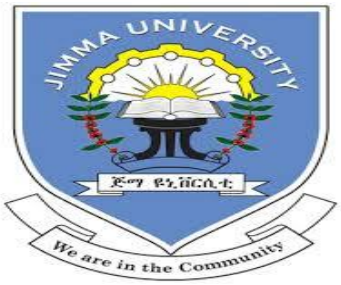
MAGNITUDE; ASSOCIATED FACTORS AND OUTCOME OF NEURAL TUBE DEFECTS AMONG NEWBORNS ADMITTED TO JIMMA MEDICAL CENTER SOUTH WEST ETHIOPIA LONGITUDINAL STUDY

A Research Thesis To Be Submitted To The Department Of Pediatrics And Child Health, Faculty Of Medical Sciences Institute Of Health, Jimma University For The Partial Fulfilment Of The Requirement Of Speciality Certificate In Pediatrics And Child Health

INVESTIGATOR; DR. BITSIET TADELE (MD)



JIMMA UNIVERSITY

INSTITUTE OF HEALTH

FACULTY OF HEALTH SCIENCES

SCHOOL OF MEDICINE

OCTOBER, 2022

JIMMA, OROMIA, ETHIOPIA

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DECLARATION

Assurance of principal investigator

I Dr Bitsiet Tadele do hereby declaring that this thesis is my original work and that it has not been submitted partially; or in full, by any other person for an award of a degree in any other university/institution

Name of principal investigator	Signature	Date
Dr. Bitsiet Tadele	_____	_____

Approval of the advisor

This thesis has been submitted with my approval as university advisor

Name of the advisor	Signature	Date
Dr. Beza Eshetu	_____	_____

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LIST OF ABBREVIATIONS

ANC=Antenatal Care

GA = Gestational age

CNS = Central nervous system

JMC = Jimma Medical Center

NICU = Neonatal Intensive Care Unit

NTD = Neural tube defect

PI = Principal Investigator

VP = Ventriculoperitoneal

U/S =Ultrasound

WHO = World Health Organization

ABSTRACT

Introduction; Neural tube defects are a group of congenital defects of the central nervous system resulting from failure of the neural tube to close during the first few weeks of fetal development.These defects have a multifactorial etiology, a combination of genetic predisposition and/or environmental and dietary factors. In Ethiopia the estimated prevalence of NTD is 63.3 per 10,000 children which is quite high.Considering the high burden of the disease and the high cost of care of this condition we assessed the magnitude of the disease in our institution and its associated factors. Since our facility is doing surgical intervention, the outcome of the enrolled babies with this defect was also assessed in the study.

Objective; Assess the magnitude, associated factors and discharge outcome of Neural tube defects among newborns admitted to Jimma medical center during the study period.

Methods; Hospital based prospective longitudinal study was conducted in the neonatology unit, Department of pediatrics, Jimma Medical Center from May to October,2022. All newborns under the age of 14 days admitted to neonatology ward that fulfilled the inclusion criteria were included in the study. Socio-demographic and clinical data was collected using a standard questionnaire. Any surgical intervention and discharge outcome were documented. The data was entered in to Epidata manager version 4.6 and exported to and analyzed using SPSS version 25. Descriptive analysis and frequencies was calculated. Bivariate and multivariate logistic regression was performed to identify the associated factors for neural tube defects. And p-value of less than 0.05 was considered as statistically significant.

Results; A total of 394 newborns were included in the study the prevalence of NTD was found to be 9.9% (95% CI 6.6-12.9%). Most common type of NTD identified was myelomeningeocele (92.3%).

In multi-variable logistic regression analysis rural residence AOR=2.21, 95% CI (1.06-4.56), P=0.033) and Khat chewing AOR=4.68, 95% CI (1.82-12.04, P=0.001) were associated factors for NTD. Nine (23.1%) of newborns with NTD have died before discharge

Conclusion and recommendation: One out of ten newborns had NTD among newborns enrolled in the study. Due attention must be given by public health experts to those mothers who come from rular area and chewing khat.

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Key words; Neural tube defect, Newborn, NICU

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CHAPTER ONE

1. Introduction

1.1. Background

Birth defects are abnormalities that are evident from birth and can be structural or functional, including metabolic problems. Following congenital cardiac malformations, neural tube defects (NTDs) are the second most prevalent birth defect [1].

NTDs are a class of central nervous system congenital abnormalities that occur when the neural tube fails to close during the first few weeks of fetal development[2].

Gastrulation, primary neurulation, secondary neurulation, and dorsal midline closure of the mesodermal-cutaneous ectodermal layers are the four stages that the neural tube and its coverings develop through. The early embryonic process known as neurulation involves the structuring and folding of the neural plate to create the neural tube. At 22 days after conception, the neural folds begin to fuse at the level of the future hindbrain-cervical junction (foramen magnum). The neural tube's posterior neuropore shuts after about 26 days, and the anterior neuropore after about 24 days [3].

By considering where they are in relation to the neural tube's first fusion point,NTD can be classified as cranial dysraphism (Craniorachischisis totalis, anencephaly,encephalocele) is caused by lesions of the anterior neural tube, whereas spinal dysraphism (caudal to the foramen magnum) is caused by lesions of the posterior neural tube (myelomeningocele , myeloschisis).

Anencephaly, spina bifida, iniencephaly, and encephalocele are among the conditions that fall under the category of opened NTD, which is characterized by communication between the brain, spinal cord, or its meningeal covering and the external enviroment. Spina bifida occulta, lipoma, diastematomyelia, and diplomyelia are examples of closed NTDs in which there is no communication with the external environment. While abnormal secondary neurulation causes the majority of closed neural tube defects, disturbed primary neurulation causes the majority of open neural tube defects [4].

NTDs have an unknown specific cause. NTDs have a complicated etiology that results from a complex interaction between environmental and genetic risk factors. Low socioeconomic status,

inadequate folic acid intake before or during pregnancy, lack of antenatal care, maternal exposure to certain environmental factors (such as chemicals and pesticides), smoking during pregnancy, consanguineous marriage, prior stillbirths or abortions, alcohol use, a prior NTD-affected pregnancy, maternal insulin-dependent diabetes, use of anti-epileptic medications, obesity, and maternal use of caffeine and other stimulants are some of the risk factors mentioned [4].

Worldwide, around 10% of infant mortalities are due to nervous system defects [5].

However, the incidence of NTD is coming to decline in recent years in industrialized countries, while it still remains higher in LMICs for limited access to specialized neonatal and surgical care. Moreover; inequities in the access to high quality care affect childbearing age women, in relation to low rate of prenatal diagnosis and prevention tools (preconception folic acid supplement). In Ethiopia, the incidence of NTDs is increasing alarmingly in recent years. Primary studies that were done in different regions of Ethiopia revealed the number of children born with congenital anomalies is increasing in recent years. The burden of NTDs is relatively high in northern Ethiopia as compared with the other regions (30 per 1000 in Southern Zone of Tigray) [6].

The prognosis for people with NTD varies according to the location, the severity of the defect, the kind of nerve cells implicated, and the severity of secondary abnormalities [7].

The outcome for individuals with NTD depends on the site, the extent of the defect, the type of nerve cells that are involved and the extent of secondary abnormalities. Many children affected by neural tube defects have multiple lifelong disabilities, including varying degrees of lower limb paralysis, bowel and bladder incontinence, hydrocephalus, intellectual and learning disabilities It can also be seen as a chronic disease that affect the child and his or her entire family with complex problems throughout life .The consequences are predominantly seen in resource limited countries where preventative measures and long-term quality care for surviving NTDs patients are limited[8].

The effects of NTD go beyond the affected person to the family who must deal with the emotional and financial burden of caring for a child with special needs. The responsibility for supporting affected people with health and social care will fall largely on society as a whole. [9]

1.2. Statement of the Problem

According to WHO 2020 report worldwide an estimated 295,000 newborns die within 28 days of birth every year due to congenital anomalies. [2]

Globally, it is estimated that approximately 300,000 babies are born each year with NTDs resulting in approximately 88,000 deaths and 8.6 million disability adjusted life year. [8]

As morbidity and mortality from infectious diseases are decreasing worldwide, the contribution of birth defects to under-5 morbidity and mortality will continue to increase proportionally. In low income countries NTDs may account for 29% of neonatal deaths due to observable birth defects [10].

Africa and Asia contributed the highest prevalence of NTD-associated stillbirths, 85% of all NTD-associated stillbirths occurring globally are attributed to Africa and Asia [11].

From systematic Review and Meta-Analysis done in Africa pooled birth prevalence of spinal bifida in Africa was 0.13%. The highest burden of spinal bifida was detected in Algeria (0.43%), Ethiopia (0.32%), Tanzania (0.26%), Cameron (0.12%), Egypt (0.10%), and South Africa (0.10%) and the lowest burden of spinal bifida was detected in Libya (0.006%) and Tunisia (0.009%) [12].

The prevalence of spinal bifida is disproportionately high in Ethiopia compared to the global average; about 10,500 live born are affected annually with prevalence of 6.5 live and stillborn spinal bifida cases per 1,000 births, each year, the absolute number of cases in the country would be approximately 21,000, of which 10,500 cases would be live born and an additional 10,500 would be stillborn[14]. The burden of NTDs diverges from region to region. The burden of NTDs is relatively high in northern Ethiopia as compared with the other regions. A recent finding in Tigray region showed the overall incidence of NTDs was as high as 13

per1000 births, and the highest burden was reported in the Southern Zone of Tigray where the incidence was 30 per 1000 births [26].

The severity of NTDs depends on the level and degree of spinal cord exposure, with symptoms ranging from mild cosmetic symptoms, such as dimples or tufts of hair on the lower back in the case of spina bifida occulta, to severe paralysis, chronic infections, incontinence or retention, and Paralysis in the case of rachischisis. Patients are also at increased risk for complications such as hydrocephalus, with the majority of patients with open spina bifida developing hydrocephalus that requires ventriculoperitoneal (VP) shunts [17].

