JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

DETERMINANTS OF NEURAL TUBE DEFECT (NTD) AMONG MOTHERS AT YEKATIT 12 ABEBECH GOBENA MCH TEACHING HOSPITAL IN ADDIS ABABA, ETHIOPIA, A CASE CONTROL STUDY

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ABSTRACT

Background

NTD is related to failure of neural tube closure between 3rd and 4th weeks of embryo development. NTD is divided into two categories: cranial and spinal defects. Anencephaly, encephalocele, and spina bifida are examples of NTD. Few studies have indicated a combined role for environmental and genetic factors in the development of NTD. So, the aim was to assess the factors associated with the development of NTD

Method

An unmatched case control study design was utilized on 245 mothers, 61 cases and 184 controls at AGH MCH center of Yekatit 12 specialized comprehensive teaching hospital located at the capital city of Addis Ababa Ethiopia. All conformed cases of NTD were included with 3 controls chosen by simple random sampling method. Data collected using electronic questionnaire and analysis was done by SPSS 27.0 and presented with significant P value of 0.05 and with 95% CI.

Results

Totally Six variables were found to be related to NTD development. primi gravidity (AOR:0.055, 95%CI: 0.007,0.416), gravidity 2-4(AOR:0.035,95 CI:0.006,0.238), Not having Previous pregnancy affected with NTD (AOR:0.079,95 % CI: 0.009,0.663) , Monthly family income in birr <5000 birr (AOR: 4.224, 95%CI : 1.344, 13.273), Not taking Preconception folic acid use (AOR : 9.600,95%CI 2.151-42.834), Known chronic illness mother (AOR: 8.561,95 % CI :1.510 48.518) , Not having Preconceptional care contact (AOR : 9.209, 95% CI :1.027-82.554) were found to be significantly associated with NTDs development .

Conclusion

Preconception care and taking preconceptional folic acid supplementation will reduce the odds of having NTD so they are recommended to prevent NTD, and on the other had having Increased number of pregnancies, low monthly income, having chronic medical illness and having previous NTD affected pregnancy was found to increase the odds developing NTD so we recommend to have increased follow up and if possible, to avoid preventable factors.

1. INTRODUCTION

In humans, formation of the neural tube begins in the 3rd week after fertilization and requires that the top layers of the embryonic germ disc elevate as folds and fuse in the midline (1). The phenomenon is intricate, involves several cell processes, and when often disrupted, resulting in NTDs (1-3). Neurulation is the process of neural tube formation; it gives rise to the regions of the brain and spinal cord that extend to the lowest sacral level. NTDs occur because of a defect in the neurulation process (1, 4).

NTD is related to failure of neural tube closure between 3rd and 4th weeks of embryo development (3). The cause of NTDs is not clearly stated. Most NTDs are multifactorial in origin, having both genetic and environmental components (3, 5).

Anatomically, NTD can be classified into cranial and spinal defects. Cranial defects comprised anencephaly, encephalocele, and iniencephaly. Conversely, spina bifida occulta, meningocele, and myelomeningocele are examples of spinal defects (4, 6).

