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ORIGINAL ARTICLE

PATTERNS OF NEURAL TUBE DEFECTS AT TWO TEACHING HOSPITALS IN ADDIS ABABA, ETHIOPIA A THREE YEARS RETROSPECTIVE STUDY

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ABSTRACT

Background: *Neural tube defects (NTDs), one of the most common congenital malformations, are potentially preventable cause of perinatal morbidity and mortality.*

Objectives*: To give baseline description of NTDs and their outcome at two teaching hospitals in Addis Ababa, Ethiopia.*

Materials and Methods: *A retrospective cross sectional descriptive study conducted from September 2009 to August 2012.*

Results: *During the study period out of 28,961 deliveries 177 cases of NTDs were identified, giving an overall NTD prevalence of 6.1/1000. Only 12% (21/177) were diagnosed before 28 weeks of gestation. The mean gestational age at diagnosis of NTDs was 33.8 weeks (±5.5). Majority, 93.2% (165/177), had antenatal care (ANC) follow-up. Most, 72% (127/177), were diagnosed by ultrasound before delivery while 28% (50/177) were identified at the time of delivery or expulsion. Majority, 85.3% (151/177), never received folic acid supplementation. Only less than 1% (2/177) of the mothers started taking folic acid supplementation pre-conceptionally. Only a third, 33.3% (59/177), of the fetuses were born alive while only 13.6% (24/177) were discharged alive. Myelomeningocele, identified in 51.4% (91/177), was the commonest NTD in this study.*

Conclusion and recommendations: *The proportion of NTDs in this study is among the highest globally reported rates. The practice of periconceptional folic acid supplementation is negligible. And although most had ANC follow-up the vast majority of NTDs were diagnosed late in the third trimester. It is, therefore, highly recommended to consider implementing national preventive strategies to reduce the prevalence of NTDs in Ethiopia.*

Key words: *NTD, Myelomeningocele, Spina Bifida*

INTRODUCTION

Neural tube defects (NTDs) are a group of severe human congenital malformations caused by the defective closure of neural tube between 21 to 28 days following conception. They represent one of the most common congenital malformations in neonates worldwide (1). NTDs can be classified as open or closed, depending on whether neural tissues are exposed or covered by skin, respectively. Open NTD are more frequent and include spina bifida (myelomeningocele), anencephaly, encephalocele, hydranencephaly, iniencephaly and schizencephaly (2).

The worldwide prevalence of NTDs ranged from 1 to 10 per 1000 (3). Each year, 300,000 to 400,000 infants worldwide are born with NTDs including spina bifida and anencephaly (4). They remain an important yet potentially preventable cause of perinatal morbidity and mortality. The risk of death is dependant on the severity of the lesion and on other factors such as the availability of medical and surgical resources (5). All anencephalic children are stillborn or die soon after birth. Children with meningocele and myelomeningocele have higher survival rates, generally due to extensive medical care and surgery.

The exact cause of NTDs is not known. The aetiology, however, includes both genetic and environmental factors. Maternal socioeconomic status, geographic area, occupational exposure, maternal use of antiepileptic drugs, education, and maternal nutrient

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deficiency have been associated with variations in the incidence (6,7). The best known risk factor for foetal NTD is maternal folate deficiency (8, 9). And, screening tests for NTDs include ultrasound examination and measurement of Maternal Serum Alpha-Fetoprotein (MSAFP) at 16–18 weeks of gestation (10). Screening decreases morbidity and mortality by promoting access to earlier diagnosis, enabling families to make informed reproductive choices, and designing appropriate strategies for prenatal care and delivery.

Prenatal maternal screening programs with termination of affected pregnancies combined with periconceptional folic acid supplementation and food fortification have led to a decrease in the prevalence of NTDs where these interventions are practiced (11-17). For example, the incidence of NTDs in England and Wales declined by 96 percent between 1970 and 1997: from approximately 3.2 per 1000 births to 0.1 per 1000 births (13). Forty percent of the decline was attributed to antenatal screening with termination of affected pregnancies and 56 percent was attributed to a decline in incidence, due at least in part to an increase in dietary folate intake. In addition, randomized trials have consistently shown peri-conception folic acid supplementation to be one of the public health interventions effective in reducing the risk of NTDs (12,18). Data from randomized trials also indicate that periconceptional folic acid supplementation reduces the risk of recurrent NTDs by about 70 percent (19).

