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NEURAL TUBE DEFECTS IN SUDAN

ISMAIL SATTI^{1,2,6}

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Abstract

Background: Neural tube defects are birth defects of the brain, spine, or spinal cord happen in the first month of pregnancy, often before a woman even knows that she is pregnant. Major cause of stillbirth, neonatal and infant deaths or severe lifelong disability. Also, the impact of NTD on caregivers well documented.

Objective: to address neural tubes defects rate, pattern and risk factors in wad Medani which the center of Sudan.

Methods: Observational, prospective, descriptive, cross-sectional and hospital-based study, NTDs during the study period were 72 cases. The collected data analyzed by SPSS.



Results: NTDs represent 41.4% of congenital anomalies with the incidence of 3.6:1000. 86.11% open myelomeningocele, almost 90% of the mothers between 20-39 years. The commonly encountered risk factors; Consanguinity in 68.06%, Previous baby with NTDs in 8.33% and previous baby with other congenital anomalies in 4.17%, besides very low usage of periconceptional folic acid. Males are more affected than females. Most detected during delivery 87.5%. Hydrocephalus is the commonly found comorbidity.

Conclusion: The rate of Neural Tube Defects is very high, with a very low rate of folic acid utilization pre-conceptionally. There is a need to have more training in ultrasound and conduct another study to disclose more issues. All interest should be towards health education and food fortification with folic acid to prevent neural tube defects which cost effective while management of residual damage and handling of complications is costly and tasking.

keywords: neural tube, spina bifida, folic acid, prevention, genetics, Sudan.

ملخص الدراسة

الخلفية: عيوب الأنبوب العصبي هي عيوب خلقية في الدماغ أو العمود الفقري أو النخاع الشوكي تحدث في الشهر الأول من الحمل، وغالبا قبل ان تعرف المرأة انها حامل. وتمثل السبب الرئيسي للاملاص ووفيات المواليد والرضع أو الإعاقة الشديدة مدى الحياة.

الهدف: معرفة معدل الحدوث والنمط والعوامل المسببة لعيوب الأنبوب العصبي في مدينة ود مدني وسط السودان الطرق : دراسة وصفية بمستشفى , العدد الكلي لحالات عيوب الأنبوب العصبي اثناء فترة الدراسة قد بلغ 72 حالة وتم تحليل البيانات التي جمعت بواسطة برنامج الحزمة الاحصائية للعلوم الاجتماعية.

النتائج: تمثل حالات عيوب الجهاز العصبي 41.1% من مجمل حالات التشوهات الخلقية بمعدل 3.6 حالة لكل الف. 86.11% عبارة عن حالات قليلة نخاعية سحائية مفتوحة . 90% من الامهات تراوحت اعمارهن ما بين 20 و 39 عاما. كما تمثلت عوامل الخطر الأكثر شيوعا في : القرابة (68.06%) , طفل سابق يعاني من عيب في الأنبوب العصبي (8.33%) , طفل سابق مع تشوهات خلقية اخرى (4.17%) ونسبة ضئيلة للاستخدام المنخفض لحمض الفوليك . الذكور أكثر عرضة للإصابة من الاناث . اغلب الحالات تم اكتشافها اثناء الولادة بنسبة 85.5% . وقد كان استسقاء الراس هو الاعتلال العصبي المصاحب

الخلاصة: معدل عيوب الجهاز العصبي مرتفع جدا بجانب الاستخدام الضئيل لحمض الفوليك قبل الحمل . هناك حوجة الي المزيد من التدريب علي الموجات فوق الصوتية واجراء دراسة اخري للكشف عن المزيد من المشكلات . يجب ان يوجه كل الاهتمام نحو التثقيف الصحي و اغناء الطعام بحمض الفوليك لمنع عيوب الأنبوب العصبي التي تكون فعالة من حيث التكلفة في حين معالجة الاضرار المتخلفة والمضاعفات أكثر تكلفة .

الكلمات المفتاحية: الأنبوب العصبي، الشوكة المشقوقة، حمض الفوليك، الوقاية، الجينات، السودان.