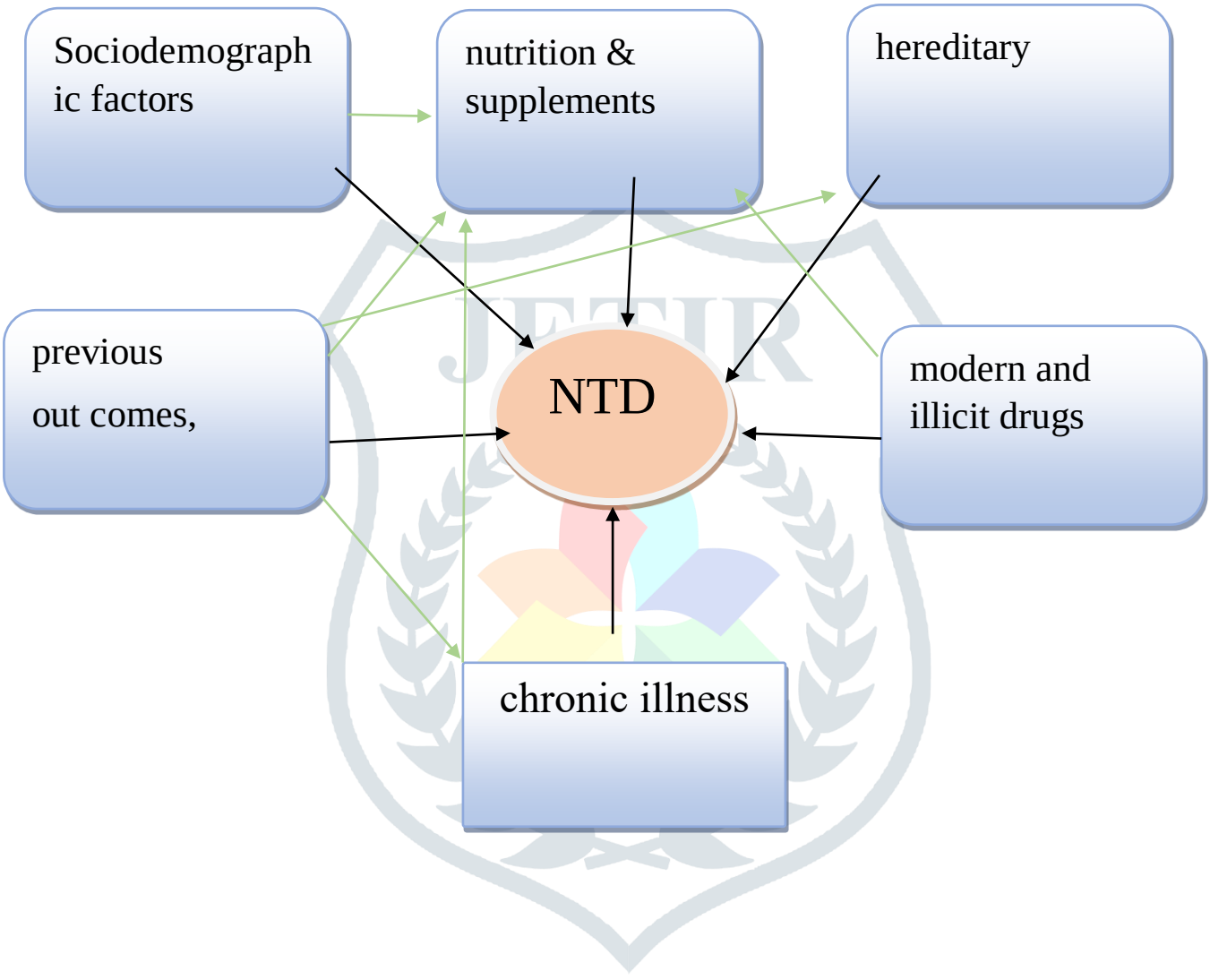
Depending on how the skin or surface is affected, neural tube defects (NTDs) can be classified as either open or closed issues (4, 7). An open NTD involves a connection between the brain or spinal cord (or their protective coverings) and the outside world. This category includes conditions such as anencephaly, spina bifida, iniencephaly, and encephalocele (7, 8). In closed NTD there is no communication with external environment which includes spina bifida occulta, lipoma, diastematomyelia, diplomyelia (4-7, 9).

People born with spina bifida usually lacks acceptance in their communities (10).its a severe birth defect has been proven to be preventable through scientific research (5, 6, 11). Many NTDs can be attributed to not getting enough folic acid around the time of conception in addition to these there are multiple factors identified as a risk factor for the development of NTD, these could be maternal diabetes , maternal exposure to certain teratogens such as valproic

acid taken by mothers who have epilepsy , lead exposure in drinking water , in utero exposure to arsenic , and mycotoxins and fungus contaminants of maize (11, 12). Other risks include hyperthermia due to maternal fever or heat exposure , maternal "flu" during the first trimester , certain parental occupations , and lower socioeconomic status (11, 12).

1.1. Conceptual framework

FIGURE 1:CONCEPTUAL FRAME WORK OF RESEARCH DONE ON AGH,2023



2. Objectives

2.1. General Objective

- To identify determinant factors of NTD among mother with follow up, termination and/or delivery at AGH.

2.2. Specific Objectives

- To identify the association that nutrition, supplementations, Genetic or hereditary, Drug use, chronic illness, Sociodemographic and other environmental factors have on the development of NTD with among mother with follow up, termination and/or delivery at AGH.

3. Method and Material

3.1. Study Design and area

Facility based unmatched case control study design was used at AGH, MCH center for Yekatit 12 specialized comprehensive teaching hospital located at the capital city of Addis Ababa Ethiopia.

Yekatit 12 hospital is one of the major teaching specialized hospitals situated in Addis Ababa giving care to over 150000 clients per year with over 500 beds at its hospital, and the past 2yrs it has opened its own MCH center with around 300 bed available and have close to 1000 deliveries per month in addition to other outpatient care and NICU care.

AGH give care to 4 sub cities of Addis Ababa with 18 health centers under these 4 sub city and one hospital which is located in Oromia region under special zone for Addis Ababa, our study has indirectly covered all these area.

3.2. Study period

Study was conducted may 2022 up to October 30, 2023 and data collection period was from June to September 2023.

3.3. Population

3.3.1. Study population

Are all women with follow up and delivery or termination done at AGH.

