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RISK FACTORS FOR NEONATAL SEPSIS IN PUBLIC HOSPITALS, SOUTHWEST ETHIOPIA: A CASE CONTROL STUDY

BY

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ABSTRACT

Background: - *Despite numerous interventions resulted in remarkable progress against neonatal death, neonatal sepsis still a major cause of mortality and morbidity worldwide with the largest share in Sub-Saharan Africa. In Ethiopia, neonatal sepsis is one of the major contributors of health problem. It is the fourth leading cause of admission and the third leading cause of mortality in the 2014/2015. Moreover, no studies were previously conducted to verify the risk factors of neonatal sepsis in the study area.*

Objective: - *To identify risk factors for neonatal sepsis in public hospitals, Southwest Ethiopia, 2018.*

Methods: - *A facility based case control study was conducted in three public hospitals of Southwest Ethiopia from March to April 30, 2018. Consecutive sampling technique was employed to enroll study subjects. Data was collected by structured questionnaire and checklists, coded and entered using Epi-data version 3.1 and analyzed by SPSS for windows version 23. Candidate variables with P-value < 0.25 in bivariate analysis were fitted in multivariable analysis to identify independent predictors and P-value <0.05 was used to declare statistically significant association.*

Results: - *A total of 65 neonates with sepsis (cases) and 139 neonates without sepsis (controls) participated in the study. Forty-three (66.2%) of cases had early onset neonatal sepsis. The independent positive predictors of neonatal sepsis in this study were being male neonate [AOR = 3.875, 95% CI (1.57, 9.569)], meconium stained amniotic fluid [AOR = 3.76, 95% CI (1.171, 12.077)], history of urinary tract infections/sexually transmitted infections [AOR = 2.963, 95% CI (1.263, 6.947)], premature rapture of membrane [AOR =3.315, 95% CI (1.34, 8.2)], being low birth weight [AOR = 3.433, 95% CI (1.044, 11.293)], low APGAR score at 5^{th} minute [AOR = 3.738, 95% CI (1.28, 10.915)] and resuscitation at birth [AOR = 3.961, 95% CI (1.743, 9.0)].*

Conclusion and Recommendation: - *socio-demographic, maternal and neonatal health related factors had contributed to the risk of neonatal sepsis. Strengthening screening of all pregnant mothers and aseptic peri-natal care of newborns are recommended.*

Key words: Neonatal sepsis, Septicemia, Risk factors, Case control Study, Southwest Ethiopia

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DEDICATION

This Thesis is dedicated to my mom, Aminat Abdu Ahmed.

Mama, can't believe you're gone. However, it's because of you

I am who I am today.

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ACRONYMS/ABBREVIATIONS

ANC	Antenatal Care
AOR	Adjusted Odds Ratio
APGAR	Appearance Pulse Grimace Activity Response
BA	Birth Asphyxia
BGSH	Bong Gebretsadik Shao Hospital
BW	Birth Weight
CoNS	Coagulase Negative Staphylococcus
COR	Crude Odds Ratio
CRP	C-reactive Protein
CSA	Central Statistical Agency
EDHS	Ethiopian Demographic and Health Survey
EONS	Early Onset Neonatal Sepsis
ESR	Erythrocyte Sedimentation Rate
FDRE	Federal Democratic Republic of Ethiopia
GA	Gestational Age
GBS	Group B Streptococcus
IMNCI	Integrated Management of Neonatal and Child Illness
IPA	Intrapartum Antibiotics
IPF	Intrapartum Fever
LONS	Late Onset Neonatal Sepsis
MoH	Ministry of Health
MSAF	Meconium Stained Amniotic Fluid
MTU	Mizan Tepi University
MTUTH	Mizan-Tepi University Teaching Hospital
NICU	Neonatal Intensive Care Unit
PROM	Premature Rapture of Membrane

PrROM	Prolonged Rapture of Membrane
PSBI	Possible Severe Bacterial Infection
SIRS	Systematic Inflammatory Response Syndrome
SSA	Sub Saharan Africa
STIs	Sexually Transmitted Infections
TASH	Tikur Anbessa Specialized Hospital
TGH	Tepi General Hospital
UTIs	Urinary Tract Infections
WHO	World Health Organization
ZHDs	Zonal Health Departments

1. INTRODUCTION

1.1. Background

According to the report of the expert meeting on neonatal and pediatric sepsis of 8 June 2010, neonatal sepsis is defined as systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection in a neonate (1). Infection could be of bacterial, viral, fungal, or rickettsial origin and also encompasses various systemic infections of the newborn, such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis etc (2,3).

Based on the onset age of the disease, neonatal sepsis is broadly classified in to two major categories as Early Onset Neonatal Sepsis (EONS) in less than 7 days of age and Late Onset Neonatal Sepsis (LONS) between 7 to 28 days of age (4,5). It can be also classified into two subtypes depending upon whether the onset of symptoms is before 72 hours of life (EONS) or later (LONS). These classifications have great contribution to diagnosis and treatment by identifying which microorganisms are likely to be responsible for sepsis during these periods and the expected outcomes of infection (6,7).

Globally, neonatal sepsis is one of the most common cause of neonatal morbidity and mortality. In spite of recent advances in health care units, it is estimated to cause 13% to 15% of all neonatal deaths worldwide. Seventeen percent of neonatal deaths in Sub Saharan Africa (SSA) are attributed to neonatal sepsis as compared to only 6% in developed nations (8). Every year 2.6 million neonates die; three fourths of these deaths occur in the first week of life, and almost all (99%) in low- and middle-income countries. Neonatal sepsis is the third leading cause of neonatal mortality, only behind prematurity and intrapartum-related complications (or birth asphyxia). It is responsible for 42% of deaths in the first week of life (9). In Ethiopia, neonatal sepsis is one of the major contributor of health problem in under five year of age. It is the fourth leading cause of admission (6.61%) and the third leading cause of mortality (5.58%) in the 2014/2015 (10).

The spectrum of organisms that causes neonatal sepsis changes over time and varies from region to region even within the same hospital. This is due to the changing pattern of antibiotic use and changes in lifestyle (11). Blood culture is the “gold standard” for diagnosis of sepsis but blood culture reports are usually available after 48 to 72 hours (7). Although blood culture is the “gold standard” for definitive diagnosis, it is not always possible to isolate a causative pathogen. Invasive

infections can occur in seemingly asymptomatic neonates. So that, assessment of history and risk factors in combination with diagnostic tests are used to identify neonates who are more likely to be infected (12).

However, early diagnosis and proper management of neonatal sepsis by rational antimicrobial therapy and supportive care can reduce mortality, it's known that prevention and reduction of neonatal mortality from neonatal sepsis requires prior identification of risk factors that predispose the newborns to acquire the condition.

This study, therefore, was aimed to identify the risk factors of neonatal sepsis in three public hospitals of Southwest Ethiopia.

1.2. Statement of the Problem

Despite various preventive and curative interventions resulted in remarkable progress against neonatal death, neonatal sepsis is still a major cause of mortality and morbidity worldwide with the largest share in SSA. Sepsis-related morbidity is an increasing concern with reported incidences that are dramatically high regardless of the improvements in the quality of neonatal assistance (13).

The incidence of neonatal sepsis in developing countries is higher than the incidence in developed countries. Reports from developed countries demonstrated that the incidence of neonatal sepsis varies from 1 to 5 cases per 1000 live births while some other population-based studies from developing countries have reported clinical sepsis rates ranging from 49-170 per 1000 live births (13). Neonatal deaths in developing countries were caused by infections (42%), asphyxia and birth trauma (29%), prematurity and low birth weight (10%), congenital abnormalities (14%) and other causes (4%). Although the infection can be caused by viruses, fungi, and parasites, bacterial infection is the leading cause in neonatal sepsis (14).

Several previous studies identified common maternal and neonatal health related risk factors for neonatal sepsis. A case control study conducted in Mekelle, Northern Ethiopia identified that 51.3% and 28.2% of neonates born to mothers who had history of UTI/STIs during the index pregnancy and intrapartum fever and 26.9% of those who delivered in health center developed neonatal sepsis, respectively (8). Similarly, another case control study conducted in Saudi Arabia disclosed that 68% of neonates born to mothers who had premature rapture of membrane and developed neonatal sepsis (15). Another case control study in rural Ghana showed among those who developed neonatal sepsis, 30% and 13% of neonates were born to mothers who had meconium stained amniotic fluid and foul smelling liquor, respectively (16). regarding neonatal health related risk factors of neonatal sepsis, a case control study conducted in Ghana showed that among neonates who developed neonatal sepsis, 61% were male neonates, 51% were premature and 14% were resuscitated at birth (16). In addition, hospital based prospective cross-sectional study conducted in Dares Salam, Tanzania indicated that 53.6% of neonatal sepsis was attributed to APGAR Score less than seven at 5^{th} minute after birth (17). Similarity, another prospective cross-sectional study conducted in Gondar University Hospital, northwest Ethiopia, disclosed that

among those who developed neonatal sepsis, 31.6% were found to be low birth weight infants (18).

In order to alleviate those risk factors, wide range of interventions against neonatal sepsis were undertaken. In low- and middle-income countries, it was underlined a need for universal provision of antenatal care for mothers as a means of decreasing mortality from neonatal sepsis. This involves educating mothers about hygienic birth practice, promoting breast feeding which contains important immunological factors, some of which have the potential to inhibit causative pathogens as well as detecting and treating important maternal risk factors for neonatal sepsis, such as asymptomatic bacteriuria (19). Recent WHO guidelines recommended that universal GBS screening of all pregnant women at 35-37 weeks of gestation, administration of intrapartum antibiotic prophylaxis at least 4 hours before the delivery with clean delivery practices by skilled birth attendants and prevention of health care-associated infections through standard precaution practices (20,21). In the presence of symptoms and signs suggestive of neonatal sepsis or signs of PSBI or for prophylaxis in neonates with documented risk factors, its recommended that empiric antibiotic therapy should be started pending the identification of the causative agent (22).

Although universal provision of ANC and clean delivery were recommended for prevention of the risk factors, the proportion of women of child bearing age in Ethiopia who received ANC from a skilled provider and utilization of institutional deliveries are 62% and 26% in 2016, respectively (23). In addition, several studies were conducted previously across the country to establish cause of neonatal infections and also many centers have studied the common causative agents of neonatal sepsis with their sensitivity patterns. However, almost all were descriptive and unable to establish causation. In the contrary, since the current study is analytic in its nature, it can quantify association so that it goes beyond descriptive statistics.

Accordingly, in order to save lives of newborns and the bottlenecks for reduction of newborn deaths from infectious causes, it is critical to identify the risk factors for neonatal sepsis. Moreover, there were little studies undertaken in the country as a whole and no studies were previously tried to verify the risk factors of neonatal sepsis in the study area. Hence, there is a necessity to carry out a study to come up with the risk factors of neonatal sepsis in public hospitals of Southwest Ethiopia.

2. LITERATURE REVIEW

This section reviews available literatures on the topic under the study. Literature search was made using relevant key words related to neonatal sepsis. Previous research findings are reviewed from international and local literatures in order to develop an understanding on and identify the sociodemographic, maternal and neonatal health related risk factors in relation to neonatal sepsis. In addition, concepts considered pertinent are cited and used as reference.

2.1. Epidemiology of Neonatal Sepsis

Prevalence of neonatal sepsis varies across the globe and there are disparities among countries from the same region. Also according to previous studies, prevalence of neonatal sepsis varies in public and private health facilities.

In public health facilities, the study conducted in Mexico, the Latin American country showed 34.8% prevalence of neonatal sepsis (24). In Asia, where 39% of neonatal mortality from the globe is present, the prevalence of neonatal sepsis varies across the countries. The study conducted in Iran showed blood culture positive prevalence of neonatal sepsis was 7.3%. Another studies in Baghdad revealed 32.5% for early onset neonatal sepsis and 65.5% for late onset sepsis, in India 64.4% for blood culture positive sepsis, again in India 42.28% blood culture positive sepsis and Thailand 44.8% for early onset neonatal sepsis (25–29). Prevalence studies conducted in Africa, the home for 38% of all neonatal deaths, showed blood culture positive neonatal sepsis in Sudan, Nigeria and Egypt was 61.3%, 33.1% and 40.7%, respectively (5,30,31) where as in Tanzania 31.4% based on clinical parameters (17).