Introduction:

Neural tube defects (NTDs) are the most common birth defects, they include: spina bifida, anencephaly, encephalocele, and iniencephaly. (Maffoni, De Giuseppe, Stanford, & Cena, 2017) They can be isolated, common or part of a syndrome they are a major cause of stillbirth, neonatal and infant deaths or severe lifelong disability, also, the impact of NTD on caregivers well documented. (Rofail, Maguire, Kissner, Colligs, & Abetz-Webb, 2013)

NTDs affect over 300,000 births each year worldwide. Spina bifida affects about 1,500 births annually in the USA, 3.5 in every 10,000 USⁱ which has decreased from around 5 per 10,000 since folate fortification of grain products. (MacHenry, Nevin, & Merrett, 1979) In Canada neural-tube defects decreased from 1.58 per 1000 to 0.86 per 1000 after food fortification, reduction greater for spina bifida than anencephaly and encephalocele. (De Wals et al., 2007) Periconceptional 400 µg of folic acid daily reduce the risk of neural-tube defects. (Ren, 2015)

NTDs are multifactorial, with genetic and environmental factors contributions (Greene & Copp, 2014) There are many factors suspected to increase risk for (NTDs), including female infant, family history of NTDs, Hispanic mothers, obesity, folate deficiency, diabetes, anticonvulsant drugs and sauna. (Mitchell, 2005). But these factors poorly predict NTD (Agopian et al., 2013). However, the extent to which these factors account for the population burden of NTDs is unknown analysis show known risk factors account for <50% of NTD cases.

Diagnosis by ultrasound, maternal serum alpha fetoprotein and the confirmatory test which not used for screening high-risk ladies; are amniotic fluid acetylcholine esterase and amniotic fluid alpha fetoprotein. 3D ultrasound can achieve a diagnostic accuracy of up to 80% (Cameron & Moran, 2009) transvaginal scan of the fetal skull before the 17th week, is an accurate method for the detection of low NTDs. (Blumenfeld, Siegler, & Bronshtein, 1993) A high prenatal detection rate for anencephaly (Boyd et al., 2000) Magnetic resonance imaging can diagnose NTDs early and accurately. (Birnbacher, Messerschmidt, & Pollak, 2002)

Wad Medani hospital is the tertiary hospital serving Gezira state in which a malarial endemic area, severe malaria is the major cause of hospital admission and 20% of severe malaria case-load and (17%) of all malaria mortality in Sudan. (Elnour, Alagib, Bansal, Abd Farag, & Malik, 2019) antifolates represent a cheap regime for treatment of chloroquine-resistant malaria, they are first-line treatment in African countries. (Hyde, 2005) Which may influence the prevalence.



NTDs cause significant morbidity and mortality in children, few studies have been done focusing on neural tube defects in Sudan. We conduct this study at Wad Medani district to assess; prevalence of NTDs, maternal use of folic acid, risk factors for NTDs and any associated congenital anomalies, and prevention of neural tube defects is cost effective while management of residual damage and handling of complications is costly and tasking.

Methodology

Observational, prospective, descriptive, cross-sectional and hospital-based study at Wad Medani hospital, during the period from March to August 2017. All Infants diagnosed with NTDs antenatally or during labour whose parents accepted to participate.

The data collected by a questionnaire including; Age, family history, Obstetrical and clinical history of the mother, consanguinity, folate consumption status, antenatal care status, and newborn clinical examination results.

All data entered in a master sheet then analyzed using SPSS (Statistical Package for Social Sciences) version 23. Frequencies, percentages, CI 95% and incidence rate.

Ethical

We obtained approval of the study from the ethical committee - Council of Obstetrics and Gynecology, Sudan Medical Specialization Board, and permission to conduct study obtained from administrative bodies.

Conflict of interest: No

Results

The rate of NTDs in our study is 0.36%, as the total number of deliveries was 20000 with 102 cases with other congenital anomalies, so NTDs is the commonest anomaly seen as they represent about 41.4% of all congenital anomalies. Male to female ratio 1.57:1. Almost, 87.5% of the cases detected for the first time during labour. (63.89%) associated with hydrocephalus, (22.22%) have musculoskeletal club foot and only one baby has VSD.

Table (1) illustrates that the disorder commonly affects the age group 30-39 years (45.84%), followed by 20-29 years (44.44%) and the least age group affected is < 20 years (9.72%). **Table (2)** represents; family history of NTD which found in 18.06% (CI=1.12 to 1.4), Consanguinity in (68.06%) (CI=1:2 to 1:1), Previous baby with NTDs in 8.33% (CI=1:37 to 1:6), Previous baby with other congenital abnormalities in 4.17% (CI=1:133 to 1:9), Current regular ANC 80.56%



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(CI=1:2 to 1:1), Current pregnancy ultrasound in 79.17% (CI=1:2 to 1:1), Preconceptional folate only 1.39% (CI=1:2 to 1:1) and only one lady was using antifolate. **Table (3)** the lesion distribution showed 86.0% open myelomeningocele, 5.6% open meningocele, 4.2% encephalocele and 4.2% anencephaly. **Table (4)** demonstrate medical disorder among mother 8.3% have diabetes Mellitus, 12.5% have hypertension and 2.8% with other systemic diseases.