3.3.2. Sample population

Case group – All mother whose pregnancy is affected with NTD and had follow up and delivery /termination at AGH and full fill the eligibility criteria for case group.

Control group - All mother whose pregnancy is not affected by NTD and had follow up and delivery /termination at AGH and full fill the eligibility criteria for control group.

3.4. Eligibility criteria

3.4.1. Inclusion criteria for case group

The inclusion criteria for the case group were all mother with follow up and delivery or termination at AGH with pregnancy affect with neural tube defect.

3.4.2. Exclusion criteria for the control

From the above all Cases with any ambiguity or multiple congenital anomalies was excluded from the study to avoid misclassification, and all elective or emergency first trimester pregnancy terminations was also not included to avoid difficulty misdiagnosis and babies delivered at other set up the health centers for our catchment centers were also not included.

3.4.3. Inclusion criteria for control group

All mother with follow up and delivery or termination done at AGH with fetus not affect with neural tube defect were included in the study.

3.4.4. Exclusion criteria for control group

Those who delivered or expelled fetus with any congenital anomalies even other than neural tube defect were excluded and finally any spontaneous or elective first trimester Abortion.

3.5. Sample size calculation

The sample size was determined by using the double population proportion formula using the Epi Info, Stat Calc, case control sample size 3 calculator. To determine the sample size, numerous factors significantly associated with the outcome variable were considered, and the larger sample size was used for this study which is exposure of folic acid (2). We took the percent of cases exposed as 4.5%, and the percent of controls exposed were 29.4 % (2), considering 95% confidence level (CI), 80% power, control to case ratio of 3: 1, it gave a minimum total sample size of 224 and out of which 56 cases of NTD and 168 controls. And the least possible odd ratio to be detected being 0.43.

Considering 10% non-respondent a total of 246 sample size was taken out of which 61 were cases and 185 were control groups. The total duration of data collection being 4-month time at Abebech Gobena hospital.

3.6. Sampling technique

Due to the rare occurrence of NTDs, we have taken each and every confirmed case of NTD who were followed, terminated or delivered at AGH as a case group and for the control group three mothers with baby not affected by NTD were selected by simple random sampling technique from that same day's delivery list on the HMIS registration.

3.7. Data collection procedure and Instrument

All intern doctors, residents, midwives, and clinical nurses was informed to report to the principal investigator whenever suspected cases of NTDs is delivered or medically terminated.

Afterwards, data was collected by trained intern doctors and residents, and before discharge of the women. The individual interns or the residents' collecting data was responsible in selecting the control group by simple random sampling using lottery method from the HMIS list.

Data was collected by face-to-face interviews using electronic based structured questionnaire adapted from the WHO birth defect surveillance tool and other similar research done previously. Some Data and maternal information were also collected from the delivery and post abortal registration form for the given period.

3.8. Data quality management

All Diagnosis were made by senior OBGYN specialists and MFM sub specialists before termination and after delivery diagnosis were made by senior OBGYN residents with support of senior OBGYN specialists. Data collectors was trained for three days with the structured questionnaire about the objectives of the study and techniques of collection and how to fill the questionnaire. Principal investigator was cross checking for completeness and accuracy of the data on regular basis. Necessary corrections were made by cross checking with the patient's chart. Data was intensively cleaned before any analysis.

3.9. Study Variables

The dependent variable was NTD affected alive or dead fetus or abortus.

In These study the independent variables were Residency, Age of mother ,Age of partner, Marital status ,educational status ,partner educational status ,occupation ,family size ,annual family income ,parity ,previous history of abortion, still birth, previous history of END, previous congenital affected delivery, preconception folic acid supplementation, number of index pregnancy , ANC place , known chronic illness ,known pregnancy associated illness, current pregnancy type ,any attempt to terminate pregnancy, contraceptive use before pregnancy, Preconception care ,Preconception supplement/drug use, use of alcohol during 1st tm px ,Drug use in 1st tm pregnancy

3.10. Data processing and analysis

Data was entered to epi info version 7 and analyzed using SPSS version 27. Coding of individual questionnaires was undertaken before data entry in to the software. Descriptive statistics, cross tabulation and binary logistic regression were used to characterize and to analyze the relationship between the dependent and independent variables. Outcome was presented as number, frequency and percentage and comparison between groups was estimated by Chi-square, odd's ratios, with 95% confidence interval and p-value set at 0.05 will be used to determine the statistical significance of the associations**.**

3.11. Operational definition

Neural tube defects (NTDs**)**: Neural tube defects (NTDs) are congenital structural abnormalities of the central nervous system and vertebral column which include anencephaly, spina bifida and Encephalocele, exencephaly, iniencephaly and others characterized with failure in the closure of neural plate(5, 23, 24).

NTDs cases: mothers who, regardless of gestational age and live birth, gave birth to a child with any kind of NTDs.