In private health facilities, study of neonatal sepsis in a Nigerian private tertiary hospital demonstrated that 34%prevalence of blood culture positive. Similarly, a ten-year review of neonatal bloodstream infections in a tertiary private hospital in Kenya showed that 152 (23%) out of 662 suspected cases of neonatal sepsis had positive blood culture. Thus, prevalence in private hospitals are lower than that of public hospitals(32,33)

In Ethiopia, the burden of neonatal sepsis is considerably high according to studies conducted in some parts of the nation. Two studies conducted in Tikur Anbessa university hospital revealed that 44.7% and 4.7% of blood culture positive prevalence of neonatal sepsis and bacterial meningitis, respectively (7,34). Another study conducted in Gondar university hospital showed, prevalence of

64% and 32.6% for early and late onset sepsis based on clinical parameters, respectively and 32% and 32.2% for early and late onset sepsis based on positive blood culture result respectively (35). The study aimed to assess incidence of neonatal sepsis, its risk factors, antimicrobials use and clinical outcomes in Bishoftu General Hospital, neonatal intensive care unit found that 72.2% incidence of neonatal sepsis (3).

2.2. Risk Factors for Neonatal Sepsis

2.2.1. Sociodemographic factors

The affiliation between sociodemographic factors and the likelihood of neonatal sepsis is marked in several studies with emphasis to maternal age and sex of the neonates as shown below.

2.2.1.1. Sociodemographic factor of index mothers:

Maternal age: numerous studies indicated that maternal age is a significant risk factor for neonatal sepsis. A retrospective cohort study conducted in northern Carolina disclosed maternal age <18 years is independent risk factor of early EOGBS compared to their counter parts [AOR=1.91, 95%CI:1.29, 2.83] (36). A case control study in Ghana showed women aged 31-40 years were 61% less likely to have neonates with sepsis compared to those aged less than 20 years [AOR=0.390, 95%CI:0.161, 0.919] (16)**.** Similarly, hospital based cross-sectional study in Dares Salam, Tanzania, demonstrated that women aged less than 20 years is 6.7 times more likely to have a neonate with neonatal sepsis compared to women aged 21-30 years [AOR=6.7,95%CI: 2.2, 3.88, P=0.001] (17)

In the contrary, a 1:4 matched case-control study conducted in china discovered that maternal age greater than 35 years is a risk factor for neonatal sepsis. A women aged greater than 35 years were approximately 5 times more likely to have neonates with neonatal sepsis than their counter parts [AOR=4.835, 95% CI: 1.170, 19.981] (37).

2.2.1.2. Sociodemographic factor of neonates:

Sex of the neonate: Several studies revealed that there is a significant difference in the proportion of male and female neonates who suffer from neonatal sepsis. A retrospective study at Tikur Anbessa Specialized Hospital (TASH) showed, 53% of subjects were male with male to female

ratio 1:0.88 (34). Similarly, a prospective study conducted in Baghdad revealed 68.7 % were male neonates (38) which is almost similar with study conducted in India where it was 66.85% (39). A case control study conducted in rural Ghana reported that neonatal sepsis was about 1.8 times more likely occur among male neonates compared with female neonates [AOR=1.806, 95% CI: 1.021, 3.224, P = 0.040] (16). In the contrary, retrospective cohort study done in Northern Carolina found that male sex to be protective of neonatal sepsis [AOR=0.80, 95% CI: 0.69, 0.92] (36).

2.2.2. Maternal Risk Factors

Maternal heath related factors such as meconium stained amniotic fluid, maternal intrapartum fever, history of urinary tract infection (UTI)/sexually transmitted infections (STIs), premature rapture of membrane (PROM), ANC follow up, intrapartum antibiotics, place of delivery and mode of delivery are major risk factors for neonatal sepsis as shown below.

Meconium Stained Amniotic Fluid (MSAF): The meconium stained amniotic fluid can be caused by infection in the uterus, prolonged fetal hypoxia in the uterus and other stress condition of fetus in the uterus. Chorioaminonitis can produce the meconium stained and foul smelling amniotic fluid because of inflammatory reaction (40).

A case control study conducted in rural Ghana demonstrated that women who had meconium stained amniotic fluid were 3.625 times more likely to give birth to infants who suffered from neonatal sepsis compared to those without meconium stained amniotic fluid [AOR=3.625, 95%CI: 1.730, 8.103, P = 0.000] (16). Similarly, another case control study in Dr. Soetomo hospital and a four-year historic cohort in southeastern Mexico disclosed MSAF is independent risk factor for neonatal sepsis [AOR=2.535, 95%CI: 1.225, 5.245, P=0.029] and [RR=1.5, 95 % CI: 1.1, 1.9, P≤ 0.005], respectively (41,42).

Maternal Intrapartum fever: Maternal intrapartum fever is found to be an important risk factor for neonatal sepsis. A case control study in Saudi Arabia disclosed maternal intrapartum temperature of ≥38°C is a significant independent risk factor [AOR=7.10, 95%CI: 2.50, 20.17] (15). Likewise, similar study in northern Ethiopia revealed intrapartum fever is a risk factor [AOR= 6.1, 95% CI:1.29, 28.31] (8).

Nested case control study conducted in Boston, Massachusetts and a retrospective cohort study in Pakistan discovered that women with highest intrapartum temperature were more likely to give birth to newborn with neonatal sepsis [AOR=2.38, 95%CI, 2.05, 2.77] (43), and [AOR=37.0, 95%CI: 3.4, 93.3] (44) respectively.

History of UTI/STIs: History of urinary Tract Infection (UTI) or sexually transmitted infections (STIs) is a major maternal health related risk factor of neonatal sepsis. A case control study in rural Ghana showed women with a history of UTI/STIs are approximately 3 times more likely to give birth to neonates with neonatal sepsis than those without history of UTI/STIs [AOR=3.007, 95%CI: 1.477, 6.425, P=0.002] (16). Likewise, similar study conducted in Mekelle, northern Ethiopia and Saudi Arabia showed that history of UTI/STIs and GBS bacteriuria are independent risk factors [AOR=5.23, 95%CI:1.82, 15.04] and [AOR=10.76, 95%CI: 1.24, 93.42, P=0.008] (8,15). Similarly, a prospective cross-sectional study conducted in Bishoftu general hospital, Debrezeit revealed that significant number of neonates born from mothers' with (UTI) developed neonatal sepsis [AOR=2.9, 95%CI: 1.489, 5.527, P= 0.02] (3).

Premature Rapture of Membrane (PROM): PROM is an important maternal health related risk factor which increases the likelihood of development of neonatal sepsis in the newborn. A case control study in Saudi Arabia disclosed that women with PROM were 9.62 times more likely to give birth to newborn with sepsis compared to women without PROM [AOR=9.62, 95%CI: 3.15, 29.42, P=0.0001](15). Similarly, case control study conducted in rural Ghana and northern Ethiopia and Nested case control study in Boston, Massachusetts revealed PROM is significant risk factor of neonatal sepsis [AOR=1.964, 95%CI: 1.742, 3.178, P=0.063], [AOR=7.43, 95%CI: 2.04, 27.1] and [AOR=3.41, 95%CI: 2.23, 5.20], respectively(8,16,43). Another retrospective cohort study in southeastern Mexico and Pakistan identified that PROM for more than 24 hours and more than 48 hours is risk factor for neonatal sepsis [RR=3.5, 95%CI:1.8, 6.6, P≤ 0.0001] and [AOR=9.6, 95%CI: 3.3, 27.1], respectively(42,44).

ANC follow up: not attending or low frequency of antenatal care is a risk factor for neonatal sepsis. A case control study in Saudi Arabia showed women who had four and above ANC visit are less likely to give birth to a newborn with neonatal sepsis compared [AOR=0.30, 95%CI: 0.09, 0.89, P=0.03] (15). Similarly, a retrospective cohort study in Brazil revealed that neonates whose

mothers had less than four antenatal visits are more likely develop neonatal sepsis [AOR=1.69, 95%CI: 1.11, 2.57] (45).

A cross sectional study conducted in Uganda demonstrated that not having ANC visit during pregnancy is an independent risk factor and women not received health education about danger signs in pregnancy are 2.37 times more likely to give birth to newborn with neonatal sepsis compared to those received health education [AOR=3.21, 95%CI:1.24, 8.33 P=0.01] and [AOR=2.37, 95%CI:1.14, 4.92, P=0.02], respectively(46).

Intrapartum Prophylactic Antibiotics (IPA): A retrospective cohort study in the Woman's Hospital of Texas, USA demonstrated that the duration of intrapartum antibiotic administration impacted the diagnosis of neonatal clinical sepsis; with the diagnosis of neonatal sepsis decreasing the longer the mother received intrapartum antibiotics. Intrapartum antibiotics for ≥4 hours reduced the risk of infants being diagnosed with clinical sepsis by 65% [AOR=0.35, 95%CI: 0.16, 0.79, P= 0.01] while Intrapartum antibiotic for less than four hours is a risk factor for neonatal sepsis [AOR=3.5, 95%CI: 1.3, 9.6, P=0.02] (47). Similarly, a case control study in Saudi Arabia disclosed that antibiotics use during labor reduces the likelihood of neonatal sepsis in the newborn [AOR=0.16, 95%CI: 0.38, 0.67, P=0.013] (15). In addition, nested case-control study conducted in Boston, Massachusetts showed that any form of intrapartum antibiotic given 4 hours before delivery is associated with decreased risk of neonatal sepsis [AOR=0.31, 95%CI: 0.13, 0.71] (43).

Place of delivery: Studies reveled that place of delivery has significant association with the risk of onset of neonatal sepsis. A case control study in northern Ethiopia showed the odds of having neonates with sepsis among mothers who gave birth at health center was 5.7 times higher compared to those who gave birth in hospitals [AOR=5.70, 95%CI:1.71, 19.00] (8). Hospital based prospective cross-sectional study conducted in Bishoftu general hospital NICU, Debrezeit-Ethiopia disclosed that significant number of neonates were born in health center and developed sepsis compared to who were born in the hospital [AOR=4.2, 95%CI: 1.934, 8.967, P=0.000] (3).

Mode of delivery: A case control study in Indonesia demonstrated newborns delivered by caesarian section are about 1.9 times more likely to suffer from neonatal sepsis compared to those delivered with spontaneous vaginal delivery [AOR=1.895, 95%CI: 1.087, 3.303, P=0.032] (41). Similarly, hospital based prospective cross-sectional study conducted in Bishoftu general hospital

NICU, Debrezeit-Ethiopia showed the risk of acquiring neonatal sepsis in newborns delivered by caesarian section and instrumental delivery is about 4.3 and 6.3 times more likely than infants born vaginal in the natural way [AOR=4.3, 95%CI: 1.025, 17.924, P=0.046] and [AOR=6.3, 95%CI: 1.252, 31.7680, P=0.026], respectively (3). Another cross sectional study in Gondar, northwest Ethiopia showed caesarean section delivery is independent risk factor [AOR=5.191, 95%CI: 2.36, 11.37] (18). In the contrary, matched case control study conducted in China revealed that caesarian section delivery reduced the risk of infants being diagnosed with neonatal sepsis by 89.7% [AOR=0.103, 95%CI: 0.041, 0.258] (37).

2.2.3. Neonatal Risk Factors

The relationship between neonatal health related risk factors and the possibility of neonatal sepsis is evident in several studies with emphasis to gestational age, birth weight, APGAR score, birth asphyxia and resuscitation at birth as shown below.

Gestational age: Prematurity or preterm baby is defined as live born newborn delivered before 37 completed weeks of pregnancy which is a major risk factor of neonatal sepsis(39). A case control study conducted in Indonesia showed that a neonates delivered before 37 weeks are about four times more likely to develop neonatal sepsis compared to term neonate [AOR=4.073, 95%CI: 2.180, 7.609, P=0.000](41). Similarly, retrospective cohort study in Indonesia and southern Mexico disclosed that gestational less than 37 weeks is independent risk factor [AOR=13.45, 95%CI: 3.91, 46.26, P=000] and [RR=2.4, 95%CI:1.7, 3.4, P< 0.0001], respectively (42,48). In addition, cross- sectional study conducted in University of Gondar Hospital disclosed preterm infants are more likely to suffer from neonatal sepsis [AOR=8.99, 95%CI: 4.175, 19.38, P<0.001] (18).

