomaly group		Normal group		Total	
	No.	%	No.	%	No.	%
No	36	72.0	17	17.0	53	35.3
Yes	14	28.0	83	83.0	97	64.7
Total	50	100.0	100	100.0	150	100.0
Odds ratio (OR) [95% CI]**12.5 [4.2– 21.7],**						**P<0.001**

Table 5 shows that Folic acid administration showed a highly significant protective effect against the anomalies, mothers who were not taking folic acid antenatally were about 12.5 folds more likely to have NTD neonates than those who were taking folic acid (OR = 12.5, P< 0.001).

DISCUSSION

The finding of this study agreed with that reported in different studies and literatures referred that Spina bifida is most common NTDs([8,11]), however scientific advances in medicine allow these anomalies to be surgically corrected through a hysterotomy, or while the fetus is still in the mother's uterus leading to reduction in the incidence rates of these anomalies[7]Furthermore, The distribution of types of NTDs according to sex revealed that spina bifida was more frequent in males than females, . Similarly, encephalocele was more frequent in males than females [12],while anencephaly was more frequent in females than males, (21.4%) versus (6.5%),these findings agreed with that reported in a large across-section observational study conducted in Iran during the period January 2001through 2005[13].

Antenatal visit: The current study revealed that the mothers who had ≤ 3visit to the antenatal care are more prone to have a neonate with NTDs, this is similar to the finding of a previous study carried out in Iraq [8]. Most of pregnant women in the studied group , unfortunately, attended the antenatal care after the first month of pregnancy when the neural tube malformation has been completed, and folic acid has lost its desired effect. however, the current study demonstrated that

Folic acid administration showed a highly significant protective effect against the NTDs, mothers who were not taking folic acid antenatally were about 12.5 folds more likely to have NTD neonates than those who were taking regularly folic acid antenatally.

Studies suggest that folic acid supplementation may affect not only the occurrence, but also the recurrence of NTDs. [14]

Recurrent abortion: In this study It had been significantly found that NTD cases were associated with abortion OR=5.5. Opinions also vary between correlation and incidence of the abortion and NTD grouping number of studies have documented an increased occurrence of spontaneous abortions in pregnancies of women who have NTD-affected infants. The widely accepted explanation for this finding is that many of these spontaneous abortions occur because the fetus is affected by an NTD or other congenital abnormality. It is believed that about half of pregnancies complicated by NTDs will end in spontaneous abortion[14]

Stillbirth: in England, The present study found that stillbirth was more frequent in those with NTDs than control group, (OR=2.2), Iranian study [13], found that 69.23% of NTDs had been seen in stillbirths, while 83% in a study carried out and Wales[15].

Parity: in our study no relation significant relation was found between parity and NTDs this finding is in contrary to the findings of other studies which had demonstrated this relation [16].

Smoking :cigarette smoke is a well-established toxin and harmful to the developing embryo, the evidence for an independent effect on the occurrence of neural tube defects (NTDs) is mixed. Smoking considered as an important risk factor due to its teratogenic effect. Recent studies reported that cigarette smoking reduces the fetal serum level of folic acid. Other studies centers on the carbon monoxide effect, which was found to reduce the oxygen carrying capacity to the fetal tissue and the nicotine which crosses the placenta, and reduces the uterine blood flow, affecting fetal oxygenation, and the acid-base balance leading to such anomalies[8]

In our study smoking mothers had higher risks of having neonates with NTDs (OR=2.25), however, the difference between cases and controls was statistically insignificant, from other point of view, higher risk estimates associated with smoking fathers (OR= 3.8), this might explains the insignificant difference with mother smoking where those mothers might affected by passive smoking of their husband which increased the incidence in both smokers and none smokers mothers. This agreed with previous Iraqi study [9], which revealed a higher risk of NTDs among the active and passive smoker mothers also demonstrated in a meta-analysis study[17]suggested that maternal passive smoking during pregnancy was associated with an increased risk of total NTDs and three NTDs subtypes in offspring[17].