In an attempt to mitigate the complications associated with open spina bifida, the standard of care in upper-middle-income countries in the acute phase includes diagnosis in utero, cesarean section rather than vaginal birth to avoid infection, surgical closure of the open lesion within 24 hours, and continued monitoring for the development of hydrocephalus, with surgical intervention as needed. Moreover, due to the complexity of their diagnoses, patients in upper-middle-income countries are monitored by multiple highly trained specialty healthcare teams. [18].

Although advances made in prevention and management of NTDs, African countries still lag behind with most countries experiencing challenges related to prevention and management. Furthermore, the health care services for children with NTDs are often more costly and may not be affordable for most families from developing countries who are mainly from low socioeconomic background.

Besides the cost of care involved with NTDS, children in developing countries face many other challenges such as harsh social economic conditions, harmful taboos, religious beliefs, and inadequate medical personnel and facilities, which all lead to late presentation of patients for appropriate health care. Additionally, surgical services in most developing countries are only found in big cities making it difficult for the poor rural communities to access the services. This may result in late presentation for surgery, high mortality rates and severe secondary complications for those who survive [19].

Outcomes research on pediatric spina bifida in sub-Saharan countries remains limited. In a 10-year survival study of Ugandan infants following myelomeningocele closure, most deaths were not directly related to myelomeningocele, but rather to infection and neglect. Furthermore, post hospitalization complications arise due to cultural beliefs or poverty, resulting in improper or lack of treatment. Stigmas surrounding medical disabilities and birth defects further complicate spina bifida treatment and outcomes; and severely impact the lives of patients and their caregivers, particularly those from lower socioeconomic backgrounds [20].

1.3 Significance of the study

This study was conducted to determine the magnitude, associated factors and outcome of NTDs at Neonatal Intensive care unit, JMC. Although our Hospital is giving surgical intervention for NTDs, there is no data on outcome of surgically intervened newborns with NTD at JMC.

These identified associated factors of NTDs are important to health planners, policy makers, governmental and nongovernmental organizations (NGOs) that are working on neural tube defect prevention. It is also important for stakeholders such as health professionals in designing interventional projects towards improving child health and reducing morbidity and mortality due to neural tube defects. It can also extend the existing knowledge and skill of health professionals towards prevention of NTDs.

CHAPTER TWO

2. Literature review

2.1 Magnitude Of Neural Tube Defect

A retrospective study conducted in tertiary hospital in northern Ghana from January 2010 to December 2014. A total of 35,426 deliveries were recorded at the facility during the study period with 57 cases of neural tube defects, giving a prevalence of 1.6 per 1000 births. The most common defect was hydrocephalus representing 57.9%, spinal bifida 38.6% and encephalocele 5.3%. Among the spinal bifida cases, myelomeningocele account 59.1%, meningocele 40.9% [23].

Between April 2013 and December 2013, a prospective study was done on all live-born neonates at three particular hospitals in Nigeria. Male to female ratio of the 1456 newborns recruited for the study was 1:1, and there were 4 neonates (2 boys and 2 girls) with NTDs, giving a birth prevalence of NTD of 2.75/1000 live births. The neonates with NTDs had a mean gestational age of 38 weeks (SD 2.16 weeks) and a mean birth weight of 2.93 kg (SD 0.51 kg). Only 5.03 percent of the moms in the study supplemented with folic acid-containing multivitamins at least one month before or throughout the index pregnancy [24].

A hospital-based cross-sectional and unmatched case-control study was conducted at three teaching hospitals of Addis Ababa University (Tikur Anbessa Specialized Hospital (TAH), Zewditu Memorial Hospital (ZMH), and Gandhi Memorial Hospital (GMH). During seven months (February to August 2016), there were 55 cases of NTDs out of 8677 births after 28 weeks of gestation with birth prevalence of 63.4 per 10,000 births A total of 115 cases were medically terminated after 12 weeks of gestation of which of these 56 terminations (48.7%) were due to NTDs. The total prevalence of NTDs after 12 weeks' gestation is 126 per 10,000 births [25].

From October 2016 to June 2017, a cross-sectional study was undertaken in eight randomly chosen large public hospitals in the Tigray area of Ethiopia: Mekelle and Ayder Hospitals, Lemelem Karl Hospital, St. Mary Hospital, Sihul Hospital, Adigrat and Wukro Hospital, and Kahsay Abera Hospital. All pregnancies' outcomes were checked for any birth abnormalities that might be seen from the outside. A total of 195 children with neural tube defects were born during

the research period out of 14,903 births. Anencephaly and spinal bifida affected 66.4 and 64.4 newborns out of every 10,000 births, respectively. In this study, the incidence rate of NTDs was 131 per 10,000 live births, with 23% of live births and 77% of stillbirths [26].

2.2. Risk Factors of Neural Tube Defect

These disorders have a complex etiology, a mix of genetic predisposition and/or environmental factors; the mechanism of NTD genesis has not yet been discovered. However, the main cause of NTDs worldwide is unquestionably a diet deficient in folate. NTD can be caused by teratogen exposure, chromosomal problems (such as trisomies of chromosomes 2, 7, 9, 13, 14, 15, 16, and 21 and duplications of chromosomes 1, 2, 3, 6, 7, 8, 9, 11, 13, 16, and X), syndromes, or other factors (e.g., aminopterin, thalidomide, valproic acid, carbamazepine) [3].

Lack of dietary folic acid (FA) causes plasma homocysteine (Hcy) levels to rise. An amino acid called Hcy, which contains sulfur, is produced by the homocysteine-methionine cycle and the transsulfuration pathway to cysteine. The lower availability of FA in the hyperhomocysteinemia condition jeopardizes nucleic-acid synthesis, which is essential for maintaining rapid and intense cell proliferation as well as the synthesis and expression of the genes and proteins that take place during early embryogenesis [4].

Numerous causes of NTDs have been identified in studies conducted around the world. Low socioeconomic status, tobacco use during pregnancy, consanguineous marriage, being a passive smoker, genetic factors, radiation exposure, a history of stillbirth or abortion, the use of anticonvulsants during pregnancy, pregnancy at a late maternal age, inadequate folic acid intake before or during pregnancy, a higher glycemic index, and the absence of antenatal care are some of these risk factors [19].

Prospective study conducted from January 1st, 2011 to June 30th, 2016 in Moroco women whose fetus or newborn showed an isolated or combined neural tube defect. The risk factors detected during this study include consanguinity (34%), consumption of fenugreek or other plants (36%), diabetes (4.5%) and medication (2.2%). A family history of malformation was reported in 6.8% of cases and among siblings in 4.5% of cases, 59% of mother did not take folic acid supplementation during the first trimester of pregnancy and none of them took B9 vitamin during the periconceptional period [27].

Case control study was conducted in four public hospitals at Bale Zone. Folic acid supplementation was identified as protective factor for NTDs, while, consanguinity, being passive smokers and women between the ages of 15-24 years, were the risk factors associated with NTDs [28].

A hospital-based cross-sectional study conducted from October 2019 to January 2020 in HFSUH, Harar. A total of 420 newborn the magnitude of neural tube defects was 5.71% Approximately 83.5% of infants had spinal bifida and 16.5% anencephaly. Preterm birth, low birth weight, maternal coffee consumption a history of abortion or stillbirth, radiation exposure and intake of anticonvulsant drugs during pregnancy were factors associated with neural tube defects[29].

Data from a supplementation program in China and long-term surveillance of NTDs in nations that have successfully implemented fortification, including the United States, Canada, Costa Rica, South Africa, and Chile, suggest that folic acid interventions can lower NTD prevalence to as low as 5–6 per 10,000 pregnancies [30].

Numerous studies have shown that periconceptional folic acid supplementation reduces the incidence of neural tube defects (NTDs) by about 70%; thus, food fortification with folic acid (FA) and better dietary intake guidance greatly lower the prevalence of neural tube abnormalities.The annual rate of live births in Ethiopia with spinal bifida might drop from the current 10,500 instances to around 1,050 if basic foods are required to be fortified; this would prevent nearly 9,000 cases. Unfortunately, folic acid fortification only prevents about 10% of neural tube defects globally, despite the fact that spinal bifida has other, less common, and entirely controllable risk factors[13].

2.3. Outcome of children with neural tube defect

Unless additional serious defects are present, postnatal closure of the myelomeningocele in a newborn within 72 hours of delivery is advised to prevent infection (meningitis). In less than 20% of mid-gestational pregnancies, myelomeningocele closure in utero is an alternative[31].

Children with neural tube defects (NTDs) require timely surgical intervention coupled with long-term management by multiple highly trained specialty healthcare teams. Multidisciplinary team of specialists, including neurosurgeons, orthopedists, urologists, nephrologists, pediatricians, physical therapists, occupational therapists, advanced practice nurses, geneticists, genetic counselors, and perinatologists, fetal surgeons are required to provide comprehensive treatment. Before the 1960s, a complicated team was not needed because the majority of infants born with this defect died from infection and/or hydrocephalus. After aggressive treatment in the early 1950s and 1960s, several large multidisciplinary treatment centers began to review their treatment results; there was a realization that helping these children required many different disciplines communicating with each other and the family. In resource-limited settings, outcomes are greatly affected by the lack of coordinated management [16].

Many children affected by neural tube defects have multiple lifelong disabilities. Spinal bifida can result in varying degrees of paralysis and intellectual and learning disabilities; encephalocele may result in seizures, varying degrees of motor impairment, and vision deficits, and anencephaly is fatal. Hydrocephalus is a common complication of both spinal bifida and encephalocele, and talipes equinovarus is a common complication of spinal bifida. Approximately 75% of anencephalic infants are stillborn, and the remainder dies in the neonatal period. Study done on outcome of patients presented with spina bifida at Mulago National Referral Hospital in Uganda between January 1, 2014, and August 31, 2015, among 201 patients, the vast majority 92% were diagnosed with myelomeningocele. The median age at presentation was 6 days, the median length of stay was 20 days, and the median time to surgery was 10 days. Half of the patients had documented surgeries, with 5% receiving multiple procedures. The 1-year mortality rate was 34%. Ninety percent of the survivors have received healthcare since their initial discharge from MNRH. Hydrocephalus was diagnosed in 88% of patients. Caregivers reported physical deficits in 39% of patients (clubfoot in 18% and bowel or bladder incontinence in 12%). The surgical complication rate was 2.5% [17].

