PREVALENCE OF NEURAL TUBE DEFECTS AMONG NEONATES IN SULAIMANY MATERNITY HOSPITAL

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ABSTRACT

Background

Awareness among women about folic acid supplementation during pregnancy showed an increment. Therefore, a difference in the prevalence of Neural Tube Defects happened.

Objectives

The aim of this study was to identify the prevalence of NTDs in Sulaimani governorate and to make a comparison between the 2 periods before and after folic acid fortification of wheat in Iraq and with improved awareness of mothers.

Methods

This observational study was conducted in Sulaimani Maternity Teaching Hospital in two different periods. The first period extending from 1/7/2005 to 31/12/2006, out of 19831 livebirths, records of neonates with anencephaly, meningocele, meningomyelocele and encephalocele were reviewed. The second period extending from 1/7/2012 to 31/12/2013, out of 26841 live births, a combined record revision and direct interview of mothers who had delivered a newborn with Neural Tube Defects was followed.

Results

Results showed that during the first period of study, out of 19831 Live Births, 52 cases of Neural Tube Defects were encountered making a prevalence rate of 2.6/1000 Live Births. The total number of deliveries during the second period was 26841 Live Births and the number of newborns having Neural Tube Defects was 31, making a prevalence rate of 1.16/1000 Live Births.

Conclusion

It was found that Neural Tube Defects are common in our area and that fortification of wheat flour with folic acid together with providing folic acid to pregnant mothers at the antenatal clinics had an overall effect in decreasing the prevalence of this defect.

Keywords: *NTD=neural tube defect.*

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INTRODUCTION

Internationally, NTDs are among the most common birth defects. They exhibit marked geographical variation, with the incidence being higher in Great Britain and lower in Japan [1]. Of human birth defects, those affecting the neural tube account for 0.5-2 per 1000 pregnancies worldwide, with variations in prevalence ranging from 0.2 to 10 per 1000 in specific geographical locations [2].

Among the 22 Arab states, published data on the birth rates of NTDs were retrieved from 13 countries. The rate varied from 0.62 to 13.8/1000 births. Variable rates were reported from the same country depending on the study methodology, year of study, and before and after folic acid supplementation [3].

Encouraging women to consume a supplement containing 400 microgram of folic acid daily has limitations as a primary public health program, as high percentage of pregnancies are unplanned. It has been suggested that well-implemented mandatory fortification programs have been implemented in many countries to maximize their effects and reduce the high costs associated with prevention programs such as education campaigns and other interventions that require behavioral changes [4].

Beginning in 1998, the United States mandated fortification of enriched cereal grain products with 140 µg of folic acid per 100 g [2]. Immediately after mandatory fortification, the birth prevalence of NTD cases declined. Fortification was estimated to avert approximately 1,000 NTD-affected pregnancies annually [5]. The birth prevalence per 1000 decreased, fallen 93% from 3.6 in1964 to 0.3 in 2004, 59% due to an underlying decrease in the prevalence of NTDs and 34% due to screening diagnosis and subsequent termination of affected pregnancies [6].

Studies in the US using various methodolies have shown a decrease of 19-32% in the prevalence of NTDs overall since the implementation of folic acid fortification in 1998. Larger decreases have been found in programs that were able to capture NTD cases using prenatal information, including elective terminations [7].

The Flour Fortification Initiative (FFI) is a network of partners working together to make flour fortification a standard practice worldwide so that people receive essential nutrients through staple food products [8]. Wheat and flour fortification is a preventive food based approach to improve micronutrients status of the population (9).Well documented studies in the United States, Canada and Chile have documented decreases of 26, 42 and 40%in the rate of NTDs affected births after implementation of national regulations mandating wheat flour fortification with folic acid [9].

Flour fortification has been widely implemented in countries of the Eastern Mediterranean, Middle East and North Africa region. The WHO Regional Office for the Eastern Mediterranean with support from the United Nations Children's Fund (UNICEF) and the Micronutrient Initiative (MI) launched an initiative in 1999 which subsequently led to nearly all the countries in the region fortifying wheat flour with at least iron and folic acid by 2009 [10].

In Iraq 19 August 2006 - Launching its nationwide Wheat Flour Fortification (WFF) project in August 2006, Iraq has achieved a notable milestone in combating anaemia and assisting in the optimal early development of the child [11], this is supposed to benefit the entire population.