NTDs controls: women who gave birth to children who were free of congenital defects and other NTDs.

3.12. Ethical clearance

Ethical clearance & permission letter was obtained from the Institutional Review Board (IRB) of Yekatit 12 specialized medical college. Confidentiality was maintained during data collection, analysis and interpretation by avoiding recording of names and impartiality in questioning and collection process.

4. Results

Socio-demographic characteristics of the study participants was a total of 246 participants with 61 cases and 185 controls were included. Among the total 61 NTDs cases 29 (47%) were anencephaly, 20 (33%) spina bifida open and closed and 9(15%) encephalocele and combination of 2 NTD 3 (5%). It was discovered that 69% of the mothers were between the ages of 25 and 35. And 63% of the fathers were in the range of 25-35. About 93.4% cases and 93.5% control are married. In terms of employment, 106(57.3%) of the controls and over 29(47.5%) of the cases were housewives, with office work coming in second.

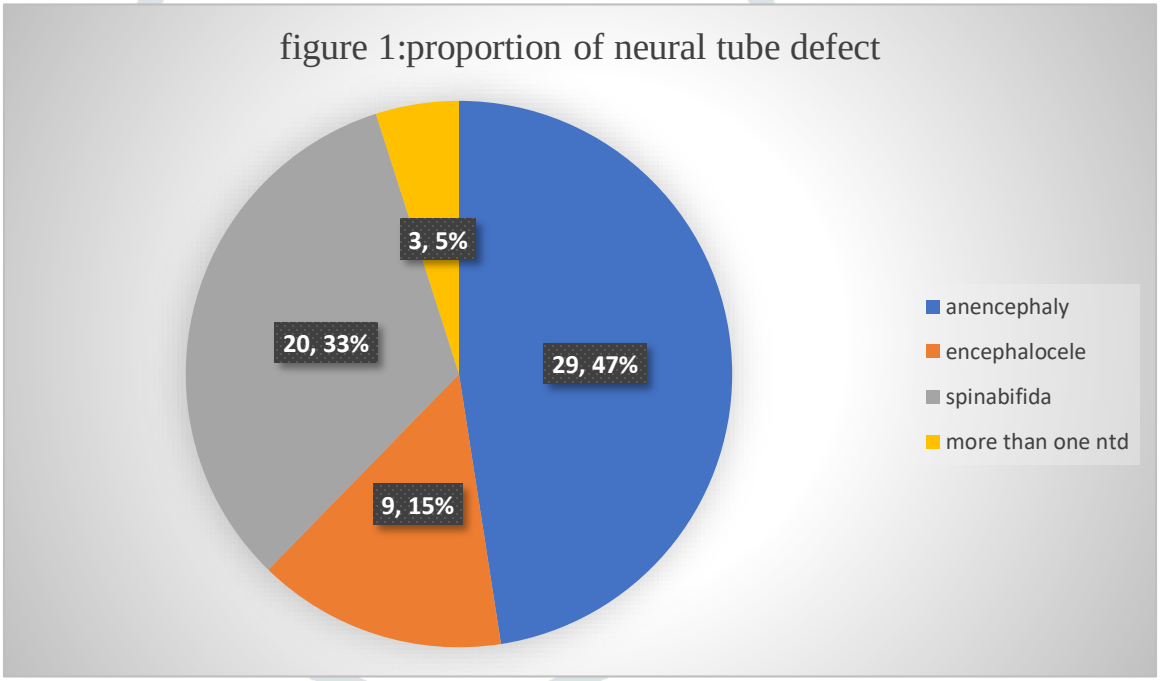


FIGURE 2:PROPORTION OF NEURAL TUBE DEFECT ON STUDY DONE AT AGH,2023

Totally 73% of our mothers have high school and secondary school educational level for both the case and the control collectively with only 4.9% case and 8.6 % control having no formal education. Additionally, 66.7% of the fathers in the case and control have completed high school and secondary education, with only 4.9% of the case and 7.1% of the control having never attended any formal education.

TABLE 1: SOCIO-DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS ON STUDY DONE AT AGH,2023