Maternal age : Although in our study, most of the mothers with infants having NTDs were less than 35 years, but the older maternal age(≥ 35 years) associated with higher risk of development of NTDs (odds ratio 1.95), however, difference between cases and controls didn't reach the statistical significance (P>0.05),a number of studies have reported maternal age risk for NTDs to be highest among youngest and oldest women, while other studies have found the risk to decrease with advancing age or the reverse.[18] This could be due to several other

maternal factors have also been established as a risk for NTDs, including socioeconomic class, various environmental factors, genetic factors, and maternal illness or medication during pregnancy, or due to nutritional deficiency problems which could predispose these mothers to NTDs.

Paternal age: The present study found that paternal age ≥ 40 years, associated with higher risk of development of NTDs, where neonates whose father age more ≥ 40 years are about 4 folds higher risk to have NTDs than those whose father age < 40 (OR=4.04) (95% CI: 1.55 – 10.55) these findings agreed the finding of the study done in Norway conducted in 2004 [(19)]in which the risk estimates were 2.5-fold (95% CI: 1.2–5.5) for fathers aged between 45 and 49 years compared with the reference age group (25–29 years),this could be due to gene mutations specially of the sperm which increased with increasing the age due to chronic disease, using medications and other stress full conditions of the life.

Education level: In the present study illiterate mothers had the higher risk of having neonates with NTDs compared to women with other educational levels, the risk estimates were 4.86 folds (95% CI: 2.2 – 10.9), this risk varied by the education profile of the neighborhood: women who did not graduate from high school and lived in less educated neighborhoods exhibited a higher risk. The higher risk associated with low education levels might attributed in part, to the diet pattern, socioeconomic status, and lack of awareness for the potential benefit of folic acid supplements in preventing NTDs among women with low education. A previous study done [(20)] .

Residence:The current study revealed that the parents who live in rural areas are more susceptible to have a neonates with NTDs with a risk estimates of about 4 folds than those who live in urban areas, this agrees with that found in the previous Iraqi study at 2010[(8)], but not agreed with that's done in Ireland s[(21)], in which the rural area have lower NTDs percentage than those in big cities, this may be due to the difference in culture and nutritional effects.

Consanguinity : In clinical genetics, a consanguineous marriage is defined as a union between two individuals who are related as second cousins or closer, with the inbreeding coefficient (F) equal or higher than 0.0156 where (F) represents a measure of the proportion of loci at which the offspring of a consanguineous union is expected to inherit identical gene copies from both parents The consanguineous marriage has its impact on the incidence of the NTDs, the current study reported consanguineous marriage in 78% of the cases, this finding was not unexpected in our country, in Iraq like in other countries in the Middle East consanguineous marriage is traditional and respected where intra-familial unions collectively account for 40 – 50% of all marriages [(22)]. The higher rate of consanguineous marriage in our country might related primarily to social factors, where people thought that consanguineous marriage could enforce the couples' stability due to higher compatibility between husband and wife, as well as the compatibility between the couple and other family members. There is a general belief that marrying within the family reduces the possibilities of hidden uncertainties in health and financial issues. It is believed that consanguinity strengthens family ties and enforces family solidarity, with cousin marriage providing excellent opportunities for the transmission of cultural values and cultural continuity.[(22)]In a previous Iraqi study (Iraq-Dohuke, 2007)[(23)], consanguinity was present in 41% of NTD cases which was lower than the 78% reported in our study), and 70% in Jordan[(24)].