A four year prospective longitudinal study conducted on treatment outcome of children operated for Neural tube defect in Addis Ababa. A total of 88 children primary operated for NTD closure in the period July 2013 to August 2014. The median age at primary NTD closure was 29 days. The commonest site of defect was lumbar (60.2%) followed by lumbosacral (11.4%). There was no perioperative mortality; however, 26.1% of the children developed wound-related complications including cerebrospinal fluid leak and infection. Preoperative CSF leakage was associated with risk of postoperative complications. At 4 years, 41% of these children had died. Presence of hydrocephalus and reduced motor function were found to be negative predictors for survival [21].

2.4. CONCEPTUAL FRAMEWORK

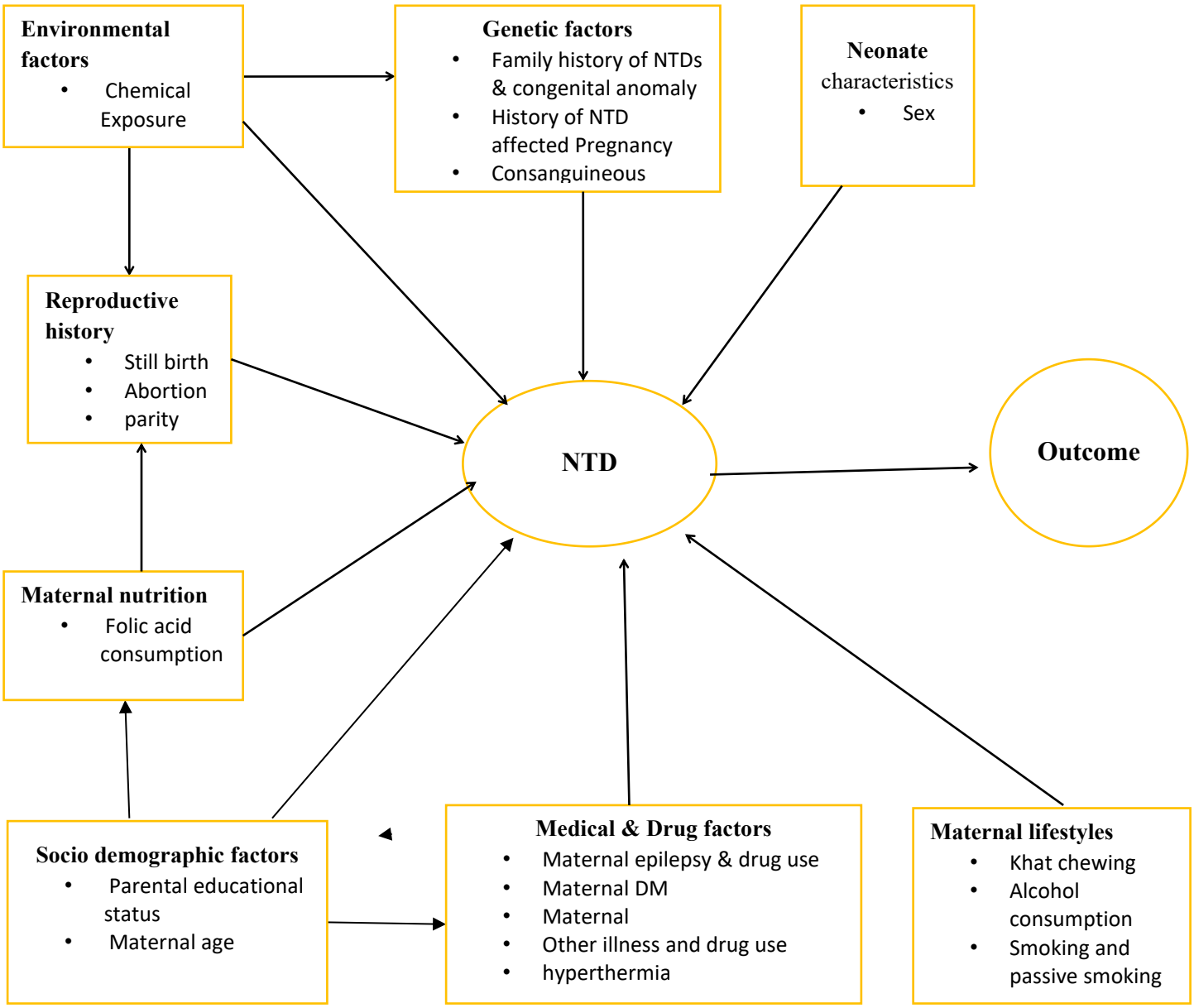

Figure 1 Conceptual frame work to assess the magnitude , associated factors and outcome of NTD among newborns admitted to NICU, JUMC, South West Ethiopia, 2022

CHAPTER THREE

OBJECTIVE

3.1. General objective:

- ✓ To assess the magnitude, associated factors and outcome of NTD in Jimma medical center., Oromia, Ethiopia.

3.2. Specific objective:

- ✓ To assess the magnitude of NTD among neonates admitted to JMC, Neonatology ward from May to October 2022
- ✓ To assess factors associated with NTD among neonates admitted to JMC, Neonatology ward from May to October 2022
- ✓ To assess discharge outcome of neonates with NTD both surgically managed and admitted to JMC, Neonatology ward May to October 2022

CHAPTER FOUR

MATERIALS AND METHODS

4.1 Study area and period

The study was conducted at the neonatology ward of Jimma Medical Center (JMC), a tertiary hospital in Southwest Ethiopia from May to October, 2022, and 350 km south west of, Addis Ababa. Jimma zone comprises Jimma town and nearby Woredas with estimated population of 2,486,155. JMC is a referral and teaching hospital which gives inpatient and outpatient services with catchment area of 15 million populations in the South West of the country.

4.2 Study design

Prospective Longitudinal study design was employed

4.3 Source population

All newborns from birth up to age of 14 days who are admitted to JMC neonatal ward during the study period.

4.4 Study population

All newborn-mother pair from birth up to age of 14 days who were admitted to JMC neonatal ward during the study period meeting the inclusion criteria

4.5 Inclusion and exclusion criteria

4.5.1 Inclusion criteria

All newborns up to age of 14 days who are admitted to JMC neonatal ward and whose parents are willing to participate

4.5.2 Exclusion criteria

Newborns whose parents declined to give consent or are unable to get consent from parents due to different reasons

4.6 Sample size determination

The minimum sample size was calculated using by using a single population proportion formula with the assumption of 95% level of confidence, 5% marginal error, the proportion of NTD 57.1% was taken from study conducted at Hiwot Fana Specialized University Hospital Harar, Ethiopia is used..

$$n = \frac{(Z\text{-}\alpha/2)^2 \, p\,q}{d^2}$$

Where:

- Z-α/2- is the standard normal variable with 95% accuracy and 5% margin of error and its Value equals to 1.96
- p- is the estimated proportion of population studied is 0.571 taken from prevalence NTD from study conducted at Hiwot Fana Specialized University Hospital, Harar, Ethiopia
- q- is 1-p
- d- is the margin of error tolerated (5%) = 0.05

A sample size of 394 was reached by adding 5% non-response rate.

4.7. Study variables

4.7.1. Dependent variable

- Neural tube defect
- Discharge Outcome

4.7.2. Independent variables

Socio-demographic

- Age sex, marital Status, educational status, occupation, residency, and income.

Maternal nutrition

- , Folic acid supplementation, dietary history

Reproductive history

Still birth,Abortion, Parity,ANC visit

Genetic factors

- History of NTDs affected pregnancy, consanguineous marriage , family history of NTDs or congenital anomaly

Maternal behavioral factors/lifestyles

- Alcohol consumption , Smoking/exposure to external smoking , Other (herbal use)

Medical & Drug factors

- Maternal chronic illness and maternal drug use , Maternal fever/febrile illness during pregnancy

Environmental factor

- Chemical exposure
- Radiation/heat exposure

Neonate characteristics

- Neonates sex , Birth weight

4.8. Operational definitions

- ✓ **Neonates:** all children under the age of 28 days.
- ✓ **NTDs:** structural defect of the central nervous system that affects the brain, spine and spinal column during the first month of embryonic development.
- ✓ **Myelomeningocele:** is a condition where the spinal cord and the tissues covering it protrude out of an opening in the back

- ✓ **Encephalocele:** is a kind of neural tube defect that results in a sac like protrusion of the brain and its surrounding membranes through an opening in the skull.
- ✓ **Anencephaly:** is characterized by an open defect in the calvaria and skin, such that the cranial neural tube is exposed.
- ✓ **Craniorachischisistotalis:** most severe form of NTD in which almost the entire brain and spinal cord remain open
- ✓ **Myeloschisis:** a flat neural tube defect characterized by cleft spinal cord without a layer of skin covering ,owing to failure the neural plate to form a complete neural tube, or rupture of the neural tube after closure
- ✓ **Spinal bifida occulta:** a midline defect of the vertebral bodies without protrusion of the spinal cord or meninges. Maybe covered with patches of hair, lipoma, or discoloration of overlying skin.
- ✓ **Hydrocephalus:** is buildup of fluid in the cavities (ventricles) deep within the brain
- ✓ **Iniencephaly:**is a rare and complex NTD involving the occiput and inion, resulting in extreme retroflection of the head , variably combined with occipital encephalocele or rachischis of cervical or thoracic spine
- ✓ **Diastematomyelia :** also known as a split cord malformation, refers to type of spina bifida when there is a longitudinal split in the spinal cord
- ✓ **Diplomyelia:** a condition in which the spinal cord is double, or is made to appear so by a deep fissure which separates it in to distinct halves
- ✓ **Periconceptional period:** a time one month before conception until 12 weeks of gestation.
- ✓ **Periconceptional folic acid supplementation**: standard recommendation of folic acid (400µg/day) for all women from the moment they begin trying to conceive until 12 weeks of gestation should take a folic acid supplements
- ✓ **Consanguineous marriage:** a union between two individuals who are related by birth as second cousins or closer (familial marriage).
- ✓ **Grand multiparous**: a woman who has already given five or more birth
- ✓ **Alive:**a newborn survived and discharged
- ✓ **LAMA:** newborn whose parents refused the care and left from hospital without completing/receiving care

- ✓ **Death** – the cessation of all biological function in the hospital

4.9.Data Collection Instruments and Procedures

Data was collected using a structured questionnaire adapted from previous literature. Data was collected by 2 neonatal nurses and 1 general practitioner using face-to-face interviews with maternally related variables (sociodemographic characteristics, obstetric characteristics , medical history, maternal nutritional history and folate and multivitamin supplementation during pregnancy, maternal life style (maternal smoking /passive smoker , alcohol intake during pregnancy, radiation exposure).