Table 1: distribution of mothers according to age n= 72.

Age group	< 20	20-29	30-39	Total
Number	7	32	33	72
Percentage	9.72	44.44	45.84	100

Table (2): Distribution of mothers according to risk factor n= 72.

Risk factor	Yes	No	95% CI	Incidence rate
Family history of NTD	13	59	1.12 to 1.4	1:6
Consanguinity status	49	23	1:2 to 1:1	1:2
Previous child history of NTD	6	66	1:37 to 1:6	1:14
Previous child with other congenital abnormalities	3	69	1:133 to 1:9	1:27
Current pregnancy ANC status	58	14	1:2 to 1:1	1:1
Current pregnancy U/S status	57	15	1:2 to 1:1	1:1



Preconceptional folate status	1	71	1:1 to 1:1	1:1
Anti Folate agent	1	71	1:2844 to 1:13	1:72

Table (3): Lesion distribution n= 72.

Type	Anencephaly	Encephalocele	Open meningocele	Open myelomeningocele	Total
Number	3	3	4	62	72
Percentage	4.2	4.2	5.6	86.0	100

Table (4): Medical disorders among mothers n= 72.

Medical disorder	DM	HTN	OTHER	NO DISORDER
NUMBER	6	9	2	55
PERCENTAGE	8.3	12.5	2.8	76.4

Discussion

All respondents found that looking after baby with NTDs with comorbidities exert a substantial burden on parents by; increase workload, decrease their quality of life, decrease time for work and income.

The rate of NTDs in our study is 3.6:1000 is higher than 2.8:1000.(Omer, Abdullah, Mohammed, & Abbasher, 2016) in our study male to female ratio is 1.57:1 which higher than



another study, this may be because that study done among alive children's in neurology center which revealed a ratio of 1:1.2, also the usage of periconceptional folic acid in our study is lower, as only one lady used folic acid pre-conceptionally, unlike 69%.(Sadik, Babikir, & Arbab, 2017) Another study in maternity hospital which didn't address geographical distributions, revealed a same rate of 3.48/1000.(Elsheikh & Ibrahim, 2012)

Unfortunately, 87.5% of the cases detected for the first time during labour and there is no study found to address this issue, however, over 79% of the ladies have regular antenatal care and did ultrasound during current pregnancy, ultrasound has a high detection rate for NTDs, we need more training in anomaly screen by ultrasound as all these cases missed.

In Our study 63.89% associated with hydrocephalus which increase the morbidity and health services exhaustion, African study revealed that Hydrocephalus in found in 11.8% with myelomeningocele and in 0.5% of encephalocele.(Warf, 2011)

In this study, the commonly affected age group is 30-39 years (45.84%) followed by 20-29 years (44.44%) which is not agree with that concluded at Omdurman maternity hospital. It may be because of method as they found that 55.5% of the mothers were less than 25 years.(Elsheikh & Ibrahim, 2012)

family history of NTD found in 18.06% but its lower in another study in other part of Sudan which revealed (10.7%).(Omer et al., 2016)

in our study we found that Consanguinity in 68.06%, Previous baby with NTDs in 8.33% and previous baby with other congenital abnormalities in 4.17% all these findings points towards genetic predisposition to NTDs, Genetic studies in NTDs concentrating on folate-related genes, however, few evidence concluded linking between both, so there is growing evidence on genes involved in neurulation.(Bassuk & Kibar, 2009)

In our study 86.11% open myelomeningocele which the most severe type of NTDs, but at Omdurman it is around 50%.(Elsheikh & Ibrahim, 2012; Omer et al., 2016)

Our study showed 8.34% of the mothers have Diabetes mellitus, about 10% of fetuses from diabetic pregnancy display congenital malformations in different systems; cardiovascular, gastrointestinal, genitourinary and neurological, among which the neural tube defects (NTDs) were more frequently.(Dheen et al., 2009) oxidative stress inhibit *Pax-3* expression, and reduce *Pax-3* in the neural tube could explain NTD because of diabetes.(Chang et al., 2003)



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Conclusion

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