Published data on NTDs in Ethiopia is very limited. One retrospective review of 115 children with neural tube defect (NTD) conducted from January, 2001 to June 2005 at Ethio Swedish Children's Hospital at Tikur Anbessa Hospital showed the most common defect seen to be myelomeningocele (64.4%); followed by meningocele (18.3%) and encephalocele (13.0%). Associated anomalies like clubfoot undescended testis, different types of hernias, hydroceles etc. were noted in 28.7% of the patients (20).

Neurosurgical service provided in Ethiopia is also very limited. A local study done in neurosurgical department on pediatric patients awaiting admission to Tikur Anbessa Hospital (TAH) from July 2006-February 2007 demonstrated that there were 338 children in waiting lists out of which 41% were myelomenigeocele and 29% were hydrocephalus. In addition, the average waiting time for admission was 447 days and the patients had to travel 300 miles on average as most of them come from rural part of Ethiopia (21).

Neither routine supplementation of folic acid for women of reproductive age group nor routine screening for NTDs is practiced in the country. This study was conducted at two teaching hospitals in Addis Ababa, Ethiopia. And it is designed primarily to give a baseline description of neural tube defects and their outcome in our setup.

MATERIALS AND METHODS

This is a hospital based cross sectional descriptive study done from September, 2009 to August, 2012 at Tikur Anbessa Hospital (TAH) and Gandhi Memorial Hospital (GMH), Addis Ababa, Ethiopia. It was done through a retrospective review of charts of all mothers who were admitted to the two teaching hospitals and delivered or aborted a fetus with NTD. Their Medical Record Numbers (MRN) identified from admission log books in the maternity ward and Neonatal Intensive Care Unit (ICU) were used to retrieve medical records/charts. Data was collected by the investigator using a pre-tested questionnaire from medical records of the study participants. The collected data was coded, cleaned and analyzed using SPSS version 20 statistical software. Summary tables and charts were used for describing data.

Ethical clearance was obtained from the research and publication committee of the department of Obstetrics & Gynecology, and IRB of Addis Ababa University. Permission was also obtained from the Hospitals to access the medical records of mothers included in the study.

RESULT

During the study period there were a total of 28,961 deliveries in the two teaching hospitals. And, a total of 177 mothers the outcome of whose pregnancies was complicated with NTDs were identified. The overall occurrence of NTDs in this study, hence, was 6.1/1000 births (live birth and fetal deaths). The mean and median ages of the participant mothers were 27.1 (±5.6) and 27 (IQR 7) respectively. Majority were house wives and from Addis Ababa with proportions of 48.6% (86/177) and 77.4% (137/177) respectively. (Table 1)

Table 1: Socio-demographic characteristics of mothers whose pregnancy outcome was complicated with NTDs at two teaching hospitals, Addis Ababa, Ethiopia, 2009-12.

	Characteristics	Frequency	Percentage (n=177)
Address	Addis Ababa	137	77.4 %
	Out of Addis Ababa	40	22.6 %
Marital Status	Married	163	92.1 %
	Divorced	1	0.6 %
	Single	13	7.3 %
Occupation	House Wife	86	48.6 %
	Governmental Employee	27	15.2 %
	Private Employee	21	11.9 %
	Factory worker	15	8.5 %
	Student	14	7.9 %
	Others	14	7.9 %

Primigravidity and gravida II were the commonest gravidities each accounting for 43.5% (77/177) and 32% (57/177) respectively. The mean gravidity was 2±1.2 while the median gravidity was 2 (IQR = 2). Only 12% (21/177) of the cases were diagnosed before 28 weeks of gestation. The mean gestational age at diagnosis of NTDs was 33.8 weeks (±5.5). Majority of the mothers, 93.2% (165/177), had ANC follow up. The ANC follow up in 72.3% (128/177), 13% (23/177) and 8% (14/177) of the mothers was in a health center, private clinic and hospitals respectively.

Most of the NTDs, 72% (127/177), were diagnosed by ultrasound before delivery while 28% (50/177) of cases were identified at the time of delivery or expulsion. Majority, 85.3% (151/177), never received folic acid supplementation throughout the entire pregnancy. Only less than 1% (2/177) of the mothers started taking folic acid supplementation pre-conceptionally. The rest, 3.4% (6/177) and 10.2% (18/177), of the mothers received folic acid in the first and after first trimesters respectively. (Table -2).