We demonstrated to the mothers the commonly used formulations of folic acid/iron-folate and asked them if they have received such tablets during the current pregnancy maternal smoking during pregnancy was determined based on mothers self-report and was defined as the a "smoker" if she smoked at least 1 cigarettes per day during pregnancy; a "passive" smoker if she was closely exposed to tobacco and exposures smoke by people such as her husband, family members, and co-workers, Alcohol intake during pregnancy: any amount and any time during pregnancy. We defined radiation exposure simply by asking the mothers exposures to radiation, such as from a diagnostic medical examination or therapeutic

Neonatal characteristics were collected at time of admission and a thorough review of medical records to obtain weight, gestational age. For those newborns having NTD additional information was collected subsequently after admission by the time investigations (trans-fontanel ultrasound, CT scan, MRI) was done, and from medical record. Those newborns with NTD who were surgically managed were followed for post op complecation by reviewing the chart as well as investication until the final outcome. Those newborns with NTD for whom surgical intervention was not done were also followed until the final outcome.

4.10. Data quality assurance

Although the data collectors were familiar with all the information in the data collection instrument, refreshment training was given for 1 day before the data collection.The data collection instrument was pretested in 5% (20) of the total sample size. The necessary modifications and corrections were made to the tool before being administered into the actual data collection. Each respondent's questionnaire was checked for its completeness and its

consistency at the time of data collection by collectors and principal investigators. Data coding, entry, and cleaning was performed by the principal investigator.

4.11. Data processing and analysis

Data was coded and entered into EpiData manager version 4.6 then exported and analyzed by Statistical Package for Social Science (SPSS) version 25..Binary logistic regression was done and **P value < 0.25** was used to enter to multivariable logistic regression model. **P- Value < 0.05** was considered as statistically significant. Odds ratio with **95% confidence interval** was used to report the finding

4.12. Ethical Approval

Ethical clearance was obtained from the Institutional Review Board (IRB) ofJimma University Institute of Health **(Ref. No. JUIH/IRB 122/22**). Additionally, permission letterwas obtained from JMC clinical director office and the department of pediatrics and child health before the commencement of the study. Written informed consent was obtained from all the mother/care taker of each neonate before enrollment into the study. Furthermore, confidentiality was assured throughout the process.Covid-19 prevention strategy was also followed

4.13. Plan for dissemination of results

The findings of the study will be presented to Jimma University Scientific community and submitted to department of Pediatrics and Child Health, faculty of medical sciences , institute of health, Jimma University. Recommendations will be forwarded to hospital staffs and other stakeholders based on the findings of the study. Efforts will be made to publish the findings on national and international scientific journals.

CHAPTER FIVE

RESULTS

5.1. Socio-demographic characteristics

A total of 394 neonates were included in this study with the response rate of 100.0%. The vast majority 348 (88.3%) of them were from Jimma zone followed by 12 (3.0%) from Gambela region (Anyuak Zone). The mean age of mothers was 26.11 ±5.5 years old. More than half 202 (51.3%) of them were from urban.(Table 1).

Table 1: Socio demographic characteristics among mothers/care givers of newborns admitted to JMC, South West, Ethiopia, 2022.

Variables	Category	Frequency	Percent
Address of the participant	Jimma	348	88.3
	Ilubabore	8	2.0
	Dawuro	7	1.7
	Anyuak	12	3.0
	Kaffa	9	2.3
	Benchimaji	6	1.5
	Others[1]	4	1.2
Maternal age in years	<19	41	10.4
	19 - 35	335	85
	>35	18	4.6
Marital status of the mother	Married	393	99.7
	Divorced	1	0.3
Residence	Urban	202	51.3
	Rural	192	48.7
Maternal educational status	Cannot read and write	92	23.4
	Can read and write	29	7.4
	Primary (G 1-8)	121	30.6
	Secondary (G 8-12)	99	25.1
	College/other	53	13.5
Occupation of mother/care giver	House wife	205	52.0
	Farmer	54	13.7
	Self employed	74	18.8
	Government/company	61	15.5

Father educational status	Cannot read and write	65	16.5
	Can read and write	46	11.7
	Primary (1-8)	87	22.1
	Secondary (8-12)	110	27.9
	College/other	86	21.8
Family monthly income	Low	288	73.1
	Lower-middle	106	26.9

Others [1] indicates; Yeme, Ameya, Guraga, Addis Ababa

5.2. Maternal reproductive and obstetric characteristics

The majority 363(92.1%) of the mothers had ANC follow up during the current pregnancy. Among mothers who had ANC follow up only 132 (36.4%) of mothers attend firsts visit within the first 3 months of pregnancy (Table 2).

Table 2. Maternal reproductive and obstetric history characteristics among mother of newborns admitted to NICU, JMC, Jimma , South West, Ethiopia, 2022.

Variables	**Category**	**Frequency**	**Percent**
Parity	Primi-para	140	35.5
	Multi-para	254	64.5
History of still birth	Yes	22	5.6
	No	372	94.4
History of abortion	Yes	30	7.6
	No	364	92.4
Planned pregnancy	Yes	327	83.0
	No	67	17.0
Had ANC follow up	Yes	363	92.1
	No	31	7.9
Month of pregnancy start ANC (n=363)	≤3 months	132	36.4
	>3 months	231	63.6
Examined for ultrasound during ANC	Yes	244	67.2
	No	119	32.8

5.3. Sociodemographic , reproductive and obstetric characteristics of mothers of newborns with NTD

This study revealed majority 31(79.5%) of newborns with NTD were from Jimma followed by Illubabor Zone 5(12.8%).Twenty seven (61.3%) are from rular area. Majority 24(68.6%) of mothers of newborns with NTD had started ANC follow up after 3 months of pregnancy. Fiftheen(43.9%) of them had obstetric ultrasound ,but NTD not detected for 9(60%) of them(Table 3)

Table 3: Sociodemographic , reproductive and obstetric characteristics among mothers/care givers of newborns with NTD admitted to JMC, South West, Ethiopia, 2022

Variable	Category	Frequency	Percent
Socio demographic characteristics			
Address of participants (n=39)	"Illubabor"	5	12.8
	"Jimma"	31	79.5
	Others 1	3	7.7
Residence (n=39)	urban	12	30.7
	rural	27	69.3
Reproductive and obstetric history			
History of Abortion(n=39)	Yes	3	7.8
	No	36	92.2
History of Still birth(n=39)	Yes	1	2.6
	No	38	97.4
Is pregnancy planned (n=39)	yes	32	82
	no	7	18
ANC follow up (n=39)	Yes	35	89.7
	No	4	10.3
Time to start ANC(n=35)	<=3	11	31.4
	>3	24	68.6
Obstetric US done (n=35)	Yes	15	43.9
	No	20	57.1
Abnormality (n=15)	yes	6	40
	no	9	60
Time of obstetric(n=6)	3 month	2	33.3
	6 month	3	50
	8 month	1	16.7

1= ADDIS ABEBA"DAWURO" GAMBELA"

5.4. Maternal medical and drug history related characteristics

This study revealed that about 9 (2.3%) mothers had chronic illness told by a doctor. Diabetes mellitus was reported among 7 (77.8% mothers followed by HTN and Asthma (Table 3).

Table 4; Maternal medical and drug history related characteristics among mother of newborns admitted to NICU, JMC, 2022.

Variables	Category	Frequency	Percent
History of chronic disease	Yes	9	2.3
	No	385	97.7
Type of chronic disease	Hypertension	1	11.1
	Diabetes mellitus	7	77.8
	Asthma	1	11.1
Febrile illness	Yes	15	3.8
	No	379	96.2
Month of pregnancy illness/ fever diagnosed	3	1	6.7
	4	2	13.3
	6	1	6.7
	7	2	13.3
	8	4	26.7
	9	5	33.3
Drugs took during pregnancy (n=15)	Amoxicillin	5	33.3
	Coartem	3	20.0
	Insulin	3	20.0
	Metformin	2	13.3
	Methyl dopa/Nifidipin	1	6.7
	Salbutamol	1	6.7
Month of pregnancy herbal took	7 month	2	
	8 month	1	
Oral contraceptive use	Yes	53	13.5
	No	341	86.5
For how long OCP use (in years)	1	29	54.7
	2	13	24.5
	3	10	18.9
	5	1	1.9

5.5. Maternal nutritional characteristics

About 60 (15.2%) of mothers have received folic acid during the current pregnancy, of which 38 (63.3%) took within the first 3 months of their pregnancy and 22(36.7%) took after the third month of pregnancy. (Table 4).

Table 5; Maternal folic acid and multi-vitamin supplementation among mother of newborns admitted to NICU, JMC, 2022.