Family history: The current study found that fathers positive family history was a significant risk factor for NTDs, family history studies suggest the recurrence risk for first-degree relatives of affected individuals is approximately 1 in 30. For second-degree relatives (the children of the mother's sisters and brothers) the risk is

approximately 1 in 220, However, the authors of the same study state there is not yet agreement upon the accurate recurrence risk data for family members.[25]

Neonatal factors: The current study found that gestational age at labor of < 37 weeks associated with the higher risk of having NTDs (OR= 2.13, 95% CI: 1.1 – 4.3) this consistent with that reported by a study[26] which concluded that premature infants (<37 weeks' gestation) were more than two times as likely to have birth defects than term infants.

CONCLUSIONS:

1. Paternal family history with NTDs have positive effect on formation defects in CNS in the neonates but father family history are more stronger in its effect than mother family history.
2. The following are the main maternal risk factors have strongly effect in NTDs of neonates :- Lack of folic acid supplementations in peri consumption period , Mothers with poor ante natal care (3visit and less) to PHC, Mother with previous abortion and or previous history of stillbirth, Mothers illiterate or with low education while mothers with higher education was protected them neonates from NTDs .
3. Found the number of the parity have no effect on NTDs.
4. Paternal smoking has positive effect in NTDs but father smoking (maternal Passive smoking) have stronger effect than mothers smoking in NTDs formation.
5. Consanguinity in marriages has stronger effect in NTDs than stranger's marriages.
6. Residence in rural area is more risky to have NTDs than residence in urban area.
7. Paternal age have effects on NTDs in neonates, its more in male > 40 years old and female > 35 years old.
8. Maturity of neonates have effect on NTDs, were premature (less than 37 week of gestation) more liable to have NTDs .
9. Neonates delivered with underweight (less than 2.5 Kg) were more risky to have NTDs than normal weight.

RECOMMENDATIONS:

1. Further population based studies are needed in different areas in Iraq and prefer including more risk factors.
2. As much as avoidance the consanguinity in marriage especially with families have congenital anomalies especially with positive paternal family history.
3. Opened Primary health care centers in rural areas to encourage antenatal care and folic acid supplementation and casual vaccination.
4. All women in reproductive age (15-45 years) should supply with prophylactic dose of folic acid which is (5Mg) for positive family history specially before 3 months of conception and 400 microgram for negative family history.
5. Women with recurrent abortions or previous still birth should complete investigation before next pregnancy, expansion of rubella immunization, peri-conceptional supplementation of folic acid, provision of adequate prenatal care including nutrition counseling, control of maternal infections.
6. Encouraging women to complete reproduction before 35 years of age.
7. Avoid smoking and the exposed to smoking as much as possible during pregnancy. Encourages the families on daughters education to let them understanding prevention methods of congenital anomalies.

REFERENCES:

1. Al-AlawiNA,Jubrael JM, Hughson M. Molecular characterization of ß-thalassemia defects in Dohuk –Iraq. **Hemoglobin** 2006;30(4):479-86.
2. National Institute of Child Health and Human Development. "How many people are affected by or are at risk for neural tube defects?". Neural Tube Defects (NTDs). U.S. National Institutes of Health.2012.
3. Cheschier N.ACOGpractice bullein.Neural tube defects. **Int J Gynaecol Obstet** 2003; 83:123-133.
4. Johnston MV, Kinsman S. Neural tube defects. In :Behrman RE, Kliegman RM, Jenson HB, eds. NelsonTextbook of Pediatrics. 17th ed. Philadelphia: WB Saunders;2009.
5. López-Camelo JS, Orioli IM, da Graça Dutra M, et al. Reduction of birth prevalence rates of neural tube defects after folic acid fortification in Chile. **Am J Med Genet A**. 2005; 135:120.
6. Li Z, Ren A, Zhang L, Ye R, Li S, Zheng J, et al. Extremely highprevalence of neural tube defects in a county area in ShanxiProvince, **China. Birth Defects Res A Clin Mol Teratol** .2006;76: 237-240.
7. Al-Ani Z, Sahar J, Suhaib M. Neural tube defects among neonates delivered in Al-Ramadi Maternity and Children's Hospital, western Iraq. **Saudi Med J.** 2010; Vol. 31 (2): 163-169.
8. Blencowe H, Cousens S, Modell B, Lawn J Folic acid to reduce neonatal mortality from neural tube disorders. **International Journal of Epidemiology**. 2010; 39: 110 – 121
9. Mills JL,Carter TC.Invited Commentary :Preventing neural tube defects and more via food fortification .**AMJ Epidemiol**. 2009;169:18.
10. International Clearinghouse for birth defects Surveillance and Research. **Annual Report** .Italy (Rome ;ICBDSR:2008.
11. Mahmood AKA. Neural tube defects among infants delivered of mothers with tobacco smoke exposure. **Medical Journal of Basrah University** .2007; 25: 25-28.
12. Kurinczuk JJ, Hollowell J, Boyd PA, Oakley L, Brocklehurst P, Gray R; .The contribution of congenital anomalies to infant mortality. National perinatal epidemiology unit, university of Oxford. Inequality in infant mortality project **briefing paper**. 2010, 1–13.
13. Safdar O, Al-Dabbagh AA, Abu Elieneen WA, Kari JA. Declinein the incidence of neural tube defects after the national fortification of flour. **Saudi Med J.** 2007; 28:1227-29.
14. TadmouriGO, Nair P, Obeid T, Al Ali MT, Al Khaja N, Hamamy HA Consanguinity and reproductive health among Arabs. **Reprod Health**. 2009; 6:17-23.
15. Hamamy H. Consanguineous marriages Preconception consultation in primary health care settings.**J Community Genet** .2012; 3:185–192.
16. Grewal J, Carmichae S L , Song J, Shaw G M, Neural tube defects: an analysis of neighbourhood- and individual-level socio-economic characteristics. **Paediatr Perinat Epidemiol.** 2009 March ; 23(2): 116-124.
17. Morris JK, Wald NJ.Prevalence of neural tube defect pregnancies in England and Wales**. J Med Screen**. 2007;14(2): 55-59.
18. Mandiracioglu A, Ulman I, Liileci E, Ulman C The incidence and risk factors of neural tube defects in Izmir, Turkey: a nested case-control study, the Turkish **Journal of Pediatrics**. 2004; 46: 214-220.

19. Kazaura M, Lie RT, Skjaerven R. Paternal age and the risk of birth defects in Norway. **Ann Epidemiol**. 2004 ;14(8):566-570.
20. Teckie G, Krause A, Kromberg JG, Neural tube defects in Gauteng, South Africa: Recurrence risks and associated factors. **The south African Medical Journal**. 2013; 103 (12):973-7.
21. Baey H, Wahhudi M, Hashim H et al. Smoking among Health Care Providers, Identification of Associated Factors in Hilla City. **Medical Journal of Babylon**. 2011; 8- No. 4 -201.
22. Wang M, Zhi-Ping W, Zhang M. Maternal passive smoking during pregnancy and neural tube defects in offspring: a meta-analysis. **Arch gynecolobstet** .2014 13;289(3):513-21.
23. Abdurrahman K. The prevalence of neural tube defects among newborns delivered in Azadi Hospital in Dohuk City, Kurdistan Region, Iraq. **Dohuk Medical Journal**. 2007; 1 (1): 42 – 48.
24. Grewal J, Carmichae S L , Song J, Shaw G M, Neural tube defects: an analysis of neighbourhood- and individual-level socio-economic characteristics. **Paediatr Perinat Epidemiol**. 2009 March ; 23(2): 116-124.
25. Farley TF, Hambidge SJ, Daley MF. Association of low maternal education with neural tube defects in Colorado. **Public Health**. 2002; 116: 89-94
26. Rasmussen SA, Moore CA, Paulozzi LJ, Rhodenhiser EP. Risk for birth defects among premature infants: A population-based study**. J Pediatr**. 2001;138: 668-673.