Wheat is the most important cereal in Iraq, both in terms of production and consumption, with average consumption up to 223 g/person/day - it was thus selected as the best carrier for these micronutrients. In February 2004 UNICEF worked closely with national and other partners on finalizing a National Plan for WFF, after which 215 "feeders" were provided; UNICEF further supported the training of Iraqi engineers on installation, operation and maintenance of the feeders and delivered 164 tons of pre-mix (containing the iron and folic acid), sufficient for an initial three months, to 175 mills throughout Iraq [11].

The aim of this study was to identify the prevalence of NTDs in Sulaimani governorate and to make a comparison between the 2 periods before and after folic acid fortification of wheat in Iraq and with improved awareness of mothers.

METHODS

This is a hospital based study that is conducted in the Maternity Teaching Hospital in Sulaiamni Governorate. This province is situated in Kurdistan Region, North of Iraq. Its estimated population is about one million and five hundred thousand persons.

It has been conducted in 2 different periods, the first one extending from 1/7/2005 to 31/12/2006 and out of 19831 L.B in the period, 111 newborns were found to have

been diagnosed with congenital anomalies on clinical examination, out of which 52 have been diagnosed with anencephaly, spina bifida cystica (meningocele and meningomyelocele) and encephalocele. While the second period extended from 1/7/2012 to 31/12/2013, and the total deliveries 26841 L.B. In the second period a total of 205 newborns were found to have been easily diagnosed with congenital anomalies, out of which 31 were found to have NTDs.

A previous record of collected data was available with the author for the first period, so to make comparison between the two periods, the two sets of data were compared. To do so the following actions were implemented in the second period to collect the parameters needed for the study to be completed:

Interviewing with mothers of the neonates having clinically detectable congenital anomalies.Clinical record revision of the pregnant women who attended the hospital for delivery and found to have babies suffering from congenital anomalies.

All live neonates (mature and premature) were included in this study. Aborted fetuses and neonates who were delivered and died soon after delivery (stillbirth) before being examined by the principle investigator /pediatrics resident/pediatrician, were excluded from this study . Neonates with the signs of occult spinal bifida were not included as they are not usually detected in the clinical exam. This hospital is a referral hospital that covers Sulaimani province. After getting the approval of health ethical committee in Sulaimani health directorate, mothers informed consent were taken. All cases of grossly confirmed NTDs were studied and the mothers were interviewed regarding some personal and medical information. 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 for collecting the needed data.

Data collection was performed at the labor room and neonatal intensive care units through a structured questionnaire filled single handy by the researcher who directly interviewed the mothers. The questions included: age of mother, educational level of the mother, mother family history of NTDs, parity, number of abortions and still births, ante-natal care, peri-conception folic acid supplementation, father age, father family history of NTDs, consanguinity of the marriage and residence. In addition questions about the neonates were asked which included (age, gender and birth weight). The data were plotted into the statistical program in computer, and analyzed using the SPSS version. P value was considered significant if it was less than 0 .05.

RESULTS

The total number of births during the first period (1/7/2005 to 31/12/2006) was 19831 live births and there were 52 cases with NTDs making the prevalence rate of 2.6 per 1000 live births. In the second period of study (1/7/2012-31/12/2013) the collected number of deliveries were 26841 live births, a sum of 205 had obvious major congenital anomalies which could be easily detected by direct examination using no electronic devices , out of which 31 cases had neural tube defects making the prevalence rate of 1.16/1000 live births as shown in table1. Testing hypothesis regarding two proportions from independent samples was applied and result was, there is sufficient evidence at the α=0.05 level of significance to conclude the proportion of individuals having NTDs in the second period is less than the proportion of individuals having NTDs in the first period at the α=0.05 level of significance. Table 1 also reveals the distribution of the sample according to the type of NTDs. It also, makes a comparison between the 2 periods. It is clear that anencephaly was the highest congenital anomaly prevailing among newborns (in the first period) followed by meningomyelocele , meningocele and encephalocele respectively. But in the second period, Meningomyelocele has the greatest number constituting 12 cases followed by anencephaly, Myelocele and encephaolocele. The greatest decline occurred in the prevalence of anencephaly, because termination of pregnancy could be done legally once the mother found to have an anencephalic fetus during antenatal care.