Birth Weight: Birth weight is an important risk factor neonatal sepsis. A case control study in Ghana and Indonesia disclosed that birth weight less than 2500 grams is a significant and independent risk factor [AOR=6.177, 95%CI: 3.01, 13.643 P=0.000] and [AOR=2.75, 95%CI:1.454, 5.20, P=0.001], respectively (16,41). Similarly, a retrospective cohort study in Indonesia, Pakistan and Brazil revealed that very low birth weight (birth weight at birth less than 1500 grams) is associated with an increased likelihood of neonatal sepsis [AOR=4.9, 95%CI:1.08, 22.25, P= 0.04], [AOR=9.8, 95%CI:1.5, 65.7] and [AOR=2.46, 95%CI:1.20, 5.03, P=0.01],

respectively(44,45,48). In addition, a cross- sectional study conducted in University of Gondar Hospital showed newborns with very low birth weight and low birth weight are more likely to suffer from neonatal sepsis than their counterparts [AOR=12.37, 95%CI: 4.135, 37.04] and [AOR=2.63, 95%CI:1.149, 6.09], respectively (18).

APGAR Score: APGAR (Appearance, Pulse Rate, Grimacy Activity, Respiration) score provides a convenient shorthand for reporting the status of the newborn infant and the response to resuscitation. It was proposed in 1952 as a means of rapidly evaluating the clinical status of a newborn infant and currently remains an accepted method for newborn infant assessment at 1st and 5th minute immediately after delivery(49).

Numerous studies demonstrated that low Apgar score is a significant and independent risk factor of neonatal sepsis. A case control study in rural Ghana disclosed that Apgar score of the neonate at one minute after birth is significantly associated with the likelihood of suffering from neonatal sepsis [AOR=5.198, 95%CI: 2.800, 9.952, P=0.000] (16). Similar study in northern Ethiopia revealed that infants with Apgar score less than 7 at 5th minute are more likely develop neonatal sepsis than their counter parts [AOR=68.9, 95%CI: 3.63, 1308] (8).Likewise, retrospective cohort study in Indonesia showed Apgar score less than 7 at 5th minute is a risk factor [AOR=14.05, 95%CI: 5.48, 35.98, P= 0.000](48).

Birth asphyxia: Asphyxia remains a severe condition leading to significant mortality and morbidity. Study in Jimma showed birth asphyxia (47.5%), neonatal infections (34.3%) and prematurity (11.1%) were the three leading causes of neonatal mortality accounting for 93% (50). Birth asphyxia (BA) is defined as failure to initiate spontaneous respirations and/or 5-minute Apgar score less than 7: the most commonly used indicator to identify BA in resource limited settings (26).

As long as a baby is crying immediately at birth which indicate the initiation of spontaneous respiration and breathing normally, newborn basic resuscitation including any manipulation, such as routine suctioning, which may cause trauma or introduce infection should be avoided (51).

Birth asphyxia is an important neonatal health related risk factor of neonatal sepsis. The study conducted in Nigeria showed that birth asphyxia is the second predominant predisposing factor next to out borne delivery (68.0%), birth asphyxia (30.2%) and prematurity (21.4%) (30). A case

control study in Ghana showed newborns who cried immediately at birth are less likely to suffer from neonatal sepsis than their counter parts [AOR=0.081, 95%CI: 0.003, 0.425, P=0.001] (16). Similar study in northern Ethiopia also showed infants not crying immediately at birth are more likely to suffer from neonatal sepsis compared to who cried immediately at birth [AOR=124, 95%CI: 6.5, 2379] (8).

Resuscitation at birth: Effective resuscitation at birth can prevent a large proportion of neonatal deaths from birth asphyxia. Basic neonatal resuscitation includes suctioning of mouth, nose and trachea as needed, mechanical ventilation, and oxygen administration(52).

Studies revealed that resuscitation at birth is a significant and independent risk factor of neonatal sepsis. A case control study conducted in Ghana showed infants who were resuscitated at birth are about five times more likely to suffer from neonatal sepsis compared to those who were not resuscitated [AOR=5.274, 95%CI: 1.630, 24.558, P=0.004] (16). Similarly, a retrospective cohort study in southeastern Mexico revealed the requirements of assisted ventilation is a significant risk factor [RR=1.7, 95%CI: 1.1, 2.5, $P \leq 0.004$] (42).A hospital based cross-sectional study conducted in Dares Salaam, Tanzania also demonstrated that resuscitation at birth is independent risk factor for the development of neonatal sepsis. [AOR=1.251, 95%CI:1.22, 3.88, P=0.025] (17).

During review of the above literatures, both strength and limitations are noted. Some literatures utilized primary data, applied appropriate study design and conducted on adequate sample size whereas majorities of the studies utilized secondary data such as retrospective chart review which is more prone to inconsistencies and inaccuracy, were descriptive studies, recruited hospitalized subjects for the study which lack representativeness as well as few samples verified by wide confidence interval and non-inclusiveness of all factors such as study only on maternal risk factors.

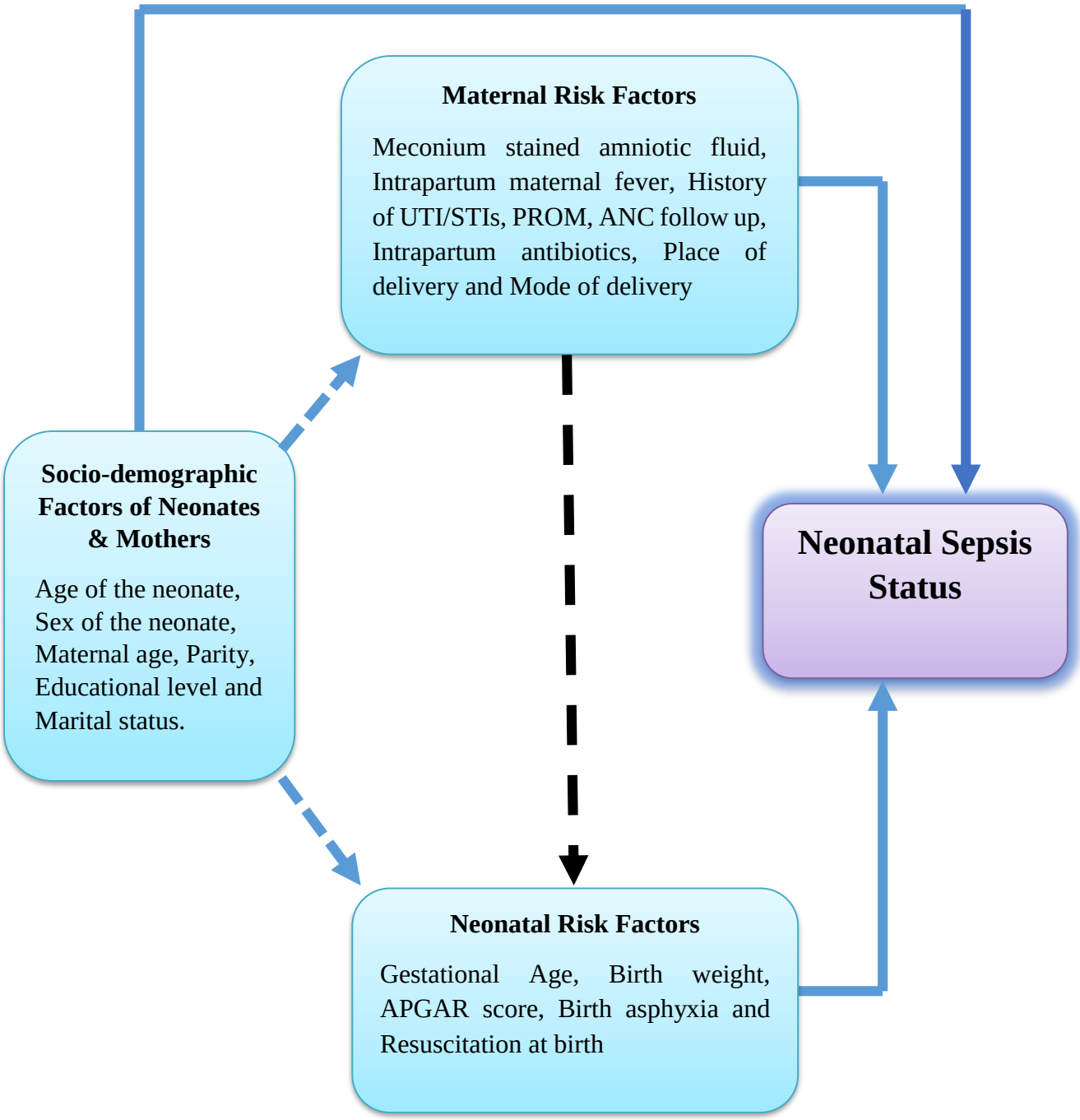

Figure 1: Conceptual Framework of risk factors for neonatal sepsis (Source: Adapted from different literatures, 2018).

Note: The relationship between independent variables was not the focus of this study.

2.3. Significance of the Study

In order to decline neonatal morbidity and mortality at the country level, local epidemiology of neonatal sepsis should be constantly updated through identification of risk factors that predispose the newborns to acquire the illness.

Evidences showed that there was variation in the magnitude of neonatal sepsis in health care delivery system in which prevalence in private health facilities are lower than public facilities. Thus, the focus of this study was public health facilities.

Findings from this study will help policy makers, partner organizations and all relevant stakeholders in providing evidences for policy choice, to plan and implement appropriate intervention measures to tackle the existing neonatal health related troubles.

Findings could help the study hospitals in improvement of those practices potentially predispose the newborn to acquire the condition during pregnancy, labor and delivery. It is also expected that, the recommendations made by this study may help as one of evidences to improve the current neonatal morbidity and mortality rates by coming up with relevant evidences for addressing the risk factors.

The study is also expected to fill gaps in this area of research and adds to the existing body of knowledge.

3. OBJECTIVE and HYPOTHESIS

3.1. General Objective

- ☑ To identify risk factors for neonatal sepsis in public hospitals, Southwest Ethiopia from March to April 30, 2018.

3.2. Specific Objectives

- ☑ To identify risk factors for neonatal sepsis in public hospitals, Southwest Ethiopia, 2018.

3.3. Hypothesis

The following are hypotheses to be tested:

1. Being male increases the likelihood of neonatal sepsis
2. Presence of meconium in the amniotic fluid increases the likelihood of neonatal sepsis
3. There is association between maternal intrapartum fever and neonatal sepsis
4. Health center delivery is associated with neonatal sepsis
5. Caesarean selection delivery increases the likelihood of neonatal sepsis

4. METHODS and MATERIALS

4.1. Study Area and Period

The study was conducted in selected public hospitals found in Southwest Ethiopia from March to April 30, 2018. In southwest Ethiopia, there are six public hospitals found in three zones of Southern Nations Nationalities and Peoples Regional State (SNNPRS): Mizan Tepi University Teaching hospital (MTUTH), Bachuma and Maji primary hospitals in Bench Maji Zone, Bonga Gebretsadik Shawo Hospital (BGSH) and Chena Meles Zenawi Memorial primary hospital in Kaffa zone, and Tepi General hospital (TGH) in Sheka zone.

Mizan Tepi university teaching hospital (MTUTH) is located in Bench Maji zone, Aman town which is 572 Kilometers to southwest of Addis Ababa, capital of Ethiopia. It was established in 1979 G.C and launched as Teaching Hospital in 2016 G.C. The hospital had 220 technical staff and is serving as referral hospital for estimated more than 1.7 million population of Bench Maji Zone, neighboring woredas of Kaffa, Sheka zones and partial Gambella regions (Majag zones) as referral center. It has a total of 109 patient beds in different departments and 8 beds in neonatal intensive care unit (NICU) for newborn infants. In the year 2017, a total of 216 neonates were diagnosed to have neonatal sepsis and treated accordingly.