Variables	Category	Frequency	Percent
Folic acid supplementation	Yes	60	15.2
	No	334	84.8
Months took folic acid after pregnancy (n=60)	≤ 3month of pregnancy	38	63.3
	>3 month of pregnancy	22	36.7
Multi-vitamin supplement during px (n=393)	Yes	43	10.9
	No	351	89.3
Start multi-vitamin supplementation (months after pregnancy) (n=43)	≤ 3month of pregnancy	33	76.7
	>3 month of pregnancy	10	23.3

Dietary assessment

During this pregnancy 107 (27.1%) of mothers were cosuming green leaf vegetables (like cabage, kale , spinach , beetroot) every day whereas 165 (41.9%), 54 (13.7%), 65 (16.5%) and 3 (0.8%) of mothers consume green leafy vegetables 3-4 times/week, once a week, sometimes and never respectively. (Figure 5).

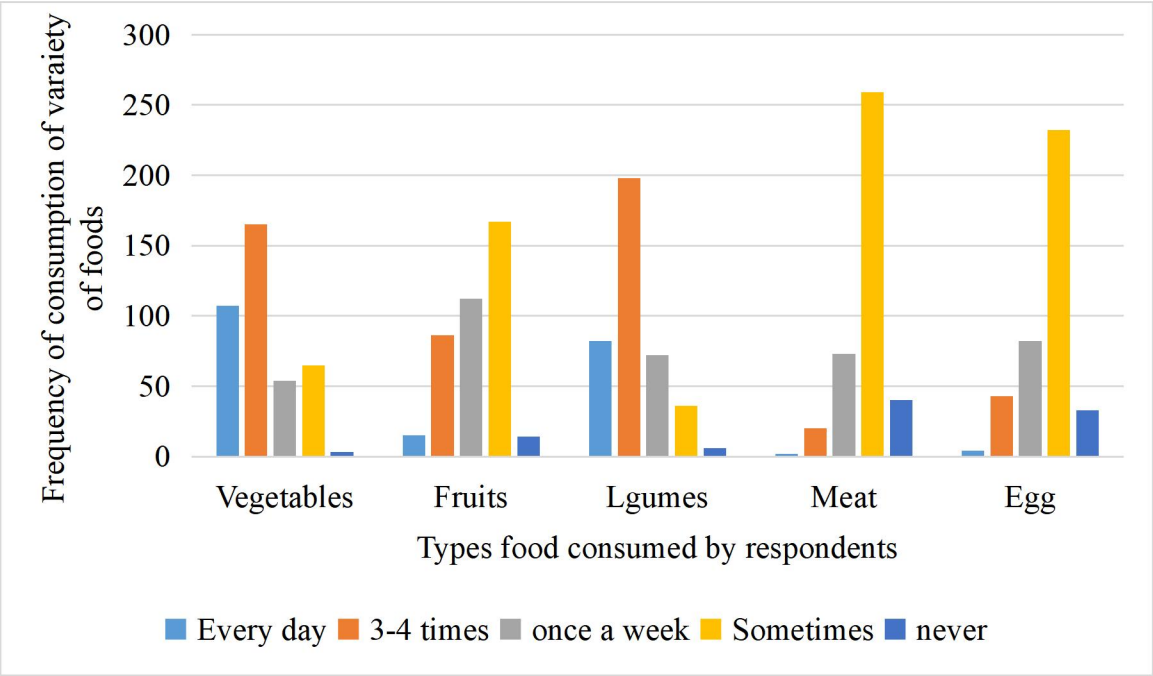

Figure 2; Distribution of consumption of variety of foods of mother of newborns admitted to NICU, JMC, 2022.

5.6. Maternal lifestyle characteristics

This study revealed that Twenty-five (6.3%) participants were chewing khat during the current pregnancy.

Table 6; Lifestyle characteristics among motherof newborns admitted to NICU, JMC, South West, Ethiopia, 2022.

Variables	Category	Frequency	Percent
Drink alcohol during this pregnancy	Yes	15	3.8
	No	379	96.2
Types of alcohol (n=15)	Beer	6	40.0
	Locally made alcohol (areka	6	40.0
	Wine	1	6.7
	Tela	2	13.3
Frequency of drinking alcohol beverage (n=15)	Sometimes	4	26.7
	Rarely	11	73.3
Number of Glasses alcohol per week	1	4	26.7
	2	4	26.7
	3	4	26.7
	4	3	19.9
Smoke cigarette during this pregnancy	Yes	1	0.3
	No	397	99.7
Was any cigarette smoker at home/ work place	Yes	17	4.3
	No	377	95.7
Chewing khat during this pregnancy	Yes	25	6.3
	No	369	93.7
Frequency of chewing khat (n=25)	Almost always	1	4.0
	Usually	5	20.0
	Sometimes	16	64.0
	Rarely	3	12.0

5.7. Environmental related characteristics

About 18 (4.6%) of study participants had history of used any pesticides/chemicals at home or work place. Among chemicals used by the respondent's herbicide was reported by 9(50%) respondents. (Table 5).

Table 7; Environmental related characteristics among mother of newborns admitted to NICU, JMC, South West, Ethiopia, 2022.

Variables	Category	Frequency	Percent
Used chemicals (insecticides ,herbicides) at home/work place	Yes	18	4.6
	No	376	95.4
Types of chemical 9n=18)	Herbicides	9	50.0
	Insecticides	5	27.7
	Pesticides	4	22.3
Use of PPE (mask, glove) (n=18)	Yes	2	11.1
	No	16	88.9
Place contacted with chemicals (n=18)	Home	5	27.8
	Farm	13	72.2
How frequent contacted with this chemicals (n=18)	Twice a week	3	16.7
	Every month	9	50.0
	Yearly	6	33.3
Factory at vicinity	Yes (Garment)	1	0.3
	No	393	99.7

5.8. Clinical characteristics of neonates

This study revealed that about 220 (55.8%) neonates were male giving male to female ratio1.3:1.In addition, more than two-third of neonates were term (37-42 weeks GA) , and 235 (59.6%) of neonates had normal birth wight (2500 -3999 g) (Table 7).

Table 8; Clinical data among newborns admitted to NICU, JMC, South West, Ethiopia, 2022.

Variables	Category	Frequency	Percent
Birth weight in (gram)	≤1000	6	1.5
	1001-1499	28	7.1
	1500-2499	107	27.2
	2500 -3999	235	59.6
	≥4000	18	4.6
Gestational age (weeks)	≤36	123	31.2
	37 - 42	271	68.8
Sex	Male	220	55.8
	Female	174	44.2

5.9. Magnitude of NTDs among neonates admitted to NICU

One out of ten 39 (9.9%, 95% CI 6.6-12.9%) newborb had NTD in the study setting (Figure 2).

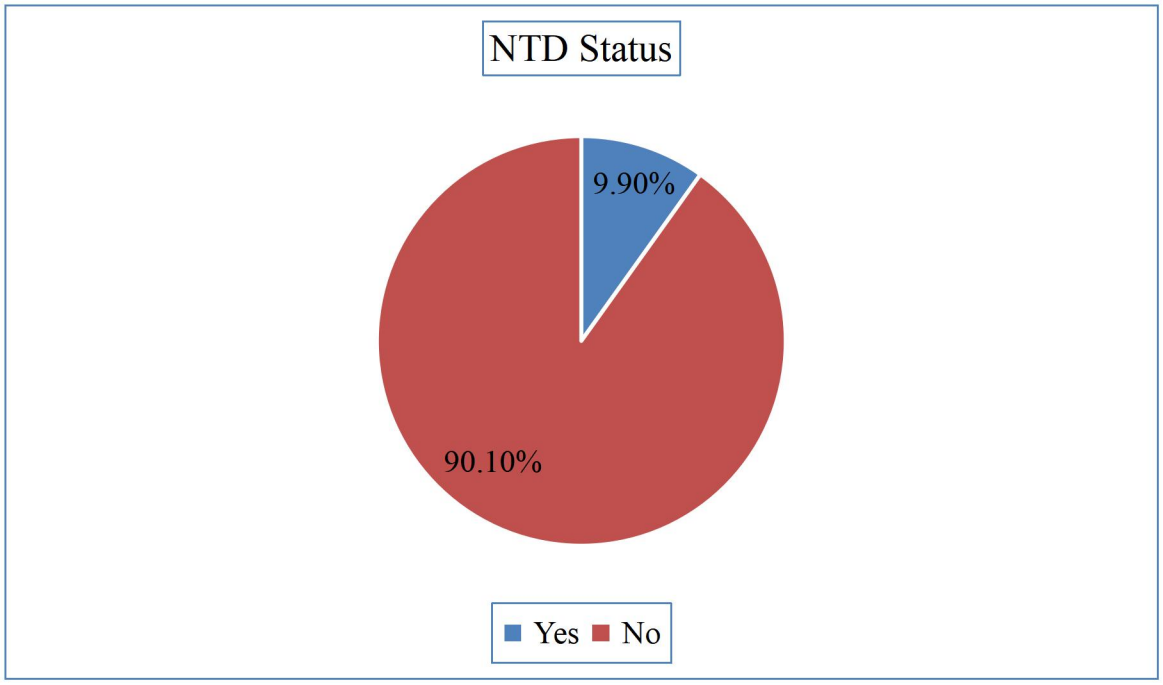

Figure 3; Magnitude of NTD among newborns admitted to NICU, JMC, South West, Ethiopia, 2022.

The vast majority 36 (92.3) of neonates were having myelomeningocele followed by meningocele 2 (5.1%) and encephalocele 1 (2.6%) . The location of NTD were lumbosacral25 (64.1%) was, lumbar 11(28.2%) , thoracolumbar 2 (5.1%) and on the skull 1 (2.5%).Thirty two (82.1%) of neonates with NTD had associated anomalies like hydrocephalus club foot, 20 paraplegia and chiari II malformation. Additionally, 19 (48.7%) of neonates with NTD had sepsis and the covering of suck is also ruptured in 27(69.2%) at presentation

Table 9; NTD related characteristics among newborns admitted to NICU, JMC, South West Ethiopia, 2022.