Medical illnesses were identified in 12.4% (22/177) of the study participants. Hypertension, identified in 3.4% (6/177) of the mothers, was the commonest medical illness, and diabetes, epilepsy and others were found in 2.3% (4/177), 1.7% (3/177) and 4.5% of the mothers respectively. The mode of delivery in about 74% (131/177) of the study participants was spontaneous vaginal. Cesarean section and laparatomy for uterine rupture were done in 17.5% (31/177) and 0.1% (2/177) of the cases respectively. The rest, 7.3 % (13/177), were terminated medically. The indications for the cesarean sections were malpresentation due to breech and transverse lie, previous C/S scar and CPD in 48.5% (16/33), 18% (6/33) and 27% (9/33) of the cesarean deliveries respectively. The diagnosis of congenial malformation was made after delivery in 39% (12/31) of the mothers who delivered by cesarean section.

Perinatal outcome: Majority of the neonates born to the study subjects were females accounting for 72.3% (128/177) with male to female ratio of 1:2.6. (Table 1) Only a third, 33.3% (59/177), of the fetuses were born alive while the rest 66.7% (118/177) were still born. The mean birth weight was 1991 gm±951gm while the median weight was 1900 gm (IQR=1650gm). Out of the 59 live born neonates 40 (67.8%) had 1st minute APGAR score of <6 whereas 19 (32.2%) had APGAR score of $\geq$6. Death within few minutes of delivery and before referral to Neonatal Intensive Care Unit (NICU) occurred in 28.8% (17/59) of the live born neonates. The rest, 71.2% (42/59) of the live born neonates, were referred to NICU. Fifteen, 35.7% (15/42), of the referred neonates died in the early neonatal period while in the NICU with the mean time of death of 6.8 hrs. Only 12.3% (24/59) of the live born neonates or 13.6% (24/177) of the total fetuses born or expelled were discharged alive with appointment to neurosurgical unit. The outcome of the admission was not documented for three of the admitted cases. (Table 3)

Table -2: Obstetric characteristics of mothers whose pregnancy outcome was complicated with NTDs at two teaching hospitals, Addis Ababa, Ethiopia, 2009-2012. (n=177)

Characteristics	Frequency	Percentage, % (n=177)
Gravidity		
I	77	43.5
II	57	32.2
III	24	13.6
IV	10	5.6
V	6	3.4
VI	3	1.7
GA at diagnosis of NTD (n=177)		
< 28 weeks	21	12
≥ 28 weeks	156	88
ANC follow up (n=177)		
Yes		
At health centre	128	72.2
At Hospital	23	13
At private facility	14	8
Sub total	***165***	***93.2***
No	12	6.8
Mode of NTD diagnosis		
Ultrasound before delivery	127	72%
Identified after delivery/ expulsion	50	28%
Received folic acid supplementation		
Yes		
Preconception	2	1.1
During first trimester	6	3.4
After first trimester	18	10.2
Subtotal	26	14.7
No	151	85.3

Table 3: Perinatal outcome of mothers whose pregnancy was complicated with NTDs at two Teaching Hospitals, Addis Ababa, Ethiopia, 2013. (n=177)

Characteristics	Frequency	Percentage, (n=177)
Sex		
Male	49	27.7
Female	128	72.3
Pregnancy outcome at the time of delivery		
Alive	59	33.3
Dead (Stillborn)	118	66.7
Pregnancy outcome at discharge		
Alive	24	13.6
Dead		
Still born	118	66.7
Death within few minutes of delivery and before referral to NICU	17	9.6
Death after referral to NICU	15	8.5
Sub total	***150***	***84.7***
Unknown	3	1.7

Myelomeningocele, identified in 51.4% (91/177) of the cases, was the commonest NTD in this study. Anencephaly, encephalocele and meningeocele were also the NTDs identified in 43.5% (77/177), 2.8% (5/177) and 2.2% (4/177) of the neonates respectively. Other associated congenital anomalies were observed in 51.8% (92/177) of the neonates. The most common associated anomaly observed was hydrocephalus identified in 37.8% (67/177).

The other associated anomalies include club foot and gastrointestinal anomalies (omephalocele, gastrochesis, imperforated anus and diaphragmatic hernia) identified in 6.8% (12/177) and 3.9% (7/177) neonates respectively. (Table -4)

Maternal post partum complications were identified in 21(11.9%) of the mothers. These complications include PPH secondary to uterine atony, uterine rupture secondary to obstructed labor due to hydrocephalus and genital laceration occurring in 7 (4%), 2 (1.1%) and 12 (6.8%) of the mothers respectively.