Bonga Gebretsadik Shawo Hospital (BGSH) is located in Kaffa zone, Bonga town which is 460 Kilometers to southwest of Addis Ababa, capital of Ethiopia. It was established in 1997 G.C and is serving as the only general hospital for estimated 1, 042, 878 population of Kaffa Zone. It has a total of 103 patient beds in different departments and 10 beds in neonatal intensive care unit (NICU) for newborn infants. In the year 2017, a total of 120 neonates were diagnosed to have neonatal sepsis and treated accordingly.

Tepi General hospital (TGH) which is located in Sheka zone, Tepi town which is 603 Kilometers to southwest of Addis Ababa, capital of Ethiopia. It was upgraded from health center in 2014 G.C and is serving as the only general hospital for estimated 1.2 million population of Sheka Zone, neighboring woredas of Kaffa zones and partial Majag zone of Gambella regions. It has a total of 111 patient beds in different departments and 9 beds in neonatal intensive care unit (NICU) for newborn infants. In the year 2017, a total of 120 neonates were diagnosed to have neonatal sepsis and treated accordingly.

4.2. Study design

Facility based case-control study was conducted.

4.3. Population

4.3.1. Source Population for Cases and Controls

All neonates attending care in all (six) public hospitals found in southwest Ethiopia.

4.3.2. Study Population

4.3.2.1. Study Population for Cases

Neonates (65 as cases) attending for care in selected public hospitals of southwest Ethiopia during the study period.

4.3.2.2. Study Population for Controls

Neonates (139 as controls) attending for care in selected public hospitals of southwest Ethiopia during the study period.

4.3.3. Case Definition

4.3.3.1. Definition of Cases

Neonates in the presence of one or more of the established IMNCI clinical [Either of fever (≥37.5°C) or hypothermia (< 35°C), fast breathing (respiratory rate ≥ 60 breaths per minute), nasal flaring, grunting, bulging fontanels, pus draining from the ear, redness around umbilicus extending to the skin, chest indrawing, not feeding well, reduced movements or movement only when stimulated, convulsion, and lethargic or unconscious] along with two or more of the hematological criteria [Total Leukocyte Count (<4,000 or >12,000 cells/mm^3), Absolute Neutrophil Count (<1500 cells/mm^3 or >7500 cells/mm^3), I: T ratio (> 0.2), Erythrocyte Sedimentation Rate (> 15/1 hour) and platelet count (<150,000 or >440,000 cells/mm^3)] (1,9).

4.3.3.2. Definition of Controls

Neonates in the absence of those IMNCI clinical criteria but attending for services such as follow up, immunization and postnatal care with their index mothers.

4.3.4. Inclusion and Exclusion Criteria

4.3.4.1. Inclusion Criteria

☑ Delivery at home and public health facilities.

4.3.4.2. Exclusion Criteria

☑ Neonates with congenital anomaly with their index mothers.

4.4. Sample Size and Sampling Technique

4.4.1. Sample Size Determination

A two population proportion formula using Epi-info version-7 was used to estimate the sample size required for the study. Sample size was calculated using eight different exposure variables and variable with largest sample size is taken. By considering the proportion of mothers who had history of UTI/STIs among controls was 13% (this variable was taken as main exposure variable from previous study) (16), 95% CI, 80% power of the study, control to case ratio of 2:1 to detect an odds ratio of 3.0 (16). Accordingly, by adding 5% non-response rate, the total sample size using Fleiss w/cc method was **216** (**70 cases and 146 controls**).

Table 1: Variables for sample size determination

Main exposure variable	% of exposure among controls	% of exposure among cases	AOR	Sample Size for		Total	References
				Cases	Controls		
MSAF	11	30	3.62	52	110	162	(16)
Intrapartum fever	3	15	7.1	52	109	161	(15)
History of UTI/STIs	**13**	**30**	**3.0**	**66**	**139**	**205**	(16)
PROM	4.7	14.8	3.41	48	101	149	(43)
Health center delivery	6.2	16.9	4.2	33	38	101	(3)

4.4.2. Sampling Technique

Out of six public hospitals found in southwest Ethiopia, three hospitals; Mizan-Tepi University Teaching hospital (MTUTH), Bonga Gebretsadik Shawo Hospital (BGSH), and Tepi General hospital (TGH) were selected using simple random sampling.

The number of study subjects (cases and controls) for each hospital was allocated based on total number of neonatal sepsis cases treated in 2017. The total number of neonatal sepsis cases treated in 2017 in MTUTH, BGSH and TGH was 216, 192, and 120 with allocated sample size of 89 (29 cases & 60 controls), 78 (25 cases & 53 controls) and 49 (16 cases & 33 controls) for MTUTH, BGSH and TGH, respectively.

Study subjects were enrolled using consecutive sampling technique by which all eligible neonates with index mothers who presented for care in selected public hospitals were approached for enrollment in the study.

The selection process for cases with their index mothers undertaken at neonatology (neonatal out-patient) department and postnatal rooms while attending care in each hospital. Controls with their index mothers were selected at postnatal, immunization and follow up clinic.

The total of 204 study subjects (neonates with their index mothers) were included in this study; 83 (27 cases & 56 controls) from Mizan-Tepi University Teaching hospital, 73 (22 cases & 51 controls) from Bonga Gebretsadik Shawo Hospital and 48 (16 cases & 32 controls), from Tepi General hospital.

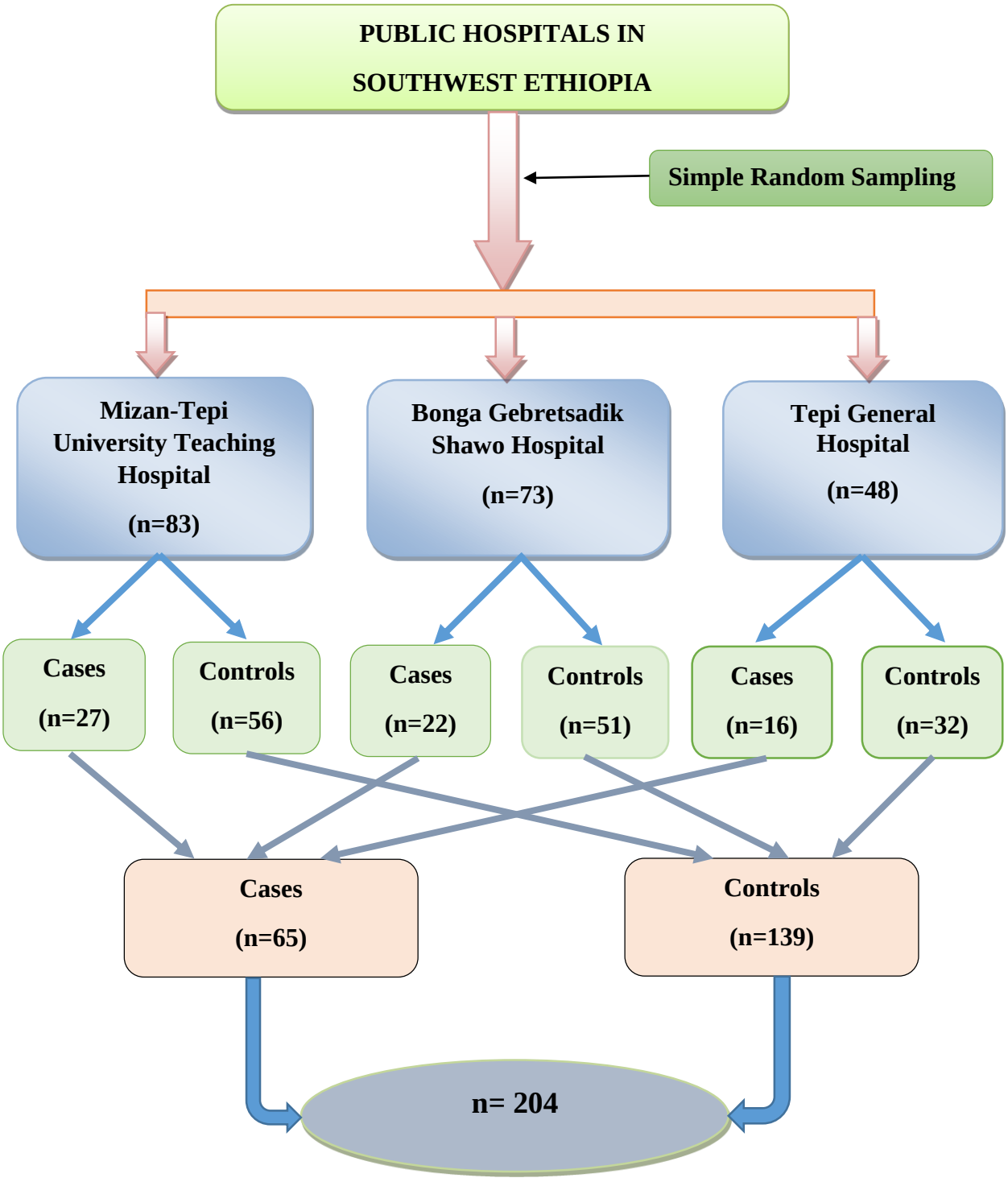

Figure 2: Schematic representation of sampling procedures, 2018.

4.5. Study Variables

4.5.1. Dependent Variable

- ☑ Neonatal Sepsis Status (Case/Control)

4.5.2. Independent Variables

- ☑ **Socio-demographic Factors:**
  - ***Socio-demographic factors of index mothers:*** includes maternal age, parity, educational level and marital status.
  - ***Socio-demographic factors of the neonates:*** includes age and **s**ex of the neonates.
- ☑ **Maternal Risk Factors (while pregnant with index neonate):** includes meconium stained amniotic fluid, maternal intrapartum fever, history of Urinary tract infection/sexually transmitted infections (UTI/STIs), premature rapture of membrane (PROM), antenatal care (ANC) follow up, intrapartum prophylactic antibiotics, place of delivery and mode of delivery.
- ☑ **Neonatal Risk Factors**: includes gestational age, birth weight, APGAR score, birth asphyxia and resuscitation at birth

4.6. Data Collection Procedure

4.6.1. Data Collection Instrument

The data was collected structured questionnaire and check list which is adapted from previous similar literature. The questionnaire was translated first into Amharic and later translated back to English by different translator to check for its consistency. The first part of the instrument was diagnostic or screening checklist containing IMNCI clinical and hematological criteria which was adapted from previous literature. The second part of the tool contains sociodemographic characteristics of neonates and index mothers, information on maternal health related risk factors and neonatal health related risk factors from neonate's records to be collected by checklist.

4.6.2. Data Collection Technique

Diagnosis of neonatal sepsis was undertaken using checklists of Integrated Management of Neonatal and Child Illness (IMNCI) Clinical [Either of fever (≥37.5°C) or hypothermia (<35°C), fast breathing (respiratory rate ≥ 60 breaths per minute), nasal flaring, grunting, bulging fontanels, pus draining from the ear, redness around umbilicus extending to the skin, chest indrawing, not feeding well, reduced movements or movement only when stimulated, convulsion, and lethargic or unconscious] and hematological criteria [Total Leukocyte Count (<4,000 or >12,000 cells/mm^3), Absolute Neutrophil Count (<1500 cells/mm^3 or >7500 cells/mm^3), I: T ratio (> 0.2), Erythrocyte Sedimentation Rate (> 15/1 hour) and platelet count (<150,000 or >440,000 cells/mm^3)] to identify (to screen) eligible and non-eligible subjects as well as to classify those eligible neonates as cases and controls by a physician who was assigned at each hospital during the study period.

After screening of cases and controls, data was collected by one BSc nurse for each hospital and one supervisor (BSc Public Health officer) using interviewer administered structured questionnaire and checklist. After informed consent was obtained, data on sociodemographic factors and maternal information was collected from index mothers using structured questionnaire. Data on neonatal health related factors was collected from neonate's records using checklist. For validation of information on laboratory investigation results, calibration of laboratory instruments was checked.