Variables	Category	Frequency	Percent
Types of NTD (n=39)	Mylomenigocele	36	92.3
	Menigocele	2	5.1
	Encephalocele	1	2.6
Location of NTD (n=39)	Lumbar	11	28.2
	Lumbosacral	25	64.1
	Thoracolumbar	2	5.1
	Skull	1	2.6
Associated anomaly (n=39)	Yes	32	82.1
	No	7	17.9
Types of associated	Hydrocephalus	21	
	Club foot	8	
	Paraplegia	20	
	Chairi II malformation	2	
	Others [2]	4	
Was the covering suck ruptured	Yes	27	69.2
	No	12	30.8
Was the covering skin infected	Yes	7	17.9
	No	32	82.1
Develop symptoms of infection (sepsis)	Yes	19	48.7
	No	20	51.3
Treated meningitis after admitted	Yes	36	92.3
	No	3	7.7

Others [2] indicates; ARM, Solitary kidney, congenital knee dislocation, hydronephrosis and omphalocele.

Pre operative trans-fontanel ultrasound and MRI was done for 25 (64.1%) and 1 (2.6%) of newborns with NTDs respectively of which 10 (38.4%) had moderate hydrocephalus and 11(42.5%) had mild hydrocephalus

Table 10; Types of investigation conducted andFindings among neonates with NTD admitted to NICU, JMC, Jimma, South West Ethiopia, 2022.

	Catagories	Frequency	Percentage
Type of preop investigation (n = 39)	Transfontanel ultrasound	25	64.1
	MRI	1	2.6
	Not done	13	33.3
Preop investigation finding (n= 26)	Mild hydrocephalus	11	42.5
	Moderate hydrocephalus	10	38.5
	Severe hydrocephalus	1	3.8
	Chiari malformation	1	3.8
	Encephalocele	1	3.8
	Meningeocele	1	3.8
	Normal	1	3.8

Majority(53.8) of newborns with NTD arrived after 72 hourss. Surgical repair was done for 27 (69.2%) of the newborns with NTD. But1 2(30.8%) newborns with NTD had no surgical intervension because 8(66.8%) newborns were critical at the time , 1 (8.3%) newborn died before surgery, intubation was failed for 1(8.3%) newborn and the schedule was prolonged for 1 (8.3%) newborn. Surgical closure was done within the first 72 hours only for 4 (14.8%) newborns while 23 (85.2%) were operated after 72 hours life.The median of age at surger was 9 days (SD 6.8 days). Fourtheen (81.5%) of operated newborns had developed post-operative complications like sepsis6(22.3%) , wound infection 8(29.6%) and hydrocephalus 8(29.6%) of which VP shunt was inserted for 2 newborns and sub dural therapeutic tap done for 1newborn (Table 9).

Table 11; Treatment related characteristics among neonates with NTD admitted to NICU, JMC, South West Ethiopia, 2022.

Variables	Category	Frequency	Percent
Age at presentation	≤72	**18**	**46.2**
	>72	**21**	**53.8**
Age at surgery (hours) (n=27)	≤72	4	14.8
	>72	23	85.2
Receive prophylaxis antibiotics before OR	Yes	27	100
Surgical intervention	Yes	27	69.2
	No	12	30.8
Reason for not doing surgery (n=12)	The patient is in critical condition	8	66.8
	Appointment (elective)	1	8.3
	Died before surgery	1	8.3
	Failed intubation	1	8.3
	Prolonged schedule	1	8.3
Trans-fontanel U/S done U/S	Yes	13	48.1
	No	14	51.9
Post operation complications (n=27)	Sepsis	6	22.3
	Surgical wound infection	8	29.6
	Hydrocephalus	8	30.6
	No complication	5	18.5
Intervention for hydrocephalus (n=8)	Sub dural therapeutic tap	1	12.5
	VP shunt	2	25.0
	Not intervention	5	62.5

5.10 Factors associated with NTD

After knowing the candidate variables through bivariate logistic regeression multivariate logistic regression was also conducted to declare the level of stastically siginificance variabls at p value <0.05 with 95% CI. During bivariate logistic regression variables like; residence, occupation of mother, father education, folic acid supplementation, chewing khat, sex and gestational age were candidate variables for multivariate logistic regression at p- value ≤ 0.25. In multivariate logistic regression model, parental rulal residence, and chewing khat were found to be significant association with NTD among newborns admitted to NICU, JMC at p- value <0.05 with 95% CI of AOR (Table 10).

This study revealed that the odds of having NTD was 2.2 times higher among neonates from rural residence as compared to neonates from urban areas (AOR=2.20 95% CI; 1.06-4.56, P=0.014). Similarly, neonates' mother who had history of chewing Khat during the current pregnancy was 4.8 times more likely to develop NTD compared to neonates' mother who didn't chewing Khat (AOR=4.68 95% CI; 1.83-12.04, P=0.001).

Table 3: Bivariate logistic regression model to identify candidate variables for fctors associated with NTD among newborns admitted to NICU, JMC, Jimma, south west, Ethiopia, 2022 (n = 394)

Variables		NTD		COR, 95%CI	P-value
		Yes (%)	No (%)		
Residence	Urban	12 (5.9)	190 (94.1)	1	
	Rural	27 (14.1)	165 (85.9)	2.53 (1.24,5.15)	0.01
ANC follow up	Yes	35(8.8)	328(83.2)	1	
	No	4(1.01)	27(6.9)	1.38(0.45,4.19)	0.56
Mother occupation	House wife	26 (12.7)	179 (87.3)	4.28(0.98,18.59)	0.07
	Farmer	7 (13.0)	47 (87.0)	4.39(0.87,22.15)	0.55
	Self employed	4 (3.4)	70 (94.6)	1.68(0.29,9.53)	0.55
	Government	2 (3.3)	59 (96.7)	1	
Father education	Can't read and write	9 (13.8)	56 (86.2)	2.60(0.82,8.18)	0.10
	Can read and write	2 (4.3)	44 (95.7)	0.73(0.13,3.95)	0.72
	Primary	16 (81.6)	17 (18.4)	3.65(1.27,10.46)	0.01
	Secondary	7 (6.4)	103 (93.6)	1.10(0.33,3.59)	0.87
	College and above	5(5.8)	81 (94.2)	1	
Folate supplementation	Yes	1 (1.7)	59 (98.3)	1	
	No	38 (11.4)	396 (88.6)	7.57(1.02,56.25)	0.04
Sex of newborn	Male	16 (7.3)	204 (92.7)	1	
	Female	23 (13.2)	151 (86.8)	1.94(0.99,3.80)	**0.05**
Khat Chewing	Yes	8 (68.0)	17 (32.0)	5.13(2.0, 12.84)	0.00
	No	306(89.7)	35(10.3)	1	
Alchol intake	Yes	1(6.7)	14(93.3)	1.56 (0.20,12.19)	0.67
	No	38(10.0)	341(90)	1	
OCP use	No	31 (8.4)	338 (91.6)	1	
	Yes	4(7.5)	49(92.5)	1.40 (0.47,4.11)	0.54
Exposure to chemicals	Yes	3(16.7)	15(83.3)	0.52 (0.14,1.91)	0.33
	No	36(9.5)	340(90.5)	1	

Table 4: Multivariate logistic regression model to identify Factors associated with NTD among neonates admitted to NICU, JMC, Jimma, south west, Ethiopia, 2022 (n = 394)

Variables		NTD		AOR, 95%CI	P-value
		Yes (%)	No (%)		
Residence	Urban	12 (5.9)	190 (94.1)	1	
	Rural	27 (14.1)	165 (85.9)	2.2(1.06,4.56)	0.033
Sex of neonate	Male	16 (7.3)	204 (927.)	1	
	Female	23 (13.2)	151 (86.8)	0.53(0.26,1.05)*	0.72
Mother occupation	House wife	26 (12.7)	179 (87.3)	2.70(0.57,12.86)	0.21
	Farmer	7 (13.0)	47 (87.0)	2.03(0.35,12.29)	0.44
	Self employed	4 (3.4)	70 (94.6)	1.39(0.23, 8.16)	0.71
	Government	2 (3.3)	59 (96.7)	1	
Father education	Can't read and write	9 (13.8)	56 (86.2)	0.92(0.22,3.877)	0.91
	Can read and write	2 (4.3)	44 (95.7)	0.35(0.05,2.34)	0.28
	Primary	16 (81.6)	17 (18.4)	2.03(0.56,7.63)	0.27
	Secondary	7 (6.4)	103 (93.6)	0.80(0.21,3.04)	0.80
	College and above	5(5.8)	81 (94.2)	1	
Folate supplementation	Yes	1 (1.7)	59 (98.3)	1	
	No	38 (11.4)	396 (88.6)	5.33(0.67,402.08)	0.11
Khat Chewing	Yes	8 (68.0)	17 (32.0)	4.68(1.82,12.04*	0.001
	No	31 (8.4)	338 (91.6)	1	

Key; * indicates variables statically significant with NTD during multivariate logistic regression

5.11 Discharge outcome of newborns with NTD admitted to NICU

Regarding to the outcome of neonates diagnosed with NTD at JMC, NICU; more than half 24 (61.5%) of them were discharged alive whereas 9 (23.1%) were died before discharge of which 6 of them died before surgical intervention