Variable	Case: n (%)	Control: n (%)	Total: n (%)
Age of mother			
<25 25-35 >35	16(26.2) 42 (68.8) 3 (4.9)	49(26.5) 128(69.2) 8(4.3)	65(26.4) 170(69.1) 11(4.5)
Age of father			
<25 25-35 >35	2(3.2) 37(60.7) 22(36.1)	6(3.3) 124(67) 55(29.7)	8(3.3) 161(65.4) 77(31.3)
Marital status			
Single /divorced Married	4(6.5) 57(93.4)	12(6.5) 173(93.5)	16(6.5) 230(93.5)
Occupation of mother			
Housewife Industry Office/private work/other	29(47.5) 6(9.8) 26(42.6)	106(57.3) 10(5.4) 69(37.3)	135(54.9) 16(6.5) 95(38.6)
Estimated income monthly			
<5000 5000-10000 >10000	32(52.4) 21(34.4) 8(13.1)	43(23.2) 86(46.5) 56(30.3)	75(30.5) 107(43.5) 64(26)
Educational status of the mother			
Nonformal education Primary school (1-8) Secondary school (9-12) College or higher-level learning	3(4.9) 25(41) 22(36.1) 11(18)	16(8.6) 63(34.1) 70(37.8) 36(19.5)	19(7.7) 88(35.8) 92(37.4) 47(19.1)
Educational status of the father			
Nonformal education Primary school (1-8) Secondary school (9-12) College or higher-level learning	3(4.9) 21(34.4) 23(37.7) 14(23)	13(7.1) 43(23.2) 77(41.6) 52(28.1)	16(6.5) 64(26) 100(40.7) 66(26.8)
Household family size			
1-3 4-6 >7	36(59.01) 21(34.4) 4(6.5)	76(41.1) 103(55.7) 6(3.2)	112(45.5) 124(50.4) 10(4.1)

TABLE 2: REPRODUCTIVE CHARACTERISTICS OF PARTICIPANTS ON STUDY DONE AT AGH,2023

Variable	Case: n (%)	Control: n (%)	Total: n (%)
Gravidity			
Gravida 1	19(31.1)	61(33)	80(32.5)
Gravida 2-4	33(54.1)	121(65.4)	154(62.6)
Gravida 5 and above	9(14.7)	3(1.6)	12(4.9)
Parity			
Para 1	26(42.6)	67(36.2)	93(37.8)
Para 2-4	35(57.4)	118(63.8)	153(62.2)
Para 5 and above	-	-	-
Previous number of abortions			
No abortion	44(72.1)	155(83.8)	199(80.9)
One abortion	12(19.6)	23(12.4)	35(14.2)
Two and above	5(8.2)	7(3.8)	12(4.9)
Number of gestations			
Singleton	61(100)	177(95.7)	238(96.7)
Twin	0	8(4.3)	8(3.3)
Previous history of IUFD			
No	60(98.4)	181(97.8)	241(98)
Yes	1(1.6)	4(2.2)	5(2)
Previous history of ENND			
No	59(96.7)	179(96.8)	238(96.7)
Yes	2(3.3)	6(3.2)	8(3.3)
previous (non NTD) congenital anomaly			
no	58(95.1)	179(96.8)	237(96.3)
yes	3(4.9)	6(3.2)	9(3.7)
Previous NTD affected delivery.			
No	54(88.5)	179(96.8)	233(94.7)
yes	7(11.5)	6(3.2)	13(5.3)
Location of ANC			
None	7(11.5)	4(2.2)	11(4.4)
Health center	50(82)	159(85.9)	209(85)
Hospital	4(6.5)	22(11.9)	26(10.6)
Attempt to terminate these pregnancy			
No	61(100)	185(100)	246(100)
Yes	0	0	0

Contraceptive use 1st year time			
No	12(19.7)	40(23.8)	56(22.8)
Yes hormonal	47(77)	140(75.7)	187(76)
Yes non hormonal	2(3.3)	5(0.5)	3(1.2)

Regarding the reproductive history of the mother most of the mothers are multi para (para 2-para 4) with percentage of 57.4% for the cases and 63.8 for the controls and 100%of the cases and 97% of the controls are single gestation. There was 1.6% and 3.3% of previous history of IUFD and ENND respectively for the case group and 2.2% and 3.2% for the control group.

There was no attempt to terminate the pregnancy in all participants and there was 76% usage of hormonal contraceptive within last year pre pregnancy with no significant variations between the groups. There was 4.9% and 3.2% history of previous congenital anomaly delivery for the case and control sequentially not including the neural tube defect delivery. For the ante natal clinic 85% of the participants were having there contact at health center level.

TABLE 3:MEDICAL, ENVIRONMENTAL AND BEHAVIORAL CHARACTERISTICS OF PARTICIPANTS ON STUDY DONE AT AGH,2023

Variable	Case: n (%)	Control: n (%)	Total: n (%)
Preconception folic supplementation			
No	58(95.1)	132(71.4)	190(77.2)
Yes	3(4.9)	53(28.6)	56(22.8)
Preconceptional visit			
No	59(96.7)	152(82.2)	211(85.8)
Yes	2(3.3)	33(17.8)	35(14.2)
Preconceptional multi vit supplements			
No	56(91.8)	152(82.2)	208(84.6)
Yes	5(8.1)	33(17.8)	38(15.4)
Pregnancy associated illness			
No	44(72.1)	149(80.5)	193(78.5)
Yes	17(27.9)	36(19.5)	53(21.5)