4.7. Data Quality Management

Data quality assurance was made through training of data collectors, questionnaire pretesting and continuous supervision at the time of data collection. A day long training was given for three physicians, three data collectors and three supervisors (BSc Public Health officers) before the actual data collection period. The training focused on study objectives, introducing the data collection tools (the questionnaire and checklists), how to approach study participants and wise use of time. Daily supervision was held at study settings by onsite supervisor and principal investigator twice a week. Data collection tool was pretested on 5% of the sample (4 cases and 8 controls) at Chena Males Zenawi Memorial hospital and modification was made on maternal exposure assessment questions. A pretested and validated questionnaire was used for the actual data collection. The data collection tools were checked each day during the actual data collection time

for completeness and consistency by supervisor and principal investigator twice a week. The code was given in completed questionnaire and the data on coded questionnaires was entered into Epi-data version 3.1 by the principal investigator.

4.8. Data Processing and Analysis

Data was checked for completeness, cleaned, assessed for missing data and analyzed using SPSS for windows version 23. Continuous explanatory variables were categorized. Descriptive analysis was carried out to generate mean, median, frequencies and proportions. Bivariate analysis using cross tabulation (chi-square test) and simple logistic regression was undertaken to ascertain sample adequacy and to identify explanatory variables associated with the outcome variable.

All co-variates showed with P-value less than 0.25 in bivariate analysis identified as a candidate variable for multivariable logistic regression model. Variable selection was made by backward LR method and multivariable logistic regression was applied. Then, only seven variables were showed an overall significant association with risk of neonatal sepsis at the 5% level of significance.

The magnitude of association between independent predictors and the outcome variable was measured by adjusted odds ratio (AOR) with 95% confidence interval (CI). A P-value less than 0.05 was used to declare the observed association is statistically significant.

Stratified analysis was undertaken to check for the presence of effect modification between maternal health related predictors and age of the neonate. Accordingly, Breslow-Day statistic showed that age of the neonates was not an effect modifier. Collinearity diagnostic was undertaken and showed there was no problem of multicollinearity.

The predictive success of the logistic regression model was assessed by looking at the classification table, showing correct and incorrect classifications of the dichotomous dependent variable. From the sampled participants included in the analysis, 82.4% of them are correctly classified on the basis of their status of the outcome as cases and controls.

Model goodness-of-fit test such as Hosmer and Lemeshow test was undertaken. Accordingly, Hosmer and Lemeshow test statistic indicated that the logistic regression model was of good fit (Chi-square = 9.048, P-value = 0.171).

4.9. Operational Definitions

***Preterm (Premature birth)*:** a live born infant delivered before 37 completed weeks of pregnancy

Term (mature birth): a live born infant delivered >=37 completed weeks

Birth weight: The first weight of a neonate measured immediately after birth & recorded in grams

Normal birth weight: is a neonate whose birth weight is between 2500 gm and 4,000 gm.

Low birth weight: is a neonate whose birth weight is between 1500 gm and 2,499 gm.

Very low birth weight: is a neonate whose birth weight is less than 1500 gm.

APGAR score: The measurement taken at 1^{st} and 5^{th} minute for reporting the status of newborn infant immediately after birth

Low APGAR score: The measurement taken at 1^{st} and/or at 5^{th} minute is less than seven.

Birth asphyxia: failure to initiate and sustain breathing at birth which is defined as APGAR score at 1^{st} minute is less than 7 and/or not crying immediately at birth.

Resuscitation at birth: suctioning of mouth, nose and trachea, mechanical ventilation, and oxygen administration for a newborn who unable to initiate breathing at birth.

Meconium stained amniotic fluid (MSAF): considered if the amniotic fluid was green in color or mixed with meconium, or appears meconium stained on the baby.

Intrapartum maternal fever: if mother suffered from fever with axillary temperature > 37.5° C during labor and delivery

***Premature rupture of membranes* (PROM):** Leakage of fluid before the onset of labor and the duration it stayed before the onset of labor in hours

Prolonged Rapture of Membrane (PrROM): the time from membrane rupture to onset of labor is more than 18 hours.

Intrapartum prophylactic antibiotics (IPA): defined as administration of any antibiotic to a mother at any time prior to delivery during her birth admission.

4.10. Ethical Considerations

The ethical approval and clearance for the study was obtained from Institutional Review Board (IRB), Institute of health, Jimma University. A support letter to the study hospitals was written by the department of epidemiology. An official letter of permission was obtained from each study hospitals. Informed consent was obtained from the index mothers of cases and control neonates

after explaining the purpose of the study. To assure confidentiality, personal identifiers was not written on the questionnaire.

4.11. Dissemination Plan

Results of this study was presented to the Jimma University, Institute of Health, as a partial fulfillment of the requirements for degree of Masters of Public Health (MPH) in Epidemiology. The findings will be delivered through hard and soft copy to the hospitals included in the study, Mizan Tepi University, Kaffa and Sheka zone health departments, and other concerned stakeholders. Repeated discussion and policy brief will be considered as needed. Efforts will be made to present the results on international and national professional conferences, and publication on peer reviewed scientific journal will also be considered.

5. RESULTS

5.1. Socio-demographic and Socio-economic Factors Related to Neonatal Sepsis

A total of 65 neonates who had neonatal sepsis (as cases) with their index mothers and 139 neonates who had no neonatal sepsis (as controls) with their index mothers included making response rate of 92.86% for cases and 95.21% for controls with overall response rate of 94.4%.

The mean age (± SD) of index mothers was 26.74 ± 5.622 for cases and 26.37 ± 5.455 for control neonates. Regarding to marital status, 59 (90.8%) index mothers of cases and 130 (93.5%) index mothers of controls were married. Twenty-five (38.5%) index mothers of cases and 45 (32.4%) index mothers of controls had not attended formal education. Forty-three (66.2%) index mothers of cases and 97 (69.8%) index mothers of controls were multiparous.

Regarding the socio-demographic characteristics of neonates, this study showed that 43 (66.2%) cases and 134 (96.4%) of control neonates were found in the age group of below 7 days. Also the proportion of male neonates was higher in the cases 49 (73.8%) compared to controls 64 (46%)

On bivariate analysis, neonatal socio-demographic factors; sex of the neonate and age of the neonate were associated with neonatal sepsis and found to be a candidate variable for multivariable analysis with P-value less than 0.25. On the other hand, maternal socio-demographic factors; maternal age, marital status, parity, educational level were not associated with neonatal sepsis and not identified as a candidate variable for multivariable analysis (See Table 2).

Table 2: Socio-demographic and Socio-economic related factors of neonates and index mothers attending MTUTH, BGSH and TGH, Southwest Ethiopia, 2018 (n=204)

Variables	Cases n=65 (%)	Controls n=139 (%)	COR (95% CI)	P-value
Maternal age				
≤ 20	10 (15.4)	25 (18)	0.747 (0.284, 1.968)	0.553
21-30	40 (61.5)	86 (61.9)	0.868 (0.418, 1.803)	0.705
31-40	15 (23.1)	28 (20.1)	1	
Marital status				
Married	59 (90.8)	130 (93.5)	0.681 (0.232, 2.0)	0.484
Other wise	6 (9.2)	9 (6.5)	1	
Parity				
Primiparous	22 (33.8)	42 (30.2)	1.182 (0.630, 2.215)	0.603
Multiparous	43 (66.2)	97 (69.8)	1	
Educational level				
No formal education	25 (38.5)	45 (32.4)	0.880 (0.368, 2.105)	0.773
Primary education	22 (33.8)	61 (43.9)	0.571 (0.239, 1.365)	0.208
Secondary education	6 (9.2)	14 (10.1)	0.679 (0.205, 2.250)	0.526
College and above	12 (18.5)	19 (13.7)	1	
Sex of the neonate				
Male	48 (73.8)	64 (46)	3.309 (1.734, 6.313)	< 0.001**
Female	17 (26.2)	75 (54)	1	
Age of the neonate				
< 7 days	43 (66.2)	134 (96.4)	1	
≥ 7 days	22 (33.8)	5 (3.6)	13.712(4.895, 38.407)	< 0.001**

- ** Significant at α=1%
- MTUTH: Mizan-Tepi University Teaching Hospital, BGSH: Bonga Gebretsadik Shawo Hospital, TGH: Tepi General Hospital

5.2. Maternal Health Related Risk Factors for Neonatal Sepsis

This study disclosed that antenatal care (ANC) visit was associated with neonatal sepsis; the majority of respondents, 35 (53.8) index mothers of cases and 99 (71.2%) index mothers of controls had received antenatal care (ANC) service for four and above visits during the index pregnancy. The study showed history of UTI/STIs during the index pregnancy was associated with neonatal sepsis; the proportion of index mother who had urinary tract infection or sexually transmitted infections (UTI/STIs) during the index pregnancy was higher among cases 30 (46.2%) compared to controls 28 (20.1%). Similarly, PROM was also associated with neonatal sepsis; the proportion of index mother who had premature rapture of membrane (PROM) was higher among cases 34 (52.3%) than controls 19 (13.7%). This study also revealed that MSAF was found to be associated with neonatal sepsis; the proportion of index mother who had MSAF was higher among cases 18 (27.7%) than controls 8 (5.8%). Likewise, intrapartum prophylactic antibiotics was associated with neonatal sepsis; twenty-four (36.9%) index mothers of cases and 15 (10.8%) index mothers of controls given intrapartum prophylactic antibiotics. In the same way, place of delivery was associated with neonatal sepsis; majorities, 50 (76.9%) cases ad 136 (97.8%) control neonates were delivered in the hospital. Likewise, mode of delivery was associated with neonatal sepsis; 43 (66.2%) cases and 116 (83.5%) of control neonates were delivered by spontaneous vaginal delivery.

As shown in table 3, all maternal health related variables were identified as a candidate variable for multivariate analysis with P-value less than 0.25 during bivariate analysis.

Table 3: Maternal health related risk factors of neonatal sepsis among index mothers of cases and controls attending MTUTH, BGSH and TGH, Southwest Ethiopia, 2018 (n=204).

Variables	Cases n=65 (%)	Controls n=139 (%)	COR (95% CI)	P-value
MSAF				
Yes	18 (27.7)	8 (5.8)	6.271 (2.557, 15.379)	< 0.001**
No	47 (72.3)	131 (94.2)	1	
Intrapartum Fever				
Yes	26 (40)	22 (15.8)	3.545 (1.808, 6.953)	<0.001**
No	39 (60)	117 (84.2)	1	
History of UTI/STIs				
Yes	30 (46.2)	28 (20.1)	3.398 (1.792, 6.444)	< 0.001**
No	35 (53.8)	111 (79.9)	1	
PROM				
Yes	34 (52.3)	19 (13.7)	6.927(3.487, 13.76)	<0.001**
No	31 (47.7)	120 (86.3)	1	
ANC follow up				
1-3 ANC follow up	30 (46.2)	40 (28.8)	2.121 (1.152, 3.906)	0.016*
4+ ANC follow up	35 (53.8)	99 (71.2)	1	
Intrapartum antibiotics				
Yes	24 (36.9)	15 (10.8)	4.839 (2.319, 10.096)	< 0.001**
No	41 (63.1)	124 (89.2)	1	
Place of delivery				
Health center	15 (23.1)	3 (2.2)	13.6 (3.776, 48.977)	< 0.001**
Hospital	50 (76.9)	136 (97.8)	1	
Mode of delivery				
C/S	12 (18.5)	12 (8.6)	2.698 (1.126, 6.461)	0.026*
Instrumental	10 (15.4)	11 (7.9)	2.452 (0.972, 6.185)	0.057
SVD	43 (66.2)	116 (83.5)	1	

- ** Significant at α=1%, * Significant at α=5%
- MTUTH: Mizan-Tepi University Teaching Hospital, BGSH: Bonga Gebretsadik Shawo Hospital, TGH: Tepi General Hospital

5.3. Neonatal Health Related Risk Factors for Neonatal Sepsis

This study discovered that, gestational age was associated with neonatal sepsis; more than three quarters of cases, 51 (78.5%) and almost all control neonates, 135 (97.1%) delivered after 37 completed weeks of gestation (term pregnancy). Similarly, weight at birth was associated with neonatal sepsis; 47 (72.3%) cases and 129 (92.8%) of controls were delivered with normal weight at birth.

Likewise, APGAR (Appearance, Pulse rate, Grimacy, Activity and Respiration) score at first minute was associated with neonatal sepsis; the proportion of neonates who had APGAR score less than 7 at first minute was higher among cases 50 (76.9%) than controls 29 (20.9%). Correspondingly, APGAR score at fifth minute was associated with neonatal sepsis; the proportion of neonates who had APGAR score less than 7 at 5^{th} minute was higher among cases 31 (47.7%) compared with controls 15 (10.8%).