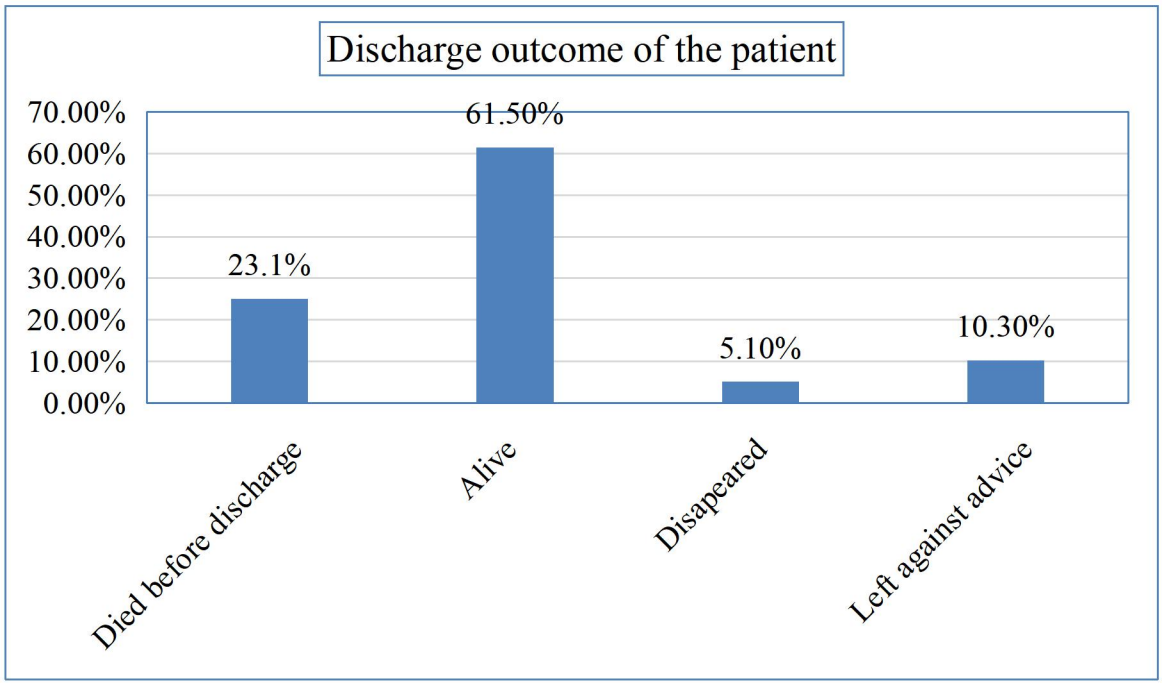

Figure 4; Discharge outcome of neonates with NTD admitted to NICU, JMC, South West Ethiopia, 2022.

CHAPTER; 6

DISCUSSION

This study attempted to assess the magnitude of NTD and associated factors among newborns admitted to NICU, JMC. The finding of this study indicated that the prevalence of NTD at our institution was 9.9%. The factors associated with NTD were rular residence, term gestational age , and chewing khat.

The finding of this study was higher compared to those studies conducted in Harar (5.71%)[30]. It is also higher than those studies done in African countries (Ghana 1.6 per 1000 births [24] , Nigeria (2.75/1000 live births) [25] and Moroko (1 per1000 births)[28]).These variations might be explained by the influence of racial, geographical, nutritional, socioeconomic, and biological differences, and parental exposure. The rates may also be affected by the differences in national NTDs prevention intervention programs in various countries settings. Study conducted in Ghana was retrospective this difference in study design may also explain the difference in the results. Referral hospitals would be expected to have higher rates than population-based studies, as many cases are referred to these hospitals for intervention NTDs.

Spina bifida and anencephaly are the two most common causes of NTDs. This study revealed that the majority (92.3%) of newborns had myelomeningocele.This is in line with studies done in Harar [29] and zambiya[20]. The location of NTD were lumbosacral 25 (64.1%) followed by lumbar 11(28.2%).

This study showed about 334 (84.8%) of mothers of newborns did not take any folate during the current pregnancy and from those who took only 39(9.9%) of them took on the recommended time. Further analysis of our study showed no significant association seen with the outcome.This is due to the fact that the vast majority of the mothers didn't take folic acid during pregnancy making similar exposure for all the study subjects which didn't give the anticipated outcome of our analysis.

This however it should not be interpreted otherwise as it is well known fact that folic acid supplementation reduces the incidence of neural tube defects (NTDs) by about 70%; thus, food fortification with folic acid (FA) and better dietary intake guidance greatly lower the prevalence

of neural tube abnormalities [14]. But other factors not assessed in our study like genetic factors could also be one major factor that could contribute to the development of NTDs.

The exact causes of NTDs remains undefined.The risk factors are multifactorial origion influenced by combination of genetic predisposition and environmental factors. Understanding the genetic and environmental factors is important to reduce the incidence and improve the outcome. In the present study, rural residence and khat chewing habits of mothers were factors contributing to the occurrence of NTDs.This study revealed newborns whose mothers chew khat were 4.6 times more likely to have infants with NTDs, which is supported by studies conducted in Ethiopia, Dessie which showed khat chewing during pregnancy as predisposing factor for the development of anencephaly[33].

In line with this, previous studies have shown that chronic khat chewing affects the nervous system. Khat contains several psychoactive components, including cathinone, cathine, cathidine and norephedrine. Such compounds may affect the development of the nervous system and be the reason for the present finding of khat as a risk factor for NTD [34].

Experimental study on animal models had showed that khat exposure during pregnancy had embryotoxic and fetotoxic evidenced by cytolysis, decidual hypoplasia, and atrophy of placenta, significant delay in embryonic and fetal development , developmental anomalies [35].

Moreover, newborns born to women living in rural area were 2.2 times affected by NTD. The possible justification is due to rural residents may not have access to start ANC follow-up early and be given folate or the pregnancy might be unplanned. In this study majority 27(69.2%) of mothers of newborns with NTD were from rular area , and only 30(8.3%) of mothers started ANC follow-up before 3 month of pregnancy and 25(6.3%) did visit Health care at all.In addition this srudy revealed eventhough obstetric ultrasound was done for 15 (43.9%) of mothers of newborns with NTD abnormality is not detected for 9(60%) of them.

Postnatal closure of the myelomeningocele in a newborn within 72 hours of delivery is advised to prevent infection (meningitis). In this study the median of age at surger was 9 days (SD 6.8 days) which is in line with study done in Uganda [17] , but much lower than study conducted in Addiss Ababa which closure was 29 days[21]

surgical repair was done within the first 72 hours only for 4 (14.8%) newborns while 23 (85.2%) were operated after 72 hours life because most of newborns were having infection and critical at the time of NICU admition. Age at presentation for majority (53.8%) of newborns with NTD was more than 72 hours because most of the patients were referral from other health facilities of which 28(71.8%) are from different weredas of Jimma zone ,followed by 5(12.8%) from illubabor zone and others from Dawuro,Gurage , Gambela each accounting (2.7%).

From newborns with NTD for whome surgical repair was done of had developed sepsis 6(22.3%) , wound infection 8(29.6%) and hydrocephalus 8(29.6%) post op complecations but VP shunt was inserted for 2 newborns. This finding is comparable with study conducted in Addis Ababa where 26.1% of the operated children developed wound-related complications including cerebrospinal fluid leak and infection[21]. However it is higher than study conducted in Uganda which where post opcomplecation was 2.5% [17].This high number of post operative complecation(infection) could be related to low infection prevention practice in our hospital.

The outcome for individuals with NTD depends on the site, the extent of the defect, the type of nerve cells that are involved and the extent of secondary abnormalities. In a 10-year survival study of Ugandan infants following myelomeningocele closure, most deaths were related to infection and neglect [21].This study showed that 9 (23.1%) of newbors with NTD died before discharge 6 of them died before surgery while the rest 3 died after surgical intervention.

6.1. Limitation of the study

some questions like dietary history are subjected to recall bias so making the interpretation weak and also dietary assessment is not detailed and simple consumption of leafy vegetables may not simply prevent NTDs as preparation and quality of the food also needs assessment , further we didn't assess for genetic predispositions which is also a major contributing factor for NTDs. And further the prevalence found in this analysis doesn't reflect the actual situation in the community so it only reflect intstitutional burden

CHAPTER; 7

Conclusion and recommendation

In conclusion, this study found that nearly one in ten neonates admitted to NICU had neural tube defects, with 36 (92.3%) of had myelomeningocele.Those mothers coming from rular area and chew khat are more likely to have child with NTD. Large percentage (81.5%) of newborns with NTD had post op complecations like hydrocephalus(29.6%) and surgical wound infection (29.6%).Only 2 patients had VP shunt inserted.Nine neonates (23.1%) with NTDs died before discharege from NICU. Attention must be given by public health experts and communities to those mothers who come from rular area and chewing Khat. Since more than half (60%) of NTD cases were missed to be detected by U/S, early detection of the abnormality and referral to delive at Hospital to be enterviened early should be given emphasis. Most patients developed surgical wound infection so infection prevention practice in our hospital should be looked at.Only few percentace of patients needing VP shunt had insertion with majority of patients having hydrocephalus so hospital should work on early intervention of hydrocephalus.

JUMC

- Should implement routinely health education programmes about the way of NTDs prevention
- Should work collaboratively with stakeholders to create awareness about NTD.
- Implement the preventive strategies of NTD as institution
- Strengthen infection prevention practices
- Work on early intervention of hydrocephalus

Health care providers

- Give health education about NTD risk factors and preventive measures for child bearing age women as well as community especially those coming from rulal area and also chewing khat
- Imrove infection prevention practice

Jimma Zonal Health Districts

- Arrange and facilitate health education programmes about prevention of NTDs for communities rular area and those chewing khat
- Give awareness about the risk and prevention methods of NTD for community in general
- Assist and give direction for health extension workers in order to give comprehensive and routine counseling service in house to house health related education.
- Should encourage and enhance health facilities to give regular health education program , early detection of NTD and referral of patients with NTDs

Researchers

- In the future researchers should conduct large scale longitudinal studies in order to know the long term outcome of surgically NTDs.

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ANNEX;QUATIONNAIRE

Information sheet and consent form /English version

Information sheet

Date_____ EC _____GC

Introduction

Dear participants!

Hello, my name is _____and I am pediatrics and child health postgraduate student in Jimma University, College of Health Science, and School of Medicine. I would like to ask few questions which take _____minutes about magnitude, associated factors and outcome of neural tube defect (NTDs) among neonates admitted to Jimma Hospital. Your genuine information that you are going to provide will help for prevention and control of NTDs. As participant of this study, you give me consent after you have understood the following information sheet:

Benefits-There is no immediate benefit in participating in this study. The result that will come out of this study will be used by the institutions and the government to solve some problems related with NTD

Incentive-There is no financial or material incentive in participating in this study.