Family history of congenital affected pregnancy			
No yes	58(95.1) 3(4.9)	178(96.2) 7(3.8)	236(95.9) 10(4.1)
Known chronic illness			
No Yes	47(77) 14(23)	174(94.1) 11(5.9)	221(89.8) 25(10.2)
Drug use for chronic illness			
No Yes	54(88.5) 7(11.5)	177(95.7) 8(4.3)	231(93.1) 15(6.1)
Alcohol beverage consumption			
No Yes	50(81.9) 11(18.1)	159(85.9) 26(14.1)	209(85) 37(15)
Illicit drug use			
No yes	56(91.8) 5(8.2)	165(89.2) 20(10.8)	223(89.8) 25(10.2)

Majority of the study participants did not have preconception clinic visit, supplementation of vitamin and folic acid total average being in the 77.2%-85.8 % (table 3).

pregnancy associated illness Like GDM, hypertensive disorder of pregnancy, anemia and so on was evident in 27.9% case and 19.5% of the controls. The amount of alcohol consumption was proportional being 18.1% for case and 14.1% for the control and the illicit drug use like smoking, chewing khat ...etc. was also 4.9% for the case and 10.8% for the control.

4.1. Factors associated with NTDs.

A bivariate and multivariate logistic regression was conducted to identify factors associated with NTDs. In the bivariate analysis variables like gravidity, previous number of abortions, Previous pregnancy affected with NTD, Location of ANC follow up, Family size in the household, Monthly family income in birr, Preconception folic acid use, Known chronic illness of the mother, Medication use for chronic illness or other illness during 1st tm and pre pregnancy, Pregnancy associated illness, Preconceptional care contact, Preconceptional multi vit supplement use were identified to have a p value of <0.25 and they were included to the final multivariate logistic regression. In the

study the correlation between the independent variables was checked and also the model fitness was also assessed with Hosmer Lemshow test and it was found to be 54 % fit.

TABLE 4: FACTORS ASSOCIATED WITH THE DEVELOPMENT OF NTD IN PARTICIPANTS WHICH STUDY WAS DONE AT AGH,2023

Variable	Case (n%)	Control (n %)	COR (95% CI)	AOR (95% CI)	P value
Gravidity					
Gravida 1	19(31.1)	61(33)	0.104(0.025-0.423)	0.055(0.007-0.416)	0.005**
Gravida 2-4	33(54.1)	121(65.4)	0.091(0.023-0.355)	0.035(0.006-0.238)	<0.001***
Gravida >5	9(14.7)	3(1.6)	1	1	
Previous number of abortions					
No abortion	44(72.1)	155(83.8)	0.397(0.120-1.314)	0.408(0.80-2.091)	0.282
One abortion	12(19.6)	23(12.4)	0.730(0.191-2.799)	1.299(0.221-7.650)	0.772
Two or more abortion	5(8.2)	7(3.8)	1	1	
Previous pregnancy affected with NTD					
Yes	54(88.5)	179(96.8	1	1	
No	7(11.5)	6(3.2)	0.259(0.083-0.802)	0.079(0.009-0.663)	0.019*
Location of ANC					
No ANC	7(11.5)	4(2.2)	9.625(1.893-48.93)	7.093(0.818-61.489)	0.075
Health center	50(82)	159(85.9)	1.730(0.569-5.257)	1.941(0.411-9.159)	0.402
Hospital	4(6.5)	22(11.9)	1	1	
Family size in the household					
1-3 individuals	36(59.01)	76(41.1)	1	1	
4-6individuals	21(34.4)	103(55.7)	0.43(0.233-0.796)	0.433(0.180-1.040)	0.061
7 and above	4(6.5)	6(3.2)	1.407(0.374-5.299)	0.645(0.044-9.356)	0.748

Monthly family income in birr					
<5000 birr	32(52.4)	43(23.2)	5.209(2.181-12.443)	4.224(1.344-13.273)	0.014*
5000-10,000birr	21(34.4)	86(46.5)	1.709(0.708-4.126)	1.850(0.587-5.827)	0.293
Above 10,000birr	8(13.1)	56(30.3)	1	1	
Preconception folic acid use					
Yes	58(95.1)	132(71.4)	1	1	
No	3(4.9)	53(28.6)	7.763(2.330-25.862)	9.600(2.151-42.834)	0.003**
Known chronic illness mother					
Yes	47(77)	177(95.7)	4.712(2.008-11.056)	8.561(1.510-48.518)	0.015*
No	14(23)	8(4.3)	1	1	
Medication use for chronic illness or other illness during 1st tm and pre pregnancy					
Yes	54(88.5)	177(95.7)	2.868(0.994-8.271)	2.473(0.291-21.029	0.407
No	7(11.5)	8(4.3)	1	1	
Pregnancy associated illness					
Yes	44(72.1)	149(80.5)	1.599(0.820-3.118)	2.004(0.827-4.854)	0.124
No	17(27.9)	36(19.5)	1	1	
Preconceptional care contact					
Yes	59(96.7)	152(82.2)	1	1	
No	2(3.3)	33(17.8)	6.405(1.489-27.539)	9.209(1.027-82.554)	0.047*