This study also showed that birth asphyxia, crying immediately after birth and resuscitation at birth were associated with neonatal sepsis; among cases, 38 (58.5%) had birth asphyxia, 36 (55.4%) were not cried after birth and 49 (75.4%) were resuscitated at birth, respectively.

In relation to types of resuscitation, the proportion of cases resuscitated at birth through suctioning of mouth and nose was higher among cases, 49 (75.4%) than controls, 34 (24.5%). Similarly, 24 (36.9%) and 11 (11.6%) of cases took oxygen via nasal catheter and mask, respectively.

As shown in table 4, all neonatal health related variables were identified as a candidate variable for multivariate analysis with P-value less than 0.25 during bivariate analysis.

Table 4: Neonatal health related risk factors of neonatal sepsis among cases and controls attending MTUTH, BGSH and TGH, Southwest Ethiopia, 2018 (n=204).

Variables	Cases n=65 (%)	Controls n=139 (%)	COR (95% CI)	P-value
Gestational age				
< 37 weeks	14 (21.5)	4 (2.9)	9.265 (2.913, 29.664)	0.001*
≥ 37 weeks	51 (78.5)	135 (97.1)	1	
Weight at birth				
Low Birth Weight	18 (27.7)	10 (7.2)	4.94 (2.128, 11.467)	< 0.001**
Normal Birth Weight	47 (72.3)	129 (92.8)	1	
APGAR score at 1st minute				
< 7	50 (76.9)	29 (20.9)	12.644 (6.233, 25.649)	< 0.001**
≥ 7	15 (23.1)	110 (79.1)	1	
APGAR score at 5th minute				
< 7	31 (47.7)	15 (10.8)	7.537 (3.655,15.545)	< 0.001**
≥ 7	34 (52.3)	124 (89.2)	1	
Birth asphyxia				
Yes	38 (58.5)	20 (14.4)	8.374 (4.226, 16.594)	< 0.001**
No	27 (41.5)	119 (85.6)	1	
Crying immediately after birth				
No	36 (55.4)	18 (12.9)	8.345 (4.161, 16.736)	< 0.001**
Yes	29 (44.6)	121 (87.1)	1	
Resuscitation at birth				
Yes	49 (75.4)	34 (24.5)	9.458 (4.772, 18.746)	< 0.001**
No	16 (24.6)	105 (75.5)	1	
Types of resuscitation				
Suctioning of mouth & nose				
Yes	47 (72.3)	34 (24.5)	8.064 (4.139, 15.709)	< 0.001**
No	18 (27.7)	105 (75.5)	1	
Suctioning of trachea				
Yes	1 (1.5)	5 (3.6)	0.419 (0.048, 3.659)	0.431
No	64 (98.5)	134 (96.4)	1	
Oxygen via nasal catheter				
Yes	24 (36.9)	6 (4.3)	12.976 (4.965, 33.911)	< 0.001**
No	41 (63.1)	133 (95.7)	1	
Oxygen via mask				
Yes	11 (16.9)	2 (1.4)	13.954 (2.994, 65.036)	0.001*
No	54 (83.1)	137 (98.6)	1	

- ** Significant at α=1%, * Significant at α=5%
- MTUTH: Mizan-Tepi University Teaching Hospital, BGSH: Bonga Gebretsadik Shawo Hospital, TGH: Tepi General Hospital

5.4. Predictors of Neonatal Sepsis

In this study, bivariate analysis identified a total of seventeen candidate variables; two sociodemographic variables (sex and age of the neonate), eight maternal health related variables (MSAF, maternal intrapartum fever, history of UTI/STIs during the index pregnancy, PROM, ANC visit, intrapartum prophylactic antibiotics, place of delivery and mode of delivery) and seven neonatal health related variables (gestational age, weight at birth, APGAR score at first minute, APGAR score at fifth minute, birth asphyxia, crying immediately after birth and resuscitation at birth) for multivariable analysis.

After controlling for potential confounding as shown in table 5, this study identified seven independent predictors of neonatal sepsis.

Accordingly, this study disclosed that being male neonate was significantly associated with neonatal sepsis. Specifically, the odds of neonatal sepsis among male neonates were approximately 4 times higher as compared to female neonates [AOR=3.875, 95% CI (1.57, 9.569)].

The study revealed that meconium stained amniotic fluid (MSAF) showed statistically significant association with neonatal sepsis. The odds of neonatal sepsis among neonates born to index mothers who had meconium stained amniotic fluid were nearly 4 times higher as compared to those without meconium stained amniotic fluid [AOR=3.76, 95% CI (1.171, 12.077)].

History of urinary tract infection or sexually transmitted infections (UTI/STIs) during the index pregnancy also showed statistically significant association with neonatal sepsis. This study revealed that, the odds of neonatal sepsis among neonates born to mothers who had history of UTI/STIs during the index pregnancy were about 3 times higher than those neonates born to mothers who did not have history of UTI/STIs during the index pregnancy [AOR= 2.963, 95% CI (1.263, 6.947)].

Premature rapture of membrane (PROM) was significantly associated with neonatal sepsis. The study indicated that, the odds of neonatal sepsis among neonates born to mothers who had premature rapture of membrane was about 3.3 times higher as compared to mothers who did not have premature rapture of membrane [AOR= 3.315, 95% CI (1.34, 8.2)].

The study revealed that weight at birth also showed statistically significant association with neonatal sepsis. The odds of neonatal sepsis among low birth weight neonates was 3.4 times higher as compared to neonates with normal weight at birth [AOR= 3.433, 95% CI (1.044, 11.293)].

Low APGAR score after birth also showed statistically significant association with neonatal sepsis. Specifically, the odds of neonatal sepsis among neonates with APGAR score of less than seven at 5^{th} minute after birth was approximately four times higher as compared to those neonates with APGAR score equal to or greater than seven at 5^{th} minute after birth [AOR=3.738, 95% CI (1.28, 10.915)].

Resuscitation at birth was also showed statistically significant association with the risk of neonatal sepsis. The study indicated that, the odds of neonatal sepsis among neonates who were resuscitated at birth was approximately four times higher as compared to those neonates who did not resuscitated [AOR= 3.961, 95% CI (1.743, 9.0)].

Table 5: Predictors of Neonatal Sepsis among cases and controls attending MTUTH, BGSH and TGH, Southwest Ethiopia, 2018 (n=204).

Variables	Cases n=65 (%)	Controls n=139(%)	COR (95% CI)	P-value	AOR (95% CI)	P-value
Neonate's sex						
Male	48 (73.8)	64 (46)	3.309 (1.734, 6.313)	<.0.001**	3.875 (1.57, 9.569)	0.003*
Female	17 (26.2)	75 (54)	1		1	
MSAF						
Yes	18 (27.7)	8 (5.8)	6.271 (2.557, 15.379)	< 0.001**	3.760 (1.171, 12.077)	0.026*
No	47 (72.3)	131 (94.2)	1		1	
History of UTI/STIs						
Yes	30 (46.2)	28 (20.1)	3.398 (1.792, 6.444)	< 0.001**	2.963 (1.262, 6.947)	0.012*
No	35 (53.8)	111 (79.9)	1		1	
PROM						
Yes	34 (52.3)	19 (13.7)	6.927 (3.487, 13.76)	<0.001**	3.315 (1.340, 8.2)	0.009*
No	31 (47.7)	120 (86.3)	1		1	
Weight at birth						
Low Birth Weight	18 (27.7)	10 (7.2)	4.94 (2.128, 11.467)	< 0.001**	3.433 (1.044, 11.293)	0.042*
Normal Birth Weight	47 (72.3)	129 (92.8)	1		1	
APGAR score at 5th minute						
< 7	31 (47.7)	15 (10.8)	7.537 (3.655,15.545)	< 0.001**	3.738 (1.28, 10.92)	0.016*
≥ 7	34 (52.3)	124 (89.2)	1		1	
Resuscitation at birth						
Yes	49 (75.4)	34 (24.5)	9.458 (4.772, 18.746)	< 0.001**	3.961 (1.743, 9.0)	0.001*
No	16 (24.6)	105 (75.5)	1		1	

- Adjusted for age of neonate, intrapartum maternal fever, ANC visit, intrapartum prophylactic antibiotics, place of delivery, mode of delivery, gestational age and birth asphyxia.
- ** Significant at α=1%, * Significant at α=5%
- MTUTH: Mizan-Tepi University Teaching Hospital, BGSH: Bonga Gebretsadik Shawo Hospital, TGH: Tepi General Hospital

6. DISCUSSIONS

This study was aimed to assess risk factors for neonatal sepsis in order to contribute in tackling the burden of the problem and its consequences. Thus, this study revealed being male neonate, meconium stained amniotic fluid, history of maternal UTI/STIs during the index pregnancy, PROM, being low birth weight, low APGAR score at 5th minute and resuscitation at birth were independent positive predictors of neonatal sepsis.

According to this study, the odds of neonatal sepsis among male neonates was nearly four times higher as compared to female neonates. This finding is in line with other previous studies conducted in rural Ghana and Northern Carolina which showed being male as a significant risk factor (16,36). Even though the biological mechanism underlying why male babies are at higher risk than female is not clearly understood, early circumcision could be a possible contributing factor (16). It also implied that since the male sex was a risk factor for low birth weight and as this factor have also been associated with neonatal sepsis, then it is likely that the relationship between sex and neonatal sepsis is mediated by birth weight (41).

On the other hand, the usual male predominance in neonatal sepsis has suggested the possibility of sex–linked factor in host susceptibility. A gene located in X-chromosome and involved with function of the thymus or with synthesis of immunoglobulin has been postulated and female has double the number thus might possess a greater resistance to infection (41,48). Some people however, hold on to the myth that female neonates may have stronger immunity than males, but evidence supporting this entitlement is scanty (35).

Inconsistent with the finding of this study, being male neonate was protective of neonatal sepsis in findings of study done in Northern Carolina (36). The possible explanation for this dissimilarity could be the difference in the study subjects that index mothers included in the northern Carolina study were Group B Streptococcus (GBS) colonization negative in ANC screening whereas their status was unknown in this study.

In previous studies, maternal age of under 20 years was identified as a risk factor for neonatal sepsis (17,36). However, this study did not observe the association between maternal age and neonatal sepsis. The possible explanation for this discrepancy might be due to proportion of index mothers under the age of 20 years was relatively scanty for both cases and control neonates in the study area.

According to this study, the odds of neonatal sepsis among neonates born to index mothers who had MSAF were nearly 4 times higher as compared to those without MSAF. This is in agreement with findings from studies done in Ghana, Indonesia and Southern Mexico where turbid or foul smelling liquor or meconium stained amniotic fluid was found as a significant risk factor for neonatal sepsis (8,41,42). The implication this finding could be when there is meconium in amniotic fluid due to prolonged fetal hypoxia, advanced gestational age and other stress condition of fetus in the uterus, there is a greater chance of the fetus being born with low APGAR score, which frequently leads to neonatal sepsis (16,41,42). This might also imply that when the neonate is being delivered with low APGAR score from mothers with MSAF, perinatal asphyxia causes an immunological insult and resuscitation procedures following birth asphyxia tend to expose newborns to pathogenic microorganisms. Thus, it might possibly increase the likelihood of sepsis (26,28).

In this study, the odds of neonatal sepsis among neonates born to mothers who had history of UTI/STIs during the index pregnancy was three times higher compared to those without history of UTI/STIs during the index pregnancy. This finding is in line with studies done previously in Mekelle, northern Ethiopia, Saudi Arabia, Ghana and Bishoftu, Ethiopia which disclosed that maternal UTI/STIs during the index pregnancy as a significant risk factor (3,8,15,16). Since in this study, more than three quarters, 159 (77.9%); 43 (66.2%) cases and 116 (83.5%) control neonates were delivered by spontaneous vaginal delivery, it might imply that following the colonization of the birth canal by the infectious agent, maternal UTI or STIs especially if untreated during the third trimester pregnancy or labor, the baby is likely to aspirate some of these pathogenic microorganisms as it is being delivered through the birth canal that might increase the likelihood of sepsis in neonates (14–16).