Confidentiality- - Any information forwarded will be kept private and your name will not specify.

Participant rights- Your participation is entirely voluntary and up to you to decide. There is no penalty if you do not agree to participate. Also you have the right not to answer any questions you do not want to. You may also withdraw from the study at any time. If in the middle you decide to stop filling questions and no longer participate, you can stop without worry. If you have any question, you can ask at any time. If you have additional questions about the study, you can contact with:

Name of the interviewer _____ Sign_____ Date _____

Name of the supervisor _____Sign _____ Date_____

Thank you for your cooperation. If you are voluntary to participate in the study we kindly request you to provide your response for the questionnaire in the next page.

Informed consent

If you have read this form or it has been read to you in the language you comprehend and understood all conditions stated above. Therefore, would you willing to participate in this study.

Yes_____ No_____

Respondent's signature_____

Interviewer name_____ Name of principal investigator _____

Jimma Medical Center

ID #_____

MRN._____

Zone_____

Woreda _____

Kebele_____

Tel –number _____

Other _____

Health extension worker tel _____

Part I: Socio-demographic factor

1.1. Age of the mother (years) _____

1.2. Marital status 1. Married 2. Single 3. Divorced 4. Widowed

1.3. Residence of the parents_____ 1. Urban 2. Rural

1.4. Educational status of mother

1. None 2. Read and Write only 3. Grade 1 - 8 4. Grade 8 -12 5. College/other

1.5. Occupation of mother/care giver:

1. House wife 2.Farmer 3.Self-employed 4.Government/company 5. Other

1.6. Educational status of father

1. None 2. Read and Write only 3. Grade 1 - 8 4. Grade 8 -12 5. College/other

1.7. Family monthly income (estimate) :_____(birr)

Part II: maternal reproductive and obstetric history

2.1. Parity (number of delivery >28 weeks)? _____

2.2. Do you have previous history of still birth (fetal death >28 weeks)? 1. Yes 2. No

2.3. Do you have previous history of abortion (fetal death <28weeks)? 1. Yes 2. No

2.4. Was the current pregnancy planned? 1. Yes 2. No

2.5. Do you have ANC follow-up on current pregnancy? 1. Yes 2. No

2.6. If yes when did you start ANC visit for the current pregnancy? _____ Months

2.7. Was ultrasound done during the ANC follow-up? (If no skip Qn 15-18) 1. Yes 2. No

2.8. If yes at what month of pregnancy was it done? _____

2.9. Was any abnormality detected during the ultrasound evaluation? 1. Yes 2. No

2.10. What is the identified problem? _____

2.11. Are you informed of the problem? 1. Yes 2. No

Part III: maternal medical and drug history related factors

3.1. Do you have any chronic illness told by a doctor? 1. Yes 2. No

3.2. If yes which chronic disease?

1 Hypertension 2. Epilepsy 3. Diabetic mellitus 4. Goiter 5.Other (specify)_____

3.3. Did you have fever during this pregnancy? 1. Yes 2. No

3.4. If yes, at what month of pregnancy was your illness/fever? _____

3.5. Did you take any of the following drugs during this pregnancy?

1. Phenobarbital 2.phenytoin 3. Others (specify) _____

3.6. Did you use any traditional herbal medicine during this pregnancy? 1. Yes 2. No

3.7. If yes, at what month of pregnancy did you took herbal medicine? _____

3.8. Did you use oral contraceptive before conception? 1. Yes 2. No

3.9. If yes, for how long?_____

Part IV: Maternal Genetic Factors

4.1. Did you have history of NTDs affected pregnancy/live birth baby (show the picture)?

1. Yes 2. No

4.2. Was there any close family member had history of NTDs affected pregnancy/live birth baby? 1. Yes 2.No

4.3. Was there any close family member had history of congenital anomalies?

1. Yes 2.No

4.4. Do you have genetically relationship with your husband? 1. Yes 2. No

Part V: Maternal nutritional and folic acid supplementation

5.1. Did you take folic acid during this pregnancy? (Show the mother the tablet) 1. Yes 2. No

5.2. If yes when did you start taking folic acid? _____months prior / after pregnancy

5.3. Did you take multivitamin supplement during this pregnancy? 1. Yes 2. No

5.4. If yes when did you start taking multivitamins? _____months prior / after pregnancy.

5.5. How often did you eat vegetables (such as spinach, kale, cabbage, and broccoli,Salad, beetroot, tomato) during this pregnancy? 1. Every day 2.3 – 4 times/week

3.Once a week 4. Sometimes 5. Never

5.6. How often did you eat fruits (such as orange, grapes, and lemons) during this pregnancy?

1. Every day 2.3 – 4 times/week 3. Once a week 4. Sometimes 5. Never

5.7. How often did you eat legumes (lentils, beans, peas) during this pregnancy?

1. Every day 2.3 – 4 times/week 3. Once a week 4. Sometimes 5. Never

5.8. How often did you eat meat such as beef, lamb, goat, chicken during this pregnancy?

1. Every day 2.3 – 4 times/week 3. Once a week 4. Sometimes 5. Never

5.9. How often did you eat eggs during this pregnancy?

1. Every day 2.3 – 4 times/week 3. Once a week 4. Sometimes 5. Never

Part VI: Maternal lifestyle

6.1. Did you drink any alcoholic beverages during this pregnancy? 1. Yes 2. No

6.2. If yes which of the following alcoholic beverages you took during this pregnancy?

1. Beer 2. Locally made alcohol (Areke) 3. Wine 4. Whisky 5.Others (specify) _____

6.3. How frequently did you drink the alcoholic beverage?

1. Almost always 2. Usually 3. Sometimes 4.rarely

6.4. How many glass of alcoholic beverage did you took per week (average)?_____

6.5. Did you smoke cigarette during this pregnancy? 1. Yes 2. No

6.6. Was there any cigarette smoker in your home or occupational place? 1. Yes 2. No

6.7. Do you chew Kat during this pregnancy? 1. Yes 2. No

6.8. If yes how frequently did you chew khat? 1. Almost always 2. Usually 3. Sometimes 4.rarely

Part VII: Environmental factor

7.1. Did you use any pesticides/chemicals (insecticides, herbicides or fungicides) at home / work? 1. Yes (specify)_____ 2. No

7.2. If yes do you use any PPE (mask , glove)? 1. Yes 2. No

7.3. Where were you in contact with this chemical during pregnancy?

1. Home 2. Farm 3. Work place

7.4. How frequently do you come in contact with this chemical?

1. Every day 2.twice a week 3. Once a week 4 every month

5. Others (specify)_____

7.5. Did you have exposure to diagnostic radiation (X-ray) one month before or after this pregnancy? 1. Yes 2. No.

7.6. Do you have exposure to therapeutic radiation one month before or after this pregnancy

1. Yes 2. No.

7.7. Is there any factory in your vicinity? 1. Yes 2. No

7.8. If yes what manufacturing factory? _____

7.9. How far is the factory from your living area?_____

Part VIII: Neonatal clinical data

8.1. Age of newborn at presentation?_____

8.2. What is the Gestational age of the baby (by Ballard/Ultrasound/LNMP) _____(wks)

8.3. What is the Birth weight (if present?) _____ (grams)

8.4. What is the Weight at presentation? _____ (grams)

8.5. What is the sex? 1. Male 2. Female

8.6. Does the neonate have NTD? (If no skip remaining questions) 1. Yes 2. No

8.7. If yes what is the type of NTD? 1.Anencephaly 2. Myelomenigocele 3.Menigeocele

4. Encephalocele 5. Others (specify)_____

8.8. What is the anatomical location of neural tube defect?

1. Lumbar 2. Lumbosacral 3. Thoracolumbar 4. Cervical 5. Skull

8.9. Does he/she has associated abnormality? 1. Yes. 2. No

8.10.If yes what anomaly does he/she has?

1. Hydrocephalus 2. Club foot 3. Paraplegia 4. Chiari II malformation 5. Other (specify)_____

8.11. What is the size of meningeomyelocele sac _____?

8.12. Was the covering skin ruptured at presentation? 1. Yes 2.No

8.13. Was the overlying skin infected at presentation? 1. Yes 2.no

8.14. Did the patient have any symptoms of infection/sepsis during presentation?

1. Yes 2.No

8.15. Is the patient treated for meningitis after admission? 1. Yes 2.No.

8.16. Did the patient receive prophylactic antibiotics before surgery? 1. Yes 2.No

8.17. Was any of the Investigation done before surgery?(more than one answer is possible)

1. Ultrasound 2. CT-scan 3. MRI 4. Not done

8.18. What was the finding onimaging?_____

8.19. Was surgical intervention done? 1. Yes 2.No

8.20. If no to Qn.no .8.19 what was the reason for not doing the surgery?

1. The patient has infection 2. The patient is critical 3. Unavailability of OR Materials /anesthesia drugs 4. Family refused surgery 4. Other ----------

8.21. If yes to Qn.no.8.18 at what age of the newborn was the surgical intervention done_____ (days)?

8.22. What was type of surgical operation done_____?

8.23. Was Trans-fontanel Ultrasound done post operatively? 1. Yes 2.No

8.24 Does he/she have any post op complications? (More than one answer is possible)

1. Infection 2 .Hydrocephalus 3. Shunt malfunction 4. Skin defect requiring flap

5. CSF leak 6. Paraplegia/Para paresis (new onset) 7.Others (specify) _____

8.25. Did the patient developed hydrocephalus post operatively? 1. Yes 2. No

8.26. If yes how was it intervened?

1. Subdural therapeutic tap 2. VP shunts 3. No 4. Others (specify)_____

8.27. What is the final outcome at discharge?

1.Alive 2. Died before discharge 3.Disappeared 4.Left against medical advice 5. Abandoned

.