Preconceptional multi vit supplement use					
Yes	56(91.8)	152(82.2)	0.411(0.153-1.106)	2.196(0.394-12.238)	0.370
No	5(8.1)	33(17.8)	1	1	

In multivariate logistic regression, primi gravidity (AOR:0.055, 95%CI: 0.007,0.416), gravidity 2-4(AOR:0.035,95 CI:0.006,0.238), Not having previous pregnancy affected with NTD (AOR:0.079,95 % CI: 0.009,0.663) , monthly family income in birr <5000 birr (AOR: 4.224, 95%CI : 1.344, 13.273), preconception folic acid use (AOR : 9.600,95%CI 2.151-42.834), known chronic illness mother (AOR: 8.561,95 % CI :1.510 48.518) , preconceptional care contact (AOR : 9.209, 95% CI :1.027-82.554) were identified to be significantly associated factors with NTDs development . On the contrary previous number of abortions, location of ANC, family size in the household, monthly family income in birr (5000-10,000birr), medication use for chronic illness or other illness during 1st tm and pre pregnancy, pregnancy associated illness, preconceptional multi vit supplement use were later found NOT to have significant association with NTDs development.

In our study increase in the total number of pregnancies is significantly associated with development of NTD, after adjusting the variables being primigravida is associated with a 94.5% lesser odd of developing NTD, and being multigravida (gravida 2-4) is associated with 96.5% lesser odds of developing NTD when we compare to mothers who are gravida five and above. With regarding heredity presence of pregnancy previously affected with NTD is significantly associated with the development of NTD, after adjusting the variables not having history of NTD is associated with 92.1% lesser odds of developing NTD and on the opposite side having history of NTD affected delivery is associated with 12.617 times greater odds of developing NTD when compared to those with no history of NTD affected pregnancy.

Estimated monthly family income (<5000 birr) is significantly associated with the development of NTD, after adjusting the variables estimated monthly family income (<5000 birr) is associated with 4.224 times greater odds of developing NTD when compared to those having monthly income >5000birr.

Considering supplementation preconceptionally folic acid usage is also significantly associated with the development of NTD, after adjusting the variables NOT taking preconceptional folic supplementation is associated with 9.6 times greater odds of developing NTD when compared to those taking the supplementation. In related topic preconceptional care visit is one of the variables which has significant associated with the development of NTD, after adjusting the variables having preconceptional visit is associated with 9.209 times greater odds of developing NTD when compared to those who didn't have any visit.

The other covariate is chronic medical illness which has significant associated with the development of NTD, after adjusting the variables having chronic medical illness is associated with 8.561 times greater odds of developing NTD when compared to those with out chronic illness.

5. Discussion

This hospital-based case control study was conducted to assess the determinants of NTDs among mothers who had abortion, follow up or delivery at AGH MCH hospital. Having pregnancy in developing countries is to be at risk for potential predisposing factors such as sociodemographic factors, nutritional deficiency, external toxic exposure, hereditary risks, reproductive infections and so on. (6) The purpose of these studies is to identify potential risk factors because knowledge of these factors is necessary to establish intervention plans for the prevention of birth defects.

In our study an increase in number pregnancy was associated with an approximately 95% increase in chance of NTD occurrence. But these finding is not always reproducible, because Studies have shown both a modest risk in mothers' risk with parity of three or more and an increased risk in primiparous mothers. No clear biological explanation has been found for these associations(1) but when seeing the odds there bound to be mild elevation in the risk of NTD with increase in the number of pregnancy.

In our study, (47%) were anencephaly, 20 (33%) spina bifida open and closed and 9(15%) encephalocele. This finding is similar to studies conducted in Addis Ababa teaching Hospitals Ethiopia (54.1%)(19) , Amhara region(48 %)(18), Tigray Northern Ethiopia (66.4 per 10,000 NTD cases) (16), Gujarat hospital, India (26%)(11) , and Southwest Iran (86.8%)(29)except saint Paul which had a higher number of spina bifida (64%) followed by anencephaly(30%)(10) . This could be justified by the fact that anencephaly is the one of the most common NTDs, and it developed before any of the central nervous system anomalies, developed within 1 month of conception.(29) Consequently, this could be the cause of its predominance in both the current study and earlier research carried out globally.