Similarly, this study indicated that, the odds of neonatal sepsis among neonates born to mothers who had premature rapture of membrane (PROM) was about 3.3 times higher compared to mothers who did not have PROM. This is in agreement with previous studies done in Mekelle, Northern Ethiopia, Saudi Arabia, Mexico and Boston, USA which showed higher odds neonatal sepsis among neonates whose mother had PROM (8,15,42,43). The implication of this finding could be after early and prolonged rupture of membrane, there is an increased chance of ascending microorganisms from the birth canal into the amniotic sac resulted in fetal compromise as well as

asphyxia, which might predispose the neonates to higher risk infections and frequently lead to sepsis (8,16).

This study indicated that maternal health related factors; MSAF, History of UTI/STIs during the index pregnancy and PROM were independent risk factors for neonatal sepsis. From the total cases included in the study, 43 (66.2%) developed EONS and were found to be within the age range of below seven days. Of which 39.53%, 84.31% and 90.69% were born to mothers who had MSAF, UTI/STIs and PROM, respectively. These findings may support for the reason that maternal factors are often associated with early onset neonatal sepsis (3,5,6). Therefore, effect modification diagnostic was undertaken to check if the association between maternal factors and the risk of neonatal sepsis could possibly have modified by age of the neonate. However, this study did not observe age of the neonate as effect modifier.

Inconsistent with this study, previous studies pointed out that ANC follow up, intrapartum fever, intrapartum prophylactic antibiotics, place of delivery and mode of delivery were well established maternal health related risk factors (3,8,15,18,43,45–47). However, this study did not observe the association between those factors and neonatal sepsis. The possible explanation for this contradiction might be attributed to adequate perinatal care of mothers and service utilization in the study area.

This study also indicated that odds of neonatal sepsis among low birth weight neonates was about 3.4 times higher as compared to neonates with normal weight at birth. This is in line with findings from studies done in Tikur Anbessa Specialized hospital, Gondar University Hospital, Ghana and Indonesia which shown low birth weight as a significant risk factor (7,16,18,41). The implication of this finding could be when neonates are born with low birth weight, they might tend to have poor host defenses with low level mucosal antibody and might be managed by some invasive, monitoring procedures. Also there is the possibility of longer duration of stay in the hospital because of the existing difficulty to diagnose sepsis early and accurately due to lack of highly sensitive and specific markers (18,41). Furthermore, they are more likely to receive parenteral nutrition and intravenous medications (16). This might also imply that, when the neonates are managed extensively by invasive, monitoring procedures as well as exposed to unhygienic birth practices on top of immature host defense, it might predispose them to higher risk of infections compared to babies of normal weight who otherwise do not receive such therapy (5,28).

APGAR score also showed statistically significant association with neonatal sepsis. The odds of neonatal sepsis among neonates with APGAR score of less than seven at 5th minute after birth was approximately four times higher as compared to those neonates with APGAR score equal to or greater than seven at 5th minute after birth. This is in agreement with previous findings from studies done in Mekelle, northern Ethiopia, Indonesia and Tanzania indicated that low APGAR score as a significant risk factor (8,17,48). The implication of this finding could be neonates with low APGAR score tend to have poor adaptation to extra uterine life due to perinatal asphyxia experienced during labor (53). It might also imply when the neonate is being delivered with low APGAR score, perinatal asphyxia causes an immunological insult and resuscitation procedures following birth asphyxia tend to explore newborns to pathogenic microbes which increase the likelihood of sepsis (26,28). Based on the existing evidence, EONS is often due to organisms acquired prenatally from the maternal genital tract whereas LONS is more frequently caused by organisms acquired from nosocomial or community sources (31). Since, maternal risk factors such as MSAF and PROM were identified as independent predictors of neonatal sepsis in this study, there might be the possibility that the newborn develops early onset sepsis and resulted in low APGAR score at birth. Therefore, reverse causality is more likely so that further research is needed.

This study also indicated that the odds of neonatal sepsis among neonates who were resuscitated at birth was approximately four times higher compared to those neonates who did not. This finding is more or less comparable with findings from studies done in Ghana, Tanzania, and Southern Mexico which showed resuscitated at birth as a significant risk factor (16,17,42). The implication of this finding is that, because the lumen of the peripheral airways of the newborn is narrow, and respiratory secretions are plentiful than in adults, resuscitation may be indicated for neonates who may not have an established breathing pattern or those who may look asphyxiated at birth (17,26). When resuscitation procedure is done vigorously, it might cause bruises to the delicate and fragile mucous membrane and if done with unsterile equipment might also introduce pathogenic microorganisms to the neonates' not yet well developed immune system (54). Therefore, this might imply that, when the neonate is exposed to invasive resuscitation procedures, insufficient infection prevention practices such as not washing hands before handling newborns and use of unsterile equipment, might predispose them to higher risk of sepsis (5,28,46).

Previous studies pointed out that prematurity and birth asphyxia are independent predictors of neonatal sepsis (16,18,30,39,41,42,48). Unfortunately, this study did not observe the association

between gestational age or birth asphyxia and neonatal sepsis. The possible explanation for this dissimilarity might be due to the fact that the proportion of preterm babies among cases and controls was relatively insignificant in this study.

This study has its own strengths and limitations. Regarding strengths of this study, first, this study tried to avoid selection bias because this study employed precise definition of cases using clinical and hematological criteria, similar process of selection by using same inclusion-exclusion criteria, collected or pulled data from multiple hospitals and case-control selection done by other than interviewers. The second strength of this study is that it utilized primary data and applied a stronger study design which is reasonably appropriate to measure risk factor. Third strength is that relatively it comprised of multiple risk factors. Unlike some previous studies which focused on a single category of risk factors, this study tried to incorporate socio-demographic, maternal and neonatal health related risk factors associated with neonatal sepsis. Fourthly, it recruited incident cases and non-hospitalized subjects for the study which prevents prevalence-incidence and berkson's bias.

Concerning limitations of this study, the first potential limitation is of recall bias. Because of the study design employed, maternal exposure assessment was done retrospectively, so that there was possibility of recall bias. Secondly, even though blood and/or cerebrospinal fluid (CSF) culture is a gold standard for the diagnosis of neonatal sepsis, this study used IMNCI clinical and other hematologic criteria for the selection of study subjects. In addition, since the study was undertaken in three different hospitals, diagnosis was made by different health care workers. Thus, these could possibility introduce information bias (misclassification of cases and controls). Third, this study did not assess the reverse causality.

7. CONCLUSION and RECOMMENDATION

7.1. Conclusion

In conclusion, this study has found socio-demographic, maternal and neonatal health related factors had contributed to the risk of neonatal sepsis. Being male neonate, meconium stained amniotic fluid, history of maternal UTI/STIs during the index pregnancy, premature rupture of membrane (PROM), low birth weight, low APGAR score at 5^{th} minute and resuscitation at birth were identified as independent positive predictors of neonatal sepsis.

This study has also witnessed that the onset of neonatal sepsis was higher in the first week of neonate's life.

On the other hand; maternal age, parity, marital status, maternal education, intrapartum maternal fever, antenatal care (ANC), intrapartum prophylactic antibiotics, place of delivery, mode of delivery, gestational age and birth asphyxia were not identified as a risk factors for neonatal sepsis.

7.2. Recommendation

Based on the findings of this study, the following recommendations are suggested.

To Mizan-Tepi University Teaching Hospital and Zonal Health Departments:

- ☑ MTUTH and ZHDs should strengthen screening of all pregnant women attending antenatal clinic for UTI and/or STIs and treatment if positive for.

To Study Hospitals and Health Professionals working:

- ☑ Study hospitals should strengthen screening of all pregnant women attending antenatal clinic for UTI and/or STIs and treatment if positive for.
- ☑ Health professionals working in the study hospitals should strengthen and demonstrate peri-natal aseptic care of newborns especially during provision of immediate newborn care and resuscitation at birth.

To researchers:

- ☑ Since this study is the first study in the study area, its scope was limited to public hospitals and did not assess reverse causality, further large scale research is recommended.

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ANNEXES

Annex 1: Questionnaire (English version)

Participant Information Sheet and Informed Consent Form:

Jimma University

Institute of Health

Faculty of Public Health

Department of Epidemiology

1. Date of data collection _____ / _____ / _____
2. Participant ID number: _____
3. Name of health facility: _____

My Name is _____. I am working as a data collector for the study being conducted in this health institution on the risk factors for neonatal sepsis among neonates in public hospitals by Abeje Kebede, who is studying for his Master's degree at Jimma University, Institute of Health, department of Epidemiology. I kindly request you to lend me your attention to explain you about the study and being selected as a study participant.

The study title: Risk factors for neonatal sepsis among neonates in public hospitals, Southwest Ethiopia: Unmatched case control study

Purpose of the study: the main objective of this study is to identify risk factors for neonatal sepsis in public hospitals of Southwest Ethiopia. Thus, the findings will be used as evidence and as input for the zonal health departments, regional health bureau, ministry of health and other partner organizations to address the problem and improve the health status of newborns by implementing appropriate interventions. Moreover, the aim of this study is to write a thesis as a partial requirement for the fulfillment of a Master's of public health degree in epidemiology for the principal investigator.

Procedure and duration: I am interviewing you using questionnaire to investigate the risk factor for neonatal sepsis. Therefore, provide me with pertinent data that is helpful the study. All of your

responses and procedures done are completely confidential. You are kindly requested to answer every question, but you may stop at any time you want to. However, your honest answers to these questions will help for better understanding of risk factors of neonatal sepsis in these vulnerable groups. The total time needed for answering the questions will be about 30 minutes.

Risks and benefits: The risk of participating in this study is almost none, but only taking 30 minutes from your time. There would not be direct payment for participating in this study.

Confidentiality: The information you provide us will be confidential. There is no information that is identifying in particular. The findings of the study are general for the study community and will not reflect anything particularly of individual persons. The questionnaire is coded to exclude showing names. No reference is made in oral or written reports that could link participants to the research.

Rights: Participation for this study is fully voluntary. You have the right to declare to participate or not in this study. If you decide to participate, you have the right to withdraw from the study at any time and this is not labeling you for any loss of benefits which you otherwise are entitled. You do not have to answer any question that you do not want to answer.

Contact address: If there are any questions or enquires any time about the study, please contact in this address: Abeje Kebede, Email: abejek2014@gmail.com or Mob. 0912-105096(Principal Investigator)

Do you agree to participate in the study? (encircle) 1. Yes 2. No

Signature of the participant _____

Signature of data collector_____

If respondent disagree, stop here.