The collected data report that in the first period hydrocephalus was found as an associated anomaly in only 7 of the cases, However Microcephaly was detected in 2 of the cases and other two cases had associated abnormalities of the viscera and skeletal abnormality for each case separately in addition to having NTD.

Meanwhile, in the second Period the associated malformations were found in only 9 of the cases, hydrocephalus in 4 of them, renal problems in 3, cardiac anomaly in one and eye anomaly in one of the cases.

Furthermore, Patients' characteristics are shown in

table 2. In addition the distribution of cases according to sex and sex ratio was obtained. The sex ratio (male to female ratio) was 0.85 for the first period and 1.06 for the second period. Also, association with birth order was evaluated and the outcomes indicate that the anomalies under focus are more common among first order pregnancies and are decreased with subsequent births but the malformations rose up in fourth and above birth order.

Table 1. Prevalence of NTDs and its different types in Sulaimani Maternity Hospital in Two different Period

Type of NTD	First period 1st period No.(%)	Second period 2nd period No.(%)
Annencephaly	30 (57.69%)	11 (35.4%)
Meningomyelocele	11 (21.15%)	12 (38.7%)
Meningocele	8 (15.38%)	5 (16.1%)
Encephalocele	3 (5.76%)	3 (9.6%)
Total NTDs	52	31
Associated Anomalies	7	9
Total live-births	19 831	26841
Prevalence of NTDs/1000 L.B.	2.6/1000	1.16/1000

Table 2 Characteristics of Patients with NTDs

Patient characteristics	Number (%) of first period	Number (%) of second period
Total	52	31
Sex		
Male	24 (46.2%)	16 (51.6%)
Female	28 (53.8%)	15 (48.4%)
Male / Female Ratio	0.85	1.06
Birth Order		
First	25 (48.07%)	11 (35.4%)
Second	4 (7.69%)	10 (32.2%)
Third	7 (13.46%)	4 (12.2%)
≥ Fourth	11 (21.15%)	6 (19.3%)
Consanguinity	6 (11.5%)	6 (19.3%)

When the results of both mother's age and birth order were combined together they show that when the youngest age group having their first baby presents the highest figures of the anomalies, but the number decreases with increasing age and increasing birth order. As mother's age advances (35 and above) birth order are associated with multiple previous pregnancies (4th and more)

DISCUSSION

NTDs can be detected antenatally through examination of mother's amniotic fluid for alpha fetoprotein and by ultrasound examination performed at about 16 weeks of gestation [12, 13]. This screening and periconceptual folic acid supplementation has substantially decreased the incidence of NTDs in some countries. These facts

must be taken into consideration when comparing incidence among countries with different practices in the prenatal care, like in Studies in the United States, using various methodologies, have shown decreases of 19%–32% in the prevalence of NTDs overall since the implementation of folic acid fortification in 1998 [14].

The rates dropped markedly in the second period of our study to 1.16/1000 L.B. This could not be explained by single factor but by multiple approaches made for tackling this problem, including providing pregnant women with folic acid in the antenatal centers and increasing awareness of women regarding the importance of this supplementation. Added to these efforts, fortification of wheat flour with folic acid from August 2006 and acceptability of families for termination of pregnancies with fetuses inevitable for life conditions had impact on the outcome.

Two other studies done in the same area, the first was made at the neurosurgical department at Sulaimani Teaching Hospital for the period between 2006-2010. In this collection of cases, the patients were referred to this specialized center for cases who needed surgical interventions, so it did not include anencephaly cases which constituted the largest number in our series of cases [15]. The second study was done by Dr. Bakir to study risk factors for NTDs for the period between 2006-2007 where 60 cases were collected and the reason for the difference in the assumed number of cases were because the researcher gathered cases from 3 different areas namely, neonatal unit at maternity hospital, neonatal unit at the pediatrics hospital and the neurosurgical department at Sulaimani Teaching Hospital [16]. But the results of these 2 studies plus the results from our study all confirm the that NTDs are common in this area

In Oman, they also found a significant decline in the rate of spina bifida from 2.11 per 1000 deliveries in 1997 to 0.78 in 1998. The decline continued and in 2006 it was reduced by 86% of the 1997 incidence. Other NTDs did not show the same improvement during that time period [17].

From the US data (NHANES), compared to the pre-fortification (1988~1994) period , serum and erythrocyte folate concentrations in post-fortification (1999~2010) periods have increased dramatically, resulting in a 31% reduction in the occurrence of NTDs [18].