Multiple Studies indicated that giving folic acid three months before or during pregnancy can decrease NTDs by 50-70%.(14, 28)Similarly in our study NOT taking preconceptional folic supplementation is associated with 9.6 times greater odds of developing NTD. Which is similar to the studies in Addis Ababa Teaching Hospitals, Ethiopia(19), Tigray, Northern Ethiopia(16) , Northwest Ethiopia (3),Shewa(25) ,Debre Birhan(26), Sudan(27), Bangladesh(8) and Kingdom of Saudi Arabia(21) and multiple other literatures.

Having no preconceptional care is associated with a 9.2times increased risk of developing NTD. And these is similar finding in Addis Ababa Teaching Hospitals, Ethiopia(19), Tigray, Northern Ethiopia(16) , Northwest Ethiopia(3) ,Shewa(25) ,Debre Birhan(26), Sudan(27), Bangladesh(8) and Kingdom of Saudi Arabia(21) and multiple other literatures. This is due to during preconceptional care management of chronic illness and screening risk factors and supplementing folic acid is done which will affect the occurrence of NTD. (16,10)

women who had a previous history of NTDs had 12.617 higher odds of newborns with NTDs compared to their counterparts, this finding is also similar to Amhara (4-fold)(18), Addis Ababa City and Amhara Region(20), a study conducted in central Iran, and a study conducted in western Iranian obstetrical centers(29). These finding shows that NTD has some genetic, ethnicity and region-specific component which are more explained by MTHFR 677TT genotype presence associated with NTD.(8)

When seeing monthly income of the family below 5000 birr(100 dollar) monthly income is associated 4.224 times greater odds of developing NTD which is comparative to other research's like Addis Ababa three teaching hospitals 2.5 times for annual income of less than 1300 dollar(2) ,north Shewa zone hospital annual income less than 24000ETB was 3.75 times greater odds(25). And these finding is having consistency for obvious reason that good income will lead to good nutrition and avoidance of triggering agents.

Having chronic medical illness is associated with increase in NTD occurrence(12). In our study there is 8.651 times increased risk for those with chronic illness like DM, HTN, epileptic, Thyroid disease,,, Results are similar to other studies as well like Amhara 73%(18) reduction if no chronic illness identified and study conducted in Northwest Ethiopia(3). These can be explained with some diseases and the drugs given for their management is associated with decrease in folic acid or directly lead to failure of fusion of the neuronal plate(12).

6. Limitations and strength

This study has several strengths. first the study was based on all pregnancy out comes (live birth, IUFD, abortions and ENND). Second Data were also collected in the immediate postpartum period to minimize the recall bias of the periconceptional event. And also, usage of electronic questionnaire and keeping track of all data electronically with easy availability of participants data on the hospitals electronic recording is also noteworthy. Finally, the research was done in a facility with monthly delivery of close to a thousand and covering numerous sub cities of the capital.

With all its important outcomes, this study has also limitations worth to be mentioned. It is challenging to extrapolate the findings to the broader public because it is a single hospital-based study. Due the rare occurrence of NTD leading to limited study samples might affect the generalizability and the model's ability to show association between risk factors and outcome variables with a narrow level of confidence interval. The study participants' exposure status was evaluated retrospectively, and this may be affected by a recall bias and some variables included in the study might be sensitive behaviours which can lead to social desirability bias. In addition, the estimates of the model might be unstable due to the presence of very small numbers variables in some categories. Finally, the genetic, syndromic, and chromosomal causes of NTD that are not preventable by folic acid were not addressed in this study.

7. Conclusion and recommendation

The result of this study revealed that the total number of pregnancies, previous NTD affected pregnancy, low monthly family income (<5000 birr), presence of chronic medical illness was found to be a risk factor for the development of NTD. where as having preconceptional care visit and pre conceptional supplementation with folic acid was found to be preventive for the development of NTD.

Based on these, it may be advised to increase preconceptional visits, take folic acid supplements, and, if at all feasible, limit exposure to the aforementioned risk factors. periconceptional folate supplementation should be taken into account for women in the reproductive age range based on our research and the other comparable articles this paper discusses. And this task is for every physician and each responsible health office. Given that unplanned pregnancies can occur and most of our target population have low-income level folic acid fortification of food may also help lower the incidence of these preventable malformations and Addis Ababa health office with sub city level health offices is advised to take the initiative.

According to this study, there was a considerable rise in the chance of acquiring NTD in those with a history of the NTD affected delivery and those with chronic illnesses. Therefore, frequent monitoring by clinicians is advised in these individuals. I.e., for these individuals supplementing them folic acid early and closed follow up is recommended for primary and secondary prevention of NTD.

Furthermore, this study relied on self-report; further research with more accurate exposure assessments and more bigger sample size with more duration of study are important to have more specific recommendations.

LIST OF TABLES

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8. References

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