Part One: Checklist for Diagnosis of Neonatal Sepsis

S. No	Questions	Response	Skip
IMNCI Clinical criteria for diagnosis of neonatal sepsis			
101	Convulsions	1. Yes 0. No	
102	Respiratory rate ≥ 60 breaths/min	1. Yes 0. No	
103	Severe chest in drawing	1. Yes 0. No	
104	Nasal flaring	1. Yes 0. No	
104	Grunting	1. Yes 0. No	
106	Bulging fontanels	1. Yes 0. No	
107	Pus draining from the ear	1. Yes 0. No	
108	Redness around umbilicus extending to the skin	1. Yes 0. No	
109	Temperature ≥37.5ºC or <35ºC	1. Yes 0. No	
110	Lethargic or unconscious	1. Yes 0. No	
111	Reduced movements	1. Yes 0. No	
112	Not able to feed	1. Yes 0. No	
113	Not attaching to breast	1. Yes 0. No	
114	Not sucking at all	1. Yes 0. No	
Laboratory Investigations			
115	Complete blood count (CBC)	1. Yes 0. No	If No, skip to Q121
116	Total leukocyte count	_____cells/mm^3	
117	Absolute neutrophil count	_____cells/mm^3	
118	I: T ratio	_____	
119	Platelet count	_____cells/mm^3	
120	ESR	_____ /1 hour	
121	Blood culture	1. Positive 2. Negative 3. Not available	

Part Two: Risk Assessment Questionnaire

S. No	Questions	Response	Skip
Sociodemographic Factors			
201	Neonatal sepsis status	1. Cases 0. Control	
202	Maternal age (in years)	_____	
203	Marital status	1. Married 2. Single 3. Widowed 4. Divorced 5. Other (specify) _____	
204	Number of childbirths including current birth	_____	
205	Religion	1. Orthodox 2. Muslim 3. Catholic 4. Protestant 5. Other (specify) _____	
206	Ethnicity	1. Amhara 2. Oromo 3. Bench 4. Kaffa 5. Other (specify) _____	
207	Educational level	1. No formal education 2. Primary 3. Secondary 4. College & above	
208	Occupation	1. House wife 2. Civil servant 3. Business woman 4. Daily laborer 5. Student 6. Other (specify) _____	
209	Average monthly income of the household in ETB	_____ ETB	
210	Age of the neonate (in days)	_____days	
211	Sex of the neonate	1. Male 0. Female	
Maternal Health Related Factors			
212	Did the amniotic fluid was foul smelling? (Meconium stained amniotic fluid)	1. Yes 0. No	
213	Did you have any fever during the time of this labor?	1. Yes 0. No	

214	Did you have any UTI/STI during the pregnancy of this neonate?	1. Yes 0. No	If No, skip to Q216
215	If yes, were you treated?	1. Yes 0. No	
216	Did you have any fluid leakage before the onset of labor? (PROM)	1. Yes 0. No	If No, skip to Q218
217	If yes, duration of rapture of membrane before onset of labor (in hours)	_____hours	
218	Did you visit health facility for ANC during your pregnancy for this neonate?	1. Yes 0. No	If No, skip to Q220
219	If yes, how many times did you receive antenatal care during your time of pregnancy for this neonate?	_____ visits	
220	Did you received antibiotics during your birth admission after labor started?	1. Yes 0. No	
221	Where did you gave birth to this neonate /Place of delivery	1. Hospital 2. Health center 3. Home	If home, skip to Q223
222	If the place of delivery is in hospital or health center, what was the type of delivery?	1. Spontaneous vaginal 1. Caesarean section 2. Instrumental	
Neonatal Health Related Factors (From Neonate's Records)			
223	Gestational age at birth in completed weeks	_____ weeks	
224	Weight at birth	_____ grams	
225	APGAR score at 1st minute	_____	
226	APGAR score at 5th minute	_____	
227	Birth asphyxia	1. Yes 0. No	
228	Did the neonate cries immediately after birth?	1. Yes 0. No	
229	Did the neonate resuscitated at birth?	1. Yes 0. No	
230	If yes, what type of resuscitation?	1. Suctioning (mouth & nose) 2. Tracheal suctioning 3. Oxygen via nasal catheter 4. Oxygen via mask 5. Mechanical ventilation	

Annex 2: Questionnaire (Amharic version)

በጅማ ዩኒቨርሲቲ

የጥናቱ ማብራሪያ የፍቃደኝነት መጠየቂያ እና መተማመኛ ቅጽ

መረጃዉ የተሰበሰበበት ቀን _____ / _____ / _____

የተሳታፊ መለያ ቁጥር: _____

የጤና ተቋሙ ስም: _____

ስሜ _____ ሲሆን በዚህ ጤና ተቋም ዉስጥ በጨቅላ ህፃናት ላይ የደም ብክለትን በሚያስከትሉ አጋላጭ ምክንያቶች ላይ ለሚሰራ ጥናት መረጃ ሰብሳቢ በመሆን እየሰራሁ እገኛለሁ። እባክዎ ስለ ጥናቱ ስጭር ማብራሪያ እንድሰጥዎ ቢተባበረኝ

የጥናቱ ዓላማ:- የዚህ ጥናት ዋነኛ ዓላማ በደቡብ ምዕራብ ኢትዮጵያ በሚገኙ የመንግስት ሆስፒታሎች ውስጥ ጨቅላ ህፃናትን ለደም ብክለት በሽታ የሚያጋልጡ አጋላጭ ምክንያቶችን መለየት ነው። ስለሆነም ግኝቶቹ ለክልል የጤና ቢሮ ለጤና ጥበቃ ሚኒስቴር እና ለሌሎች አጋር ድርጅቶች ችግሮን ለመፍታት እና ተገቢውን ጣልቃ ገብነቶች በመተግበር ጨቅላ ህፃናትን የጤና ሁኔታ ለማሻሻል እንደማስረጃ እና እንደግኝት ያገለግላሉ።

የመረጃ አሰባሰብ ሂደትና የሚወስደዉ ጊዜ:- ጨቅላ ህፃናትን ለደም ብክለት በሽታ የሚያጋልጡ አጋላጭ ምክንያቶችን መለየት ቃለመጠይቅ እያደረግሁ ነው። ስለዚህ ለጥናቱ ጠቃሚ መረጃን በመስጠት እንዲተባበረኝ እጠይቅዎታለሁ። ሁሉም የሚሰጧቸው መልሶች ሙሉበሙሉ ሚስጥራዊናቸው የተጠበቀ ነዉ። ሁሉንም ጥያቄዎች እንዲመልሱ በአክብሮት እጠይቅዎታለሁ ነገርግን በፈለጉት ጊዜ ማቆም ይችላሉ። ይሁን እንጂ ለነዚህ ጥያቄዎች የሚሰጡት ትክክለኛ መልስ ለእነዚህ ተጋላጭነት ሳላቸው ጨቅላ ህፃናት ውስጥ ለሚከሰተዉ የተጋላጭነት ምክንያቶች የበለጠ ለመረዳት ይረዳል። ጥያቄዎቹን ለመመለስ የሚፈጀዉ ጠቅላላ ጊዜ 30 ደቂቃ ይሆናል።

ስጋቶችና ጥቅሞች: - በዚህ ጥናት መሳተፍ ምንም ዓይነት ስጋጋ አያስከትልም ነገርግን ከእርስዎ ጊዜ 30 ደቂቃ ብቻ ነው የሚወስደው። በዚህ ጥናት ለመሳተፍ ቀጥተኛ ክፍያ አይኖርም።

የመረጃዉ ሚስጢራዊነት: - ለእኛ የሰጡን መረጃ በሚስጥር የሚያዝ ይሆናል። በተሰዩ ተሰዩቶ የሚታወቅ ምንም መረጃ የለም። የጥናቱ ግኝቶች በጥናቱ ዉስጥ ለሚሳተፉ ጠቅላላ እንጂ የግለሰብን ልዩነት የሚያንጸባርቅ አይደሉም። መጠይቁ የግለሰብ ስሞችን አያካትትም።

የተሳታፊ መብቶች: - በዚህ ጥናት መሳተፍ ሙሉ በሙሉ በፈቃደኝነት ላይ የተመሰረተ ነው። በዚህ ጥናት ውስጥ ስመሳተፍ ጠይም ሳስመሳተፍ የመወሰን መብት አለዎት። ስመሳተፍ ከወሰኑ በማንኛውም ጊዜ የማቋረጥ መብት አለዎት። መመለስ የማይፈልጉትን ማንኛውም ጥያቄ መልስ መስጠት የለብዎትም።

የማነጋገሪያ አድራሻ:- ስለጥናቱ ምንም ዓይነት ጥያቄ ካለዎት በዚህ አድራሻ መጠየቅ ይችላሉ፡ አበጀ አበደ (ዋና ተመራማሪ) ሞባይል ስልክ ቁጥር 0912-105096 ጠይም ኢሜል: abejek2014@gmail.com

በጥናቱ ስመሳተፍ ይስማማሉ? [1] አዎን እስማማለሁ [2] አልስማማም

የተሳተፈዋ ፈርማ _____

የመረጃ ሰብሳቢዋ/ዉ. ፈርማ _____

መልስ ሰጪው ካልተስማሙ አመስግነዉ. እዚህ ላይ ያቁሙ

ክፍል ሁለት፡ የተጋላጭነት ዳሰሳ መጠይቅ

ተ.ቁ	ጥያቄዎች	ምላሽ	ስለፍ
ማህበራዊ እና ኢኮኖሚያዊ የተጋላጭነት ዳሰሳ			
201	የጨቅላ ህፃን የደም ብክለት	1. አለ 0. የለም	
202	የሰድሚሽ/ዎ ስንት ነዉ (በዓመታት)	_____ዓመት	
203	የጋብቻ ሁኔታሽ/ዎ	1. ያገባ 2. ያላገባ 3. መበለት 4. የተፋታ 5. ሌላ (ይግለጹ) _____	
204	የአሁኑን ጨምሮ ስንት ልጅ ወልደሻል/ዋል	_____	
205	ሃይማኖትሽ/ዎ	1. ኦርቶዶክስ 2. ሙስሊም 3. ካቶሊክ 4. ፕሮቴስታንት 5. ሌላ (ይግለጹ) _____	
206	ብሔረሰብሽ/ዎ	1. አማራ 2. ኦሮሞ 3. ቤንች 4. ከፋ 5. ሌላ (ይግለጹ) _____	
207	የትምህርት ደረጃሽ/ዎ	1. መደበኛ ትምህርት አልተማርኩም 2. የመጀመሪያ ደረጃ ትምህርት 3. የሁለተኛ ደረጃ ትምህርት 4. ኮሌጅ እና ከዚያ በላይ	
208	የሥራ ሁኔታሽ/ዎ	1. የቤት እመቤት 2. የመንግስት ሰራተኛ 3. ነጋዴ 4. የቀን ሰራተኛ 5. ተማሪ 6. ሌላ (ይግለጹ) _____	
209	የቤተሰብሽ/ዎ ወርሃዊ ገቢ	_____ ብር	
210	የህፃኑ/ዋ ዕድሜ (በቀናት)	_____ ቀናት	
211	የህፃኑ/ዋ ፃታ	1. ወንድ 0. ሴት	
የእናቶችን ጤና ያማከለ የተጋላጭነት ዳሰሳ			
212	በወሊድ ወቅት የሽርት ዉሃዉ መጥፎ ሽታ ነበረዉ?	1. አዎ 0. አልነበረዉም	
213	በምጥሽ ወቅት ትኩሳት ነበረሽ?	1. አዎ 0. አልነበረኝም	

214	በዚህ እርግዝና ወቅት የሽንት ቱቦ ኢንፌክሽን ወይም የአባላዘር በሽታ ታመሽ ነበር?	1. አዎ 0. አልታመምኩም	ወደ ጥ.ቁ 216 እለፍ/ፊ
215	መልሽስ አዎ ከሆነ ታክመሽ ነበር?	1. አዎ 0. አልታከምኩም	
216	ምጥሽ ከመጀመሪ በፊት የሽርት ዉሃ ፈሶ ነበር?	1. አዎ 0. አልፈሰሰም	ወደ ጥ.ቁ 218 እለፍ/ፊ
217	መልሽስ አዎ ከሆነ ስምን ያህል ጊዜ ወይም ሰዓታት ፈሰሰሽ?	_____ ሰዓታት	
218	በጤና ተቋም የእርግዝናና ክትትል ታደርጊ ነበር?	1. አዎ 0. አድርጌ አላዉቅም	ወደ ጥ.ቁ 220 እለፍ/ፊ
219	መልሽስ አዎ ከሆነ ስምን ያህል ጊዜ የእርግዝናና ክትትል አደረግሽ?	_____	
220	ምጥ ከጀመረሽ በሓላ መድሐኒት ተሰጥቶሽ ነበር?	1. አዎ 0. አልተሰጠኝም	
221	ደህንን ህፃን የት ነዉ የወለሽዉ?	1. ሆስፒተል 2. ጤና ጣቢያ 3. እቤት ዉስጥ	ወደ ጥ.ቁ 223 እለፍ/ፊ
222	ደህንን ህፃን በምን ዓይነት መንገድ ነዉ የወለሽዉ?	1. በተፈጥሮዋዊ መንገድ 2. በኦፕሬሽን 3. በመሳሪያ እርዳታ	

DECLARATION

I, the undersigned, declare that this thesis is my original work and has not been presented for a degree in this or any other university and all sources of materials used for the thesis have been fully acknowledged and the comments given during defense were fully accommodated.

Name: Abeje Kebede (BSc)

Signature: _____

Name of the institution: Jimma University

Date of submission: _____

Approval of Internal examiner:

This thesis has been submitted with my approval as internal examiner.

Name: _____

Signature: _____ Date: _____

Approval of Chairperson:

This thesis has been submitted with my approval as chairperson.

Name: _____

Signature: _____ Date: _____