Table 4: NTD type and associated anomalies identified in mothers whose pregnancy outcome was complicated with NTDs at two teaching hospitals, Addis Ababa, Ethiopia, 2009-2012. (n=177)

Characteristics	Frequency	Percentage, (n=177)
Type of NTD identified		
Myelomeningocele	91	51.4
Anencephaly	77	43.5
Encephalocele	5	2.8
Meningeocele	4	2.2
Associated congenital anomaly (n=177)		
Yes		
Hydrocephalus	67	37.8
Club foot	12	6.8
GI anomalies	7	3.9
Cleft lip	2	1.1
Others	4	2.2
Sub total	***92***	***52***
No	85	48

DISCUSSION

One of the Millennium Development Goals initiated by the United Nations was dedicated to reducing global child mortality rates. Since 1990, global child mortality has been declining largely due to the focus on communicable diseases (22). This reduction of mortality has led to the neglected causes of child mortality to be exposed, including that of congenital abnormalities (23). Neural tube defects (NTDs) are one of the most common major birth defects second in frequency only to congenital heart diseases (24). The incidence of NTDs varies according to the geographic conditions, race, sex of the baby and certain maternal conditions (25).

In most developed countries and many developing countries like South Africa the incidence is less than 1/1000 mainly as a result of fortification of their diet with folic acid and perinatal supplementation of folic acid. Regardless of the progress in control of NTDs observed in these countries, NTD continue to be a problem of significant public health impact in our setup. In this study the overall prevalence of NTDs was found to be 6.1/1000 deliveries.This prevalence of NTDs in this study (6.1/1000) is 5 and 9 times higher than reports from South Africa (1.4/1000) and Thailand (0.67 /1,000 births) respectively.

Only 15% of mothers were seen to have been supplemented with folic acid, 69% of which received the supplementation in the third trimester when it has no protective effect. This could be due to lack of knowledge of the importance of folic acid in reducing the prevention of NTDs by the mothers as well as health care providers (26). This is in agreement to a prior study done by Mohammed at Jigjiga University Hospital on supplement use among pregnant women in Ethiopia, in which 76.4% women claimed no awareness about the benefits of early supplementation and particularly folic acid intake was found to be negligible during the prenatal as well as antenatal period (27).

The most common type of NTD observed in this study was myelomeningocele 91(51.4%) followed by anencephaly 77(43.5%). This finding is in agreement with most other international studies (28-31). Similar study done at Tikur Anbessa Ethio-Sewdish Hospital and published in 2009 found the most common

anomaly to have been myelomeningocele (64.4%) and meningocele 18.3 % (20). The study, however, was conducted in NICU where only live neonates were referred leading to higher proportion of alive spina bifida which had better prognosis while excluding anencephalic babies which die soon after delivery.

NTDs were observed to occur more commonly in females in our study with male to female ratio of 1:2.6 which is comparable to reports from many countries. A case-control study based on the Oxford Record Linkage about 70 percent of the children with anencephaly and 60 percent of the children with spina bifida were females (32). The sex distribution in the Thailand 10 years review, however, was equal among NTD cases with 55 (48%) females, 59 (51%) males and one (1%) unidentified sex (29).

Although 95% of mothers whose pregnancy outcome complicated by NTDs had ANC follow-up only 12% of them were diagnosed before 28 weeks of gestation and the mean gestational age at the time of diagnosis was 33.9 week ±5.6 weeks. This clearly shows the failure of the ANC service in our setup to timely diagnose NTDs. Detecting lethal congenital anomalies early and termination in the first trimester could have avoided caring anomalous fetus to third trimester of pregnancy and complications associated with late termination. This problem would have been reduced by screening all mothers in the second trimester with ultrasound and determining MSAFP as demonstrated in high income countries where the prevalence was reduced by 56% just by screening and terminating the affected fetus (13).

***Limitations of the study*:** As this study is retrospective and the study population not representative of the general population the study findings may not reflect the national situation.

***Conclusion and recommendations*:** In conclusion, the prevalence of neural tube defects in this study is among the highest globally reported rates the most prevalent NTD being myelomeningocele. The practice of periconceptional folic acid supplementation in our setup is negligible. And although most had ANC follow-up the vast majority of NTDs were diagnosed late in the third trimester.

Considering the findings of this study and cost of treatment of NTDs it is highly recommended to consider implementing national preventive strategy to reduce the prevalence of NTDs in Ethiopia. And based on lessons learned from other countries; early screening and periconceptional folic acid supplementation are the two effective possible approaches to bring about the required reduction in NTD prevalence in the country.

In addition, further large scale prospective studies are needed to have reliable estimates on burden of NTDs, associated factors and cost benefit analysis of screening and preconception folic acid administration for Ethiopian set-up.

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