In Saudi Arabia, mandatory fortification of flour was adopted by the National Flour Mills Organization starting from 2001 (Year 1421 in Hijri Calendar) with the minimum requirement of 1.653 gram of folic acid for each kilogram of flour. To evaluate the effect of flour fortification with folic acid, Safdar et al compared, in a study from the Western Region, the incidence of NTDs at King Abdul-Aziz University Hospital (KAUH), Jeddah between the eras before flour fortification (1997-2000) and afterwards (2001-2005). They observed a decline in NTDs from 1.9/1000 live births in the former period to 0.76/1000 live births in the period following fortification (2001-2005) [18].

A study made at Pricess Badea Teaching Hospital, in the north of Jordan to show the effect of folic acid fortification on the incidence of neural tube defects, the incidence dropped from 1.85/births before fortification to 0.9 after fortification, 49% reduction, which is statistically significant [19].

Studies done in different parts of Iraq like the study done in Azadi Teaching Hospital in Dohuk the incidence was found 4.7/ 1000 L.B. in the period of 2004-2005 [20]. Central nervous system defects were the most common types of birth defects among live births. In Al-Anbar governorate it constituted 55% with a rate of 4.6 per 1000 live births. Similar rates were reported in Basrah for the period 1999–2000 (4.35 per 1000 births) [21], and Erbil (4.48 per 1000 live births [22]. However, higher rates of NTDs were reported in Baghdad (5.95 per 1000 births) [23] and Diwaniyah (8.4 per 1000 total births in 2000) [20] .

While in Ramadi the study was made 2007-2008 at Al-Ramanadi Maternity and Children hospital yielding an incidence of 3.3/1000 births [24]. These figures conencide with the first part of our study which shows high figures (before fortification of wheat with folic acid).

Significant declines in spina bifida and anencephaly were observed among Hispanic births and non-Hispanic white births. The prevalence ratio for non-Hispanic black births was of borderline significance for spina bifida and was not significant for anencephaly [25].

Regarding the type of NTDs in our study anencephaly was the most common anomaly among the CNS anomalies and among the top of congenital anomalies as a whole, but the figure of anenecephaly dropping in the second period was due to the fact that pregnancies diagnosed with fetuses having anencephaly are eligible for termination. But the results of the countries differ according to their geographic location and countries nearby or surrounding Iraq, some have almost the

same sequence of occurrence of the NTDs while others differ and spina bifida is more common than anencephaly. For example a study was done in Basrah showed a high prevalence on meningomyelocele during the period of 1990 to 1998 and it showed increase in the number of cases which they attribute to the exposure of Uranium as a result of Gulf War [21]. In the studies we encountered in which anencephaly was more common included the study of Tehran [26] and Izmir [27]. Also it was mentioned in the article on anencephaly by the center of Arab for Genomics Studies that in Morrocco, Palastine, Saudi Arabia, Tunisia and UAE, anencephaly is more prevalent [28]. But on the other hand all the studies performed in Jordan [29] plus that of North Iran [26] meningomyelocele is more common than anencephaly.

Data on the prevalence of NTD in Iraq are not yet published by Ministry of Health. However, searching electronic database and locally publishing journals revealed remarkable increase in the prevalence of NTD in certain localities In Iraq compared to that reported worldwide. These include the following: Ramadi (3.3/1,000 live births, 3 fold), Basra (4.3/1,000 live births, 4 fold) , Baghdad (4.4/1,000 live birth, 4 fold) , Diwaniah (8.5/1,000 live birth, 8 fold) , Najaf (27/1,000 live births, 27 fold), and Fallujah (95/1,000 live births, 95 fold) [30].

Study limitations

The total number of deliveries in the hospital under study does not represent the total number of deliveries in the government as there is a still a good number of mothers who prefer to deliver either at home or in a private hospital where recording could not be easily obtained and controlled. Added to that some families accept the idea of termination of pregnancies for an incompatable condition with life. So the figures obtained in our study does not represent actual prevalence in our region but it certainly gives clear idea that NTDs are among the most common congenital anomalies in our city as a whole and that there is a decline in the prevalence in the second part of the study.

a) Deficiency of information in the records of the patients was the major limitation.

b) No follow up of most cases recorded even those admitted to the neonatal unit.

c) Unavailability of a precise record of the pregnancies being terminated legally for medical reasons.

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