THE ASSOCIATION BETWEEN ABO/ RH BLOOD GROUP DISTRIBUTION AND INCIDENCE OF PEPTIC ULCER DISEASE AT TIKUR ANBESSA SPECIALIZED HOSPITAL, ADDIS ABABA, ETHIOPIA

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The association between ABO/ Rh blood group distribution and incidence of peptic ulcer disease at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia

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This is to clarify that thesis prepared by Yonas Teshome entitled, “The association between ABO/Rh blood group distribution and incidence of peptic ulcer disease at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia” is submitted in partial fulfilment of the Requirement for Degree of Master of Sciences in Medical Physiology, complies with the regulations of the university and meet the accepted standards with respect to the originality and quality.

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ABBREVIATIONS

AAU........................... Addis Ababa University
CCK.............................Cholecystokinin
DU...............................Duodenal Ulcer
ECL..............................Enterocromaffin like cells
Fuc .............................Fucose
Gal.............................Galactose
GalNAc..........................N-acetylgalactosamine
GI...............................Gastro-intestinal
GU...............................Gastric Ulcer
H. Pylori.......................Helicobacter Pylori
NSAID..........................Non-Steroidal Anti-Inflammatory Drugs
PUD.............................Peptic Ulcer Disease
PI...............................Principal Investigator
PGE$_2$..........................Prostaglandin E$_2$
RBC ............................Red Blood Cell
SPSS ..........................Statistical Package for the Social Science
TASH.........................Tikur Anbessa Specialized Hospital
ABSTRACT

Background: Peptic ulcer disease affects around 5-10% of the general population worldwide and is an important cause of morbidity and mortality throughout the world. Currently researches have shown that there is association between ABO/RH blood group and peptic ulcer disease. However, such studies are limited in Ethiopia.

Objective: The aim of this study was to assess the association between ABO/RH blood group distribution and the incidence of peptic ulcer disease at Tikur Anbessa Specialized Hospital.

Methods: Hospital based cross-sectional study was conducted to assess the association between ABO/ RH blood group distribution and other factors with incidence of peptic ulcer disease at Tikur Anbessa Specialized Hospital (TASH). Endoscopically diagnosed Peptic Ulcer Disease patients were selected for the test; non-peptic ulcer disease patients, hospital staffs and students were recruited as a control group. Blood was collected from study participants and their ABO/ Rh blood type were identified and recorded. Structured questionnaire was also used to collect other relevant data. The data were entered into Epi Data software version 3.1 and analyzed using SPSS version 23.

Result: A total of 126 (89 male and 37 female; mean age: 39.10 year) subjects were enrolled in the study. The ABO blood group frequency in peptic ulcer patients was 19.04% (12/63), 11.11% (7/63), 11.11% (7/63) and 50.79% (32/63) for blood group A, B, AB and O respectively, while for control groups it was 25.39% (16/63), 23.80% (15/63), 12.69% (8/63) and 38.09% (24/63) for blood group A, B, AB and O respectively. Rh positivity was found in 90.48% of peptic ulcer disease patients and 95.34% of controls. Among peptic ulcer disease patients 34.1% (22/63) had Gastric Ulcer, and 65.9 % (41/63) had Duodenal Ulcer. Patients with blood group O was found to have higher percent (56%) of H. pylori infection than other blood groups. There was statistically significant association between sex \( p=0.001, \text{AOR (95\% CI) 4.21(3.30, 7.50)} \), use of NSAID \( p= 0.001, \text{AOR (95\% 2.1 (0.41, 0.39)} \), smoking cigarette \( p=0.014, \text{AOR (95\%) 7.32 (1.48, 36.03)} \) alcohol consumption \( p=0.028, \text{AOR (95\%) 2.78 (1.11, 6.97)} \) and peptic ulcer disease.

Conclusion: Peptic ulcer disease was more prevalent among patients with blood group O than other blood group types. Additionally, blood group O had higher percent of H. Pylori infection than other blood group types. Use of NSAIDs, Smoking, and Alcohol consumption were risk factors for peptic ulcer disease.

Key words: ABO/Rh blood group, Peptic Ulcer Disease, Gastric Ulcer, Duodenal Ulcer, NSAIDs
1. INTRODUCTION

1.1 Background

It was Karl Landsteiner who discovered ABO blood group system in 1901 (Hult, 2013). Blood group is usually restricted to blood cell surface antigens and generally to red blood cell surface antigens. There are about 270 authenticated blood group antigens which fall into one of 26 blood group systems (Hult, 2013).

The ABO blood group system is the widely used type and is encoded by a gene located on the long arm of chromosome nine (Danniel, 2002). This gene control formation of A and B antigens on the surface of the red blood cells (RBCs) which are carbohydrate molecules built stepwise from saccharides such as galactosamine (GalNAc), glucosamine (GlcNAc), fucose (Fuc), galactose (Gal), and glucose (Glc) (Hult, 2013). This carbohydrate molecules are synthesized by the sequential action of the ABO glycosyltransferases that catalyze the addition of specific monosaccharides (galactosamine or galactose) on a common precursor H antigen to form distinct A and B antigens. Individuals with blood group O express only the basic H antigen (Zhang, 2012).

Therefore, Red blood cells (RBCs) of type A have the A antigen on their surfaces, those of type B have antigen B, type AB red cells bear both antigens, while type O cells bear neither antigen. The antigens are also present in the secretory fluids such as saliva, sweat and semen in the majority of humans (Thrumiaya et al., 2017). The plasma of blood group A has anti-B, blood group B has anti-A, blood group AB has no anti- body and blood group O has both anti-A and anti-B. The antibodies can be detected by the age of three month and reach the maximum level at the age of 5 to 10 years (Svensson, 2011).

The antibodies are not induced by exposure to RBCs carrying the foreign antigen. They are suggested to be stimulated by microbial structures in the normal gut flora, which are very similar to the carbohydrate blood group antigens. Without the exposure to normal gastrointestinal microbes via diet, none or very low levels ABO antibodies were produced (Hult, 2013).

The Rh blood groups are so named because of one of the eight Rh antigens (agglutinogen D), which was originally identified in Rhesus monkeys. Later the same antigen was discovered in human beings. The Rh negative blood type is relatively uncommon, representing less than 15% of the population (Wagner and Flegel 2004).
The so-called "natural" antibodies to Rh do not exist in humans, as they do for the A and B antigens. However, Rh+ cells infused into an Rh negative recipient can give rise to a strong antibody response (Danniel, 2002). Unlike the A and B antigens, the Rh antigens are located only on red blood cells. Therefore, while this antigens are important for blood transfusion, they do not normally play a role in organ transplantation (Svensson, 2011). But their roles for RBCs are preventing aggregation and adhesion to endothelial cells, protecting against mechanical damage and pathogen invasion which makes them reasons for the association ABO blood group with diseases (Hult, 2013).

Many researchs are indicating the association of ABO blood group with different types of diseases. Accordingly, blood group A was associated with the development of head, neck and gastric cancers (Kakava et al., 2016), while blood groups B and AB with tuberculosis (Rao et al., 2012). Blood O blood was said to have protective nature from venous thromboembolism (Franchini et al., 2015, Zhong et al., 2015), pancreatic cancer (Zhang et al., 2014; Laufey et al., 2009), severe malaria (Panda et al., 2011) while it is found to be prone for cholera and peptic ulcer disease (Anstee, 2017).
1.2 Statement of the problem

Peptic Ulcer Disease (PUD) is a very prevalent condition that affects around 5-10% of the general population worldwide (Lauret et al., 2015). It is an important cause of morbidity and mortality throughout the world affecting the lives of millions of people in their everyday life. In the United States, approximately four million people have peptic ulcers (duodenal and gastric), and 350,000 new cases are diagnosed each year (Schwartz et al., 2010). Around 180,000 patients are hospitalized yearly, and about 5000 people die each year as a result of peptic ulcer disease (Aro et al., 2006).

The costs of PUD, including lost work time and productivity, are estimated to be above $9 billion per year in the United States. In 1998, approximately 1.5% of all Medicare hospital costs were spent treating PUD (Schwartz et al., 2010). Poor socio-economic conditions and lack of awareness about the disease, increases the burden of peptic ulcer disease much greater. In Bangladesh it is a major cause of morbidity and significant cause of mortality having a point prevalence of approximately 15% (DU-11.98% and GU-3.58%) (Sadiqque, 2014).

If an early treatment is not initiated and peptic ulcer disease is not cured, the ulcer can perforate and become a complicated surgical case. Gastric perforation is found to be common problem in Irrua, Nigeria (Dongo et al., 2017) and in Tikur Anbessa specialized hospital, Ethiopia, perforated peptic ulcer disease is found to be the 3rd cause of surgery for acute abdomen following appendicitis and intestinal obstruction (Ersumo et al., 2004).

Through early detections, simple life style modifications and with the help of modern medical treatment, the problem of peptic ulcer disease can be largely controlled and patients with peptic ulcers can lead a prolonged and healthy life. However, researches done in relation to this problem were very limited in Ethiopia. Thus this research provides valuable information about the association of the disease with blood group distribution and help to create awareness for the people so that they can have preventive means.
1.3 Significance of the study

The relationship between blood group types and peptic ulcer disease has been widely evaluated in the world, but there is no published study on the association of ABO/RH blood group distribution and peptic ulcer disease in Ethiopia. Thus, this study was aimed to evaluate the association of peptic ulcer disease with ABO blood group distribution in TASH patients.

1.4. Hypothesis of the study

**Null hypothesis:** there is no association between ABO/Rh blood group distribution and incidence of peptic ulcer disease in Tikur Anbessa Specialized Hospital.

**Alternative Hypothesis:** there is association between ABO/Rh blood group distribution and incidence of peptic ulcer disease (PUD) in Tikur Anbessa Specialized Hospital.
LITERATURE REVIEW

There are abundant evidence that blood groups play a role in the susceptibility or resistance to various infectious and non-infectious diseases (Yang et al., 2014; Wang et al., 2012; Su et al., 2001). One of the arguments used to reinforce the role of these molecules is the higher expression of the ABO carbohydrates in body secretions and tissues that have contact with the environment such as in the skin and in mucous membranes of respiratory and gastrointestinal tracts (Hult, 2013). There are evidences that demonstrated the importance of the H antigen, expressed in gastric mucous membrane, to the attachment of Helicobacter pylori which is identified to be the major cause of peptic ulcer disease (Mattos et al., 2004).

2.1 Peptic Ulcer Disease

Peptic ulcer is a sore in the lining of gastric or duodenal mucosa which generally range between 3 mm and several centimeters in diameter (Baltimore, 2013). Under normal condition, a physiologic balance exists between gastric acid secretion and gastric and duodenal mucosal defense systems. The imbalance between defensive factors which include the function of mucus-bicarbonate barrier, prostaglandins, mucosal blood flow, cell renewal and migration, antioxidants, and aggressive factors such as hydrochloric acid, pepsin, refluxed bile, leukotrienes leads to formation of peptic ulcer (Amandeep et al., 2012).

2.2 Pathophysiology of peptic ulcer disease

The mechanism by which the defensive factors protect the stomach from digesting itself is by a gel layer that consists mucus and bicarbonate which is secreted by mucus neck cells in the stomach. This gel layer is impermeable to aggressive factors such as acid and pepsin under normal condition. But during injury, additional mechanisms help to prevent acid and pepsin from entering the epithelial cells. For example, increased blood flow removes acid that diffuses through the damaged mucosa and provides adequate bicarbonate level in the gel layer superficially to epithelial cells. Additionally, epithelial cells regulate intracellular pH by removing excess of hydrogen ions through the ion pumps in the basolateral cell membrane (Zatorski, 2017).

2.2.1 Defense Mechanisms

2.2.1.1 Superficial Gel Layer

The surface of gastric mucosa is covered by a layer formed from mucus gel and bicarbonate which will be the first line of defense for gastric mucosa. The gel layer has the ability to protect the stomach from proteolytic actions of a protein digesting enzyme pepsin on gastric epithelium (Schwartz’s et al., 2010). Gastro intestinal (GI) hormones, such as gastrin, secretin, and
prostaglandins, play a role in regulation of gastric mucus secretion. The secretion of bicarbonate into the mucus gel layer is also essential to maintain a pH gradient at the epithelial surface (Baltimore, 2013). Various factors such as prostaglandins, luminal acid, and melatonin can stimulate bicarbonate secretion. Therefore this acid neutralizing base is simultaneously produced with mucus to protect the stomach from its own hydrochloric acid. But, when the protective barrier breaks down during pathological events or under influence of injuring agents, other protective mechanisms are activated. They include intracellular acid neutralization, rapid epithelium renewal, and maintenance of mucosal blood flow (Zatorski, 2017).

### 2.2.1.2 Prostaglandins

Prostaglandins are constantly produced in the gastric mucosa especially Prostaglandin E$_2$ (PGE$_2$), which play a crucial role in the maintenance of mucosal integrity and protection against damaging factors. It has been proved that prostaglandins interact with almost all the mucosal defense mechanisms. Therefore, they have potential to reduce acid output, stimulate mucus and bicarbonate production, as well as increase mucosal blood flow (Baltimore, 2013). Prostaglandins are also responsible for acceleration of epithelial restitution (rapid replacement of sloughed or denuded surface epithelial cells by migration of adjacent cells) and mucosal healing (Wallace, 2000).

### 2.2.1.3 Epithelial Cells

The Epithelial cells have hydrophobic phospholipids on the surface which can repel water soluble acids and reduces mucosal damage by the acid. Furthermore, epithelial cells produce antimicrobial cationic peptides such as cathelicidins and beta defensins to prevent the stomach mucosa from bacterial colonization. Therefore, cationic peptides add anti-microbial character to the innate defensive system with mucosal gel layer, an acid neutralizer bicarbonate and acid repulsive epithelial cells hydrophobic phospholipids (Zatorski, 2017).

### 2.2.1.4 Mucosal Cell Renewal

There are mucosal progenitor cells which are responsible for a continuous surface epithelial cells renewal and the process of complete epithelial renewal takes about 3–7 days, while the restitution of epithelium after exposure to injuring agents occurs within minutes and depends on migration of preserved cells from the neck area of gastric glands (Schwartz’s et al., 2010). Furthermore,
prostaglandins (PGE$_2$) and gastrin interact with epidermal growth factor receptor EGFR and stimulate cell proliferation and renewal of gastric mucosa.

### 2.2.1.5 Mucosal Blood Flow

Mucosal blood flow plays a crucial role in maintaining a healthy mucosa, providing nutrients and oxygen and to remove toxic metabolites from gastric mucosa. Back-diffused acid is buffered and rapidly removed by the rich blood supply. When there is back diffusion of acid because of damage to mucosal gel layer by different factors, there is a protective increase in mucosal blood flow. If this protective response is blocked, gross ulceration can occur. The important mediators of these protective mechanisms include prostaglandins and nitric oxide (NO) produced by endothelial cells located in small vessels of the stomach. These two potent vasodilators protect the gastric mucosa against a detrimental effect of restricted blood flow (Zatorski, 2017) (Schwartz’s et al., 2010).

### 2.2.2 Aggressive Agents: Gastric Acid and Pepsin

Four types of cells are involved in the process of regulation of gastric acid secretion. These are G cells which secrete gastrin, D cells which secrete somatostatin, enterochromaffin-like cells which secretes histamine and parietal cells. Parietal cells are gastric acid secreting cells by a proton pump H$^+$/K$^+$-ATPase (Amandee et al., 2012). Gastrin, acetylcholine, and histamine stimulate the parietal cell to secrete hydrochloric acid. A large part of the acid-stimulatory effects of both acetylcholine and gastrin are mediated by histamine released from mucosal ECL cells. The mucosal D cell, which releases somatostatin, is also an important regulator of acid secretion. Somatostatin inhibits histamine release from ECL cells and gastrin release from G cells. The function of D cells is inhibited by Helicobacter pylori infection, and this leads to an exaggerated acid secretory response (Schwartz’s et al., 2010).

Gastric acid is a fluid formed in the stomach, which plays an important role in digestion of proteins by activating a protein digesting enzyme pepsin. The pH of gastric acid is 1.5–3.5 in the stomach lumen. The chief cells synthesize and release the proenzyme pepsinogen, which will be activated by the acid into pepsin. Because of its relatively high molecular size, pepsin cannot permeate the continuous adherent mucus layer within a physiologically meaningful time scale. Nevertheless, luminal pepsin at acidic pH slowly hydrolyzes and erodes the mucus layer. At the same time, mucus loss is balanced by a new. H. pylori infection and use of non-steroidal anti-inflammatory drugs are the predominant causes of peptic ulcer disease (Zatorski, 2017).
2.3 Risk actors of Peptic Ulcer Disease

2.3.1. Helicobacter pylori and Peptic Ulcer Disease

Helicobacter pylori is well recognized as major cause of gastro-intestinal diseases. The bacteria have evolved several mechanisms to evade primary host defenses such as acidity and peristalsis in order to establish persistent infection within the stomach (Tanih et al., 2010). In the first step, the bacteria disrupt the antimicrobial activity of gastric acid barrier, enter the mucous layer, and adapt to environmental conditions of gastric mucus. In the next step, H. pylori adhere to the host gastric mucosa, and this event triggers the expression of several bacterial genes, which allows the pathogen to persist in this environment and avoid clearance caused by peristaltic movements or shedding of the mucous layer. One of the important factors in H. pylori colonization is enzyme urease, which is able to convert urea into ammonia and carbon dioxide in order to elevate the pH to neutral by forming an acid-neutralizing cloud of ammonia near bacterium and thus protecting the bacterial cell from gastric acid (Zatorski, 2017).

After safe colonization, using its hemostatic factors and cytotoxins (e.g., protease, lipases and phospholipase A and vacuolating cytotoxin) the bacteria causes injury (Mustafa et al., 2015). Protease and lipase produced are responsible for degradation of gastric mucus and cell injury from back infusion of gastric acid. Furthermore, Helicobacter pylori disrupts the function of D cells which are majorly involved in regulation of acid secretion by secreting somatostatin to inhibits histamine release from ECL cells and gastrin release from G cells when there is excessive acid secretion. This leads to an exaggerated acid secretory response on degraded gastric mucus and causes peptic ulcer disease (Amandeep et al., 2012).

Because of this studies have confirmed that H.pylori infection was present in more than 90% of patients with duodenal ulcers and about 85% of those with gastric ulcers (Mustafa et al., 2015). In Yirgalem Hospital, south Ethiopia, Helicobacter pylori infection was detected in 93% of 174 patients with a peptic ulcer compared with 63% of 116 patients with normal findings (Henriksen et al., 1999).

In the same way a research done in Hong Kong shows a direct association between H. pylori infection and both duodenal ulcer (OR $\frac{1}{4}$ 15.87, 95% CI: 10.60–23.76, $P < 0.001$) and gastric ulcer (OR $\frac{1}{4}$ 3.12, 95% CI: 2.15–4.53, $P < 0.001$) (Xi et al., 2005). Therefore H pylori infection is listed among the main risk factors for PUD (OR 4.3 (95% CI 2.2; 8.3)), with tobacco smoking (3.8 (1.7; 9.8)), and NSAIDs (3.0 (1.4; 6.6)) (Rosenstock et al., 2003). Researchers also point out that the infectivity of the bacteria is associated with different factors that can enhance the bacterial pathogenicity.
2.3.1.1 Factors that can increase the H. pylori infection

There are many factors that can increase the infectivity H. pylori. Among these; tobacco smoking, chat chewing and drinking alcohol are the major one. According to a research done in Jigjiga University, the prevalence of H. pylori infection among khat chewers, drunkers and smokers were 72.4%, 74.1% and 79.4% respectively and tobacco smoking showed significant association with H. pylori infection (Alebie et al., 2016).

Blood group O had showed significant association with H. pylori infection in many researches. One of this research was a research done in Japan. This research indicate that the rate of H. pylori infection was significantly higher for type O blood compared to other blood types. In addition, the odds ratio for H. pylori infection adjusted for age, sex, and smoking and drinking habits was also significantly higher for type O blood compared to other blood types (Inoue et al., 2014). another study also demonstrated higher incidence of H. pylori among patients of blood group O with gastric ulcer (46.7%) as compared with A (20%), B (13.3%) and AB (3.3%) blood groups showing a statistically significant differences (Baqir et al., 2016). In contrary a research among Kosovo blood donors not found a significant relationship between infection with H. pylori and ABO/Rh blood group (Zhubi et al., 2011). Similarly, in Ethiopia ABO/Rh blood group was not found to be associated with H. pylori infection (Tadesse et al., 2014; Moges et al., 2006).

Because H. pylori infection is the major cause of peptic ulcer disease, it will be better if patients with Gastritis start H. pylori eradication therapy when a confirmatory test is not available but patients with dyspepsia who are over 40 years of age should undergo Endoscopy (EGD) for initial work up (Ayana et al., 2014). Maintaining hygiene is very necessary to reduce the transmission of H. pylori because studies have described the gastro-oral, oral-oral and faeco-oral he bacteria (Rastogi et al., 2014).

2.3.2. Non-steroidal Anti-inflammatory Drugs (NSAIDs)

NSAIDs interfere with mucosal defense in the stomach by direct toxic effects, diminishing the hydrophobicity of gastric mucus, cyclooxygenase inhibition and depletion of endogenous prostaglandins (Mustafa et al., 2015). Prostaglandins are produced from a precursor arachidonic acid which is catalyzed by the two cyclo-oxygenase isoenzymes, cyclo-oxygenase-1 and cyclo-oxygenase-2. The gene for cyclo-oxygenase-1, the housekeeping enzyme, maintains the homeostasis of organs. Cyclo-oxygenase-2, the inflammatory enzyme, is inducible. Literature suggests that the anti-inflammatory properties of NSAIDs are mediated through inhibition of
cyclo-oxygenase-2, and adverse effects, such as gastric and duodenal ulceration, occur as a result of effects on the constitutively expressed cyclo-oxygenase-1 (Venerito et al., 2010).

Therefore when NSAIDs block the cyclooxygenases; there is suppression of a number of prostaglandin-related protective functions. For instance, Administration of NSAIDs results in cyclooxygenase-dependent inhibition of bicarbonate secretion, which also inevitably impairs mucosal defense mechanism. Adequate blood flow in mucosal circulation will not be maintained when there is reduced prostaglandin production because of inhibitory effect of NSAIDs. This makes NSAIDs the second most common cause of peptic ulcer disease (Zatorski, 2017).

The prevalence of peptic ulcer in chronic NSAID users is about 25% (15% gastric and 10% duodenal). More than half of patients who present with peptic ulcer hemorrhage or perforation report the recent use of NSAIDs (Schwartz’s et al., 2010). Gastro-duodenal ulceration and bleeding are the major limitations to the use of non-steroidal anti-inflammatory drugs (NSAIDs) (Wallace, 2000). Therefore, in very high risk patients for both gastrointestinal and cardiovascular complications NSAID therapy should be avoided altogether (Venerito et al., 2010) or there should be concomitant use of Misoprostol. Because misoprostol found to reduce the risk of clinical ulcer complications (Rostom et al., 2002).

### 2.3.3. Smoking and peptic ulcer disease

Cigarette smoking is the most preventable risk factor for human health. According to a WHO report, 1.3 billion individuals are active smokers worldwide and smoking kills 6 million individuals each year; eventually, half of these smokers die due to smoking-related diseases (Li et al., 2014). Studies suggest that smokers are about twice as likely to develop peptic ulcer disease as nonsmokers (Schwartz’s et al., 2010). A research done in Sweden also states that smoking cigarette increases the chance of acquiring peptic ulcer disease three times (Aro et al., 2006).

Cigarette smoking increases gastric acid secretion in the stomach (Debas et al., 1971). This increased gastric acid secretion is mediated through the stimulation of H2-receptor by histamine release and due to the increase of the functional parietal cell volume or secretory capacity in smokers. Smoking also stimulate pepsinogen secretion by increasing chief cell number or with an enhancement of their secretory capacity (Maity et al., 2003). Cigarette smoking and nicotine reduce the level of circulating epidermal growth factor (EGF) and decrease the secretion of EGF from the salivary gland, which are necessary for gastric mucosal cell renewal. To this end cigarette smoke increases apoptosis but decreased cell proliferation, blood vessel formation (reduce
angiogenesis in the gastric mucosa through inhibition of nitric oxide synthesis thereby arresting cell renewal process) and mucus synthesis in the GI mucosa (L. Zhang et al., 2012).

2.3.4. Alcohol and Peptic Ulcer Disease

Alcohol at low concentrations (5%) may modestly stimulate gastric acid secretions principally by stimulating the secretion of gastrin and to a lesser extent by a direct effect on the parietal cells. To the contrary, an alcohol concentration of higher than 5% has no effect on gastric acid secretion (Baltimore, 2013). It is supposed that the process of distillation of beer, white or red wine, liquors and champagne causes a loss of their stimulating properties. This capacity of producing gastric acid stimulation has been attributed to the presence of maleic and succinic acids, which are found in non-distilled beer and wine (Stermer, 2002).

Researches indicate that alcohol consumption is primarily associated to upper gastrointestinal bleeding and potentiates the risk of Non-steroidal anti-inflammatory drug (NSAID) associated Gastrointestinal bleeding (Strate et al, 2016). This is related to alcohol-induced mucosal injury and decreased formation of prostaglandins. It is a well-known fact that alcohol consumption can cause mucosal inflammation, which may lead to mucosal damage and disrupts the gastric mucosal barrier which increases the mucosal acid permeability (Zatorski, 2017). A study conducted in Sydney Australia also showed that alcohol consumption increases H. pylori infection (OR = 9.05, 95% CI: 1.05–77.98) (Li Zhang et al., 2010).

2.3.5. Sex and peptic ulcer disease

It is well known that peptic ulcer predominates in the males. Most reports on the sex incidence of peptic ulcer in the adult give a ratio of two or five males to one female even if it is decreasing through time (Schwartz, 2010). The male to female ratio for age-adjusted duodenal ulcer mortality rates in California dropped from 5.4 in 1950 to 2.3 in 1980, whereas that for gastric ulcer mortality dropped from 4.0 to 1.8 (John et al., 1985). The rhythmic interplay in each month between the pituitary and the ovaries might provide the protective mechanism for females (David et al., 1938).

2.3.5. Coffee and peptic ulcer disease

Some studies denote that peptic ulcer disease do not have association with coffee consumption while others report correlation. A research in Japan indicate that there is no significant relationship between coffee consumption and the peptic ulcer disease (Shimamoto et al., 2013). But some other reported that coffee is highly acidic and it can stimulate the hypersecretion of gastric acid and immune system suppression caused by chronic increased levels of stress hormones induced by
caffeine intake can create a situation in which the bacteria Helicobacter pylori can grow (Rafetto et al., 2004).

In contrary, a research done in Malaysia state that subjects who drink coffee are less likely to develop H. pylori infection (41.0%) as compared to those who don’t drink coffee (54.0%). However, the difference is not statistically significant. With respect to the number of cups per day, lower percentage of H. pylori infection was detected among those who consume more than 5 cups per day (p value=0.194) (Kadhim et al., 2015).

2.3.6. ABO/Rh blood group and peptic ulcer disease

Among the associated factors, blood group polymorphism is the one. In Iraqi, one hundred and six patients with peptic ulcer disease (PUD) (43 male and 63 female; mean age: 48 ± 18 years) were enrolled and the ABO blood group phenotype frequency in peptic ulcer patients was found to be: 18.9% for blood group A, 15.1% for blood group B, 57.5 % for blood group O and 8.5% for blood group AB. Rh positivity was found in 100% of patients. Significant higher percentage of patients with both gastric and duodenal ulcer disease are those holding blood group O+ compared to other blood group phenotypes (57.5%) (p= 0.003). The study also showed higher incidence of duodenal ulcer (DU) in patients with blood group O+ compared to gastric ulcer (GU) patients (65.6% vs 54.1%) (Abdulridha, 2013).

In the same way a study done in Iran on 81 patients with PUD (51 male, 30 female with average age 49± 18 years) indicates the ABO distribution to be 37% (30/80) for blood group A, 23.4% (19/81) for group B, 35.6% (28/81) for group O and 4.9% (4/81) for group AB. RH positivity was found in 63% (51/81) of patients. In local healthy population ABO/RH blood group distribution was 33.8%, 20.7%, 34.7%, 8.4% and 89.6% for A, B, O, AB and RH indicating ABO/RH blood group has important role in patients with peptic ulcer disease (Rasmi et al., 2009).

A cohort study with a 9.9 year median length of study among 1,073,584 Swedish and Danish blood donors indicates blood donors with blood group A, B, or AB all had significantly lower risk for gastric and duodenal ulcer than those with blood group O. Accordingly, the relative risk estimates for gastric ulcers ranged from 0.77 (95% CI: 0.64, 0.91) for those with blood group AB and 0.83 (95% CI: 0.73, 0.94) for blood group B to 0.91 (95% CI: 0.85, 0.99) for blood group A. For duodenal ulcers, the estimated relative risks were 0.85 (95% CI: 0.71, 1.00) for blood group AB, 0.75 (95% CI: 0.65, 0.85) for blood group B, and 0.81 (95% CI: 0.74, 0.87) for blood group A (Edgren et al., 2010).

A study in Gezira central Sudan on 40 patients (with a mean age of 50.75 ± 18.18 years) of peptic ulcer disease which are diagnosed by esophagogastroduodenoscopy showed that 28 patients were
both H. pylori biopsy-urease and Rhesus factor positive (93.3%), while 2 patients were H. pylori positive and Rhesus negative (6.7%). Among patients who were H. Pylori urease positive; 3 were blood group A (10%), 9 were B (30%) and 18 were O (60%). Most patients 31(77.5%) had duodenal ulcers, while 9 (22.5%) had gastric ulcers at esophagogastroduodenoscopy.

Out of those who had D.U at esophagogastroduodenoscopy; 3 were Blood group A (9.7%), 10 were B (32.3%) and 18 were O (58.1%). While among those with gastric ulcer; 3 were Blood group B (33.3%) and 6 were O (66.7%). Rhesus factor was positive in 28 patients (93.3%) and negative in 2 patients (6.7%) among those who were urease positive. Patients with duodenal ulcer; 29(93.5%) were Rhesus positive and 2(6.5%) were negative. All patients with gastric ulcer (9 patients) were Rhesus positive (100%). This implies that there was statistically significant correlation between the O blood group, positive Rhesus factor and H. Pylori infection in peptic ulcer disease patients (Mohammed et al., 2015).

To sum up H. pylori infection (OR 5.6, 95% CI: 1.9-8.8), chronic intake of NSAIDs (OR 2.8, 95% CI: 1.3-4.4), Smoking (OR 2.3, 95% CI: 1.4-6.5), and male gender (OR 3.6, 95% CI: 1.2-5.8) were the main risk factors of peptic ulcer disease (Barazandeh et al., 2012). Psychosocial factors also may have effect on the development of ulcer by increasing duodenal acid load, altering local circulation or motility, intensifying Helicobacter pylori infection, stimulating corticosteroid secretion, and affecting health risk behaviors (Levenstein, 2002).

2.4. Clinical Manifestations

Over 90% of patients with peptic ulcer disease complain of abdominal pain. The pain is typically non-radiating, burning in quality, and located in the epigastrium. Timing of the symptoms in relation to meal may differentiate between gastric and duodenal ulcers. A gastric ulcer would give epigastric pain during the meal, as gastric acid production in increased as food enters the stomach. Symptoms of duodenal ulcers would initially be relieved by ingestion of food and experience pain 2 to 3 hours after a meal and at night when the stomach begins to release digested food and acid into duodenum.

Two thirds of patients with duodenal ulcers will complain of pain that awakens them from sleep. Other signs and symptoms include nausea, bloating, weight loss, stool positive for occult blood, and anemia (Schwartz et al., 2010).
2.5. Diagnosis

The diagnosis is mainly established based on the characteristic symptoms. Stomach pain is usually the first signal of a peptic ulcer. Upper GI endoscopy is the most accurate diagnostic test for PUD. It gives information about the size and the location of the lesion. The demonstration of H.pylori colonization can be made either by serologic analysis, breath test or fecal antigen detection (Lauret et al., 2015).

2.6. Treatment

Treatment of peptic ulcer disease focuses on three major targets. The first is reducing acid secretion, then eradication of H.pylori infection, and lastly increasing the mucosal layer. When the three targets are incorporated together, it is called triple management. Triple management includes: (a) Proton pump inhibitor (PPI) in standard dose + clarithromycin 500 mg + amoxicillin 1000 mg each given twice daily (b) PPI in standard dose + clarithromycin 500mg + metronidazole 400 mg, each given twice daily (c) Ranitidine bismuth citrate (RBC) 400mg + clarithromycin 500 mg + amoxicillin 1000mg, each given twice daily (d) Ranitidine bismuth citrate (RBC) 400 mg +clarithromycin 500 + metronidazole 400 mg, each given twice daily. Each of above regimen should be given for 7-14 (Mustafa et al., 2015).
3 OBJECTIVE OF THE STUDY

3.2 General objective
The main objective of this study was to assess the association between ABO/Rh blood group distribution and incidence of peptic ulcer disease at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia.

3.3 Specific objectives
- To assess the ABO/Rh blood group distribution of peptic ulcer disease patients at Tikur Anbessa Specialized Hospital during the study period.
- To evaluate the association of socio-demographic data, use of NSAID, smoking, drinking coffee and alcohol consumption, with peptic ulcer disease.
- To determine the incidence of H. Pylori infection according to ABO/Rh blood group distribution.
4. MATERIALS AND METHODS

4.1 Study area and period

The study was conducted from June 5 to April 15 at Tikur Anbessa Specialized Hospital (TASH) which is the largest and oldest teaching hospital in Ethiopia. The hospital is located in Addis Ababa and provides referral service for patients coming from all regions of the country. It has 800 beds and gives diagnostic and treatment services for patients.

4.2 Study design

Hospital based cross-sectional study design was conducted to assess the ABO/RH blood group distribution of peptic ulcer disease patients at Tikur Anbessa Specialized Hospital during the study period.

4.3 Study population

All the population of Tikur Anbessa Specialized hospital was the source population for the study. The study population was all endoscopically diagnosed peptic ulcer disease patients at Tikur Anbessa Specialized Hospital during the study period and meet the eligibility criteria.

4.4 Eligibility criteria

4.4.1 Inclusion criteria

All peptic ulcer disease patients enrolled to undertake endoscopic examination and have consent to participate in the study were included.

4.4.2 Exclusion criteria

- Patients with gastric mass
- Patients with gastric cancer
4.5 Sample size determination

Endoscopically confirmed peptic ulcer disease patients in TASH for the past two years were only 98 patients. Thus it was unfeasible to determine the sample size using sample size determination formula. Therefore considering confirmed peptic ulcer disease as a rare disease in TASH, all endoscopically confirmed peptic ulcer disease patients during the data collection period (September 14 – November 10) were included. The medical charts of endoscopically confirmed peptic ulcer disease patients within the past two years were reviewed. Then those who meet the inclusion criteria were also called and enrolled in the study.

In this way the number of study subjects reached 63 for endoscopically confirmed peptic ulcer disease patients and 63 for the control groups. Totally there were 126 study participants.

4.6 Sampling procedure

The sampling procedure was a convenient sampling method. All endoscopically confirmed peptic ulcer disease patients attending the endoscopy room during the time of data collection and are eligible to participate in the study were selected.

The purpose of the study was explained for the study participants who joined the study voluntarily. All study participants have signed the consent form.

4.7 Study variables

4.7.1 Independent variables
- Socio-demographic characteristics; age, marital status, educational level, economic status
- ABO blood group distribution
- RH factor
- Drinking Coffee
- Alcohol Consumption
- Smoking.
- H. pylori infection
- Chronic use of NSAID

4.7.2 Dependent variables
- Peptic ulcer disease
4.8 Operational definitions

**Peptic ulcer disease (PUD):** Peptic Ulcer was defined as a mucosal break at least 3 mm in diameter, with or without a necrotic base in the middle of the lesion, in either the stomach (gastric ulcer) or the duodenum (duodenal ulcer) diagnosed by endoscopic examination.

**NSAIDs users:** Those used NSAIDs at least for a month.

**NSAIDs non-users:** Individuals who do not use NSAIDs or used NSAIDs less than a month.

**Alcohol drinkers:** Those drinking one or more drinks (drink was defined as 1 bottle of beer, 1 glass of wine or 1 shot of liquor)

**Non-drinkers:** Individuals who are not drinking currently and have never drank alcohol at all.

**Smokers:** Individuals who are smoking ≥ 1cigarette per day and have smoked before.

**Non-smokers:** individuals who do not smoke and have never smoked cigarette.

4.9 Data and Blood sample collection procedures

Socio-demographic characteristics and other data that are risk factors for peptic ulcer disease was collected from the participants by face to face interview using Amharic version of the semi-structured questionnaire.

The study participant’s finger was lanced by qualified health care professionals in the hospital using a lancet and less than 3 ml of venous blood was collected. The collected blood from each study participants was dropped on 3 clean microscopic slides labeled A, B and D. Then anti-A, anti-B and anti-D antibodies were added on the slides respectively and stirred. After 2 minute the samples were checked for agglutination under microscope to determine the blood group and Rh-factor.

When a slide labeled A shows agglutination, the study participants blood group was determined to be blood group A. When a slide labeled B agglutinates, the blood group of study participants was recorded as blood group B. When both A and B slides agglutinate, the blood group of study participants was recorded as blood group AB and if blood cells of both slides A and B don’t agglutinate, the blood group of study participants was recorded as blood group O.

In the same way Rh group was determined by the presence or absence blood cells clumping (agglutination) on slide labeled as D. When the blood cells on a slide labeled D clump together the study participant’s blood was determined to be Rh positive but if no agglutination is seen on a slide labeled D, the study participant’s blood was determined to be Rh negative. Stool from study participants was also checked for presence or absence of H. Pylori using standard laboratory techniques by laboratory technician. Safety precautions was taken while handling blood and disposing it.
4.10 Data quality control and management
Data was collected and analysed by the principal investigator. All laboratory procedures were handled by laboratory technologists with a standardized tools that were used to measure and analyze the test. Data coding, entering, verifying, and cleaning were performed with a great care.

4.11 Data processing and analysis
Simple descriptive statistics such as means, frequencies, and percentages were used to present socio-demographic characteristics and distribution of blood group and peptic ulcer disease. Binary and multivariate logistic regressions were used to compute association between parameters. Data entry was done by using Epi Data statistical software version 3.1 and then exported to SPSS software version 23 for analysis. And a p-value of < 0.05 at 95% confidence level was considered to be statistically significant.

4.12 Ethical consideration
Before starting data collection and preliminary study, ethical clearance was obtained from the Departmental Research and Ethics Review Committee, Department of Medical Physiology, College of Health Sciences, Addis Ababa University. Samples and data were collected after the study participants gave full consent. Confidentiality, anonymity, neutrality, accountability and academic honesty was maintain throughout the study.

4.13 Data presentation and dissemination
Results were presented using descriptive statistics, text, frequency tables and graphs. A research report was submitted to the Department of Medical Physiology as partial fulfillment of the requirements for the award of MSc degree in medical physiology. The results of the study was communicated to AAU community and the general population of TASH.
5. RESULTS

The study was conducted on a total of 126 study participants. Sixty three (63) patients were endoscopically confirmed peptic ulcer disease patients and 63 controls without peptic ulcer disease. The study participants’ age varied between 14 years and 81 years with a mean age of 39.10 year for patients who had peptic ulcer disease and 39.41 years in those without peptic ulcer disease. The majority of the study participants were male (70.6%), married (46%) and their educational level was up to secondary school (41.3%). (Table 1)

Table 1: Socio-demographic characteristics of Peptic Ulcer Disease patients and control groups in TASH, Addis Ababa, Ethiopia, 2018

<table>
<thead>
<tr>
<th>Socio-demographic variables (N=126)</th>
<th>Frequency</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 20 years</td>
<td>10</td>
<td>7.9</td>
</tr>
<tr>
<td>21- 30 years</td>
<td>44</td>
<td>34.9</td>
</tr>
<tr>
<td>31- 40 years</td>
<td>20</td>
<td>15.9</td>
</tr>
<tr>
<td>41- 50 years</td>
<td>20</td>
<td>15.9</td>
</tr>
<tr>
<td>&gt;50 years</td>
<td>32</td>
<td>25.4</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>89</td>
<td>70.6</td>
</tr>
<tr>
<td>Female</td>
<td>37</td>
<td>29.4</td>
</tr>
<tr>
<td><strong>Religion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orthodox</td>
<td>75</td>
<td>59.52</td>
</tr>
<tr>
<td>Muslim</td>
<td>23</td>
<td>18.25</td>
</tr>
<tr>
<td>Protestant</td>
<td>25</td>
<td>19.84</td>
</tr>
<tr>
<td>Catholic</td>
<td>3</td>
<td>2.38</td>
</tr>
<tr>
<td><strong>Ethnic group</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amhara</td>
<td>49</td>
<td>38.9</td>
</tr>
<tr>
<td>Oromo</td>
<td>38</td>
<td>30.2</td>
</tr>
<tr>
<td>Tigre</td>
<td>15</td>
<td>11.9</td>
</tr>
<tr>
<td>Others</td>
<td>24</td>
<td>19.0</td>
</tr>
<tr>
<td><strong>Marital status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>49</td>
<td>38.9</td>
</tr>
<tr>
<td>Married</td>
<td>58</td>
<td>46.0</td>
</tr>
<tr>
<td>Divorced</td>
<td>11</td>
<td>3.7</td>
</tr>
<tr>
<td>Widowed</td>
<td>8</td>
<td>6.3</td>
</tr>
<tr>
<td><strong>Educational level</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary school</td>
<td>31</td>
<td>24.6</td>
</tr>
<tr>
<td>Secondary school</td>
<td>52</td>
<td>41.3</td>
</tr>
<tr>
<td>College/university</td>
<td>32</td>
<td>25.4</td>
</tr>
<tr>
<td>Postgraduate</td>
<td>11</td>
<td>8.7</td>
</tr>
</tbody>
</table>
The ABO blood group distribution among peptic ulcer disease patients was found to be 19.04% (12/63) for blood group A and B, 11.11% (7/63) for blood group AB and 50.79% (32/63) for blood group O while among control groups it was 25.39% (16/63) for blood group A, 23.80% (15/63) for blood group B, 12.69% (8/63) for blood group AB and 38.09% (24/63) for blood group O. Therefore, blood group O was found to have higher distribution among peptic ulcer disease patients than control groups (50.79% vs. 38.09%). (Figure 1)

![Figure 1: Distribution of ABO blood group among peptic ulcer disease patients and control groups in TASH, Addis Ababa, Ethiopia, 2018.](image)

Rh positivity was 90.48% among PUD patients and 95.34% among controls. (Figure 2)

![Figure 2: Distribution of Rh factor among peptic ulcer disease patients and control groups in TASH, Addis Ababa, Ethiopia, 2018.](image)
Out of the total peptic ulcer disease patients 34.1% (22/63) had gastric ulcer and 65.9% (41/63) had duodenal ulcer. The frequencies of ABO blood group among endoscopic findings (gastric ulcer versus duodenal ulcer) were 22.22% (14/63) gastric ulcer versus 28.57% (18/63) duodenal ulcer for group O, 4.76% (3/63) gastric ulcer versus 14.28% (9/63) duodenal ulcer for group A, 7.93% (5/63) gastric ulcer versus 11.11% (7/63) duodenal ulcer for group B, and 11.11% (7/63) duodenal ulcer for group AB. (Figure 3)

**Figure 3:** The distribution of gastric ulcer and duodenal ulcer among peptic ulcer disease patients according to ABO blood group type.
Out of 63 peptic ulcer disease patients, 41 (65%) was H. pylori positive. The incidence of H. pylori infection out of the total H. pylori infected patients according to the ABO blood group distribution were 56% (23/41) for blood group O, 14.6% (6/41) for blood group A, 19.5% (8/41) for blood group B and 9.7% (4/41) for blood group AB. (Figure 4)

**Figure 4:** Proportion of ABO blood group according to H. pylori infection among peptic ulcer disease patients in TASH, Addis Ababa, Ethiopia, 2018.

Furthermore, out of 32 blood group O peptic ulcer disease patients, 72% were H. Pylori infected. Therefore, when compared to other blood type, blood group O was found to have higher percent of H. pylori infection. Fifty percent of blood group A, 67% of blood group B and 57% of blood group AB were also infected by H. pylori. (Figure 5)

**Figure 5:** Comparison of ABO blood group according to H. pylori infection among PUD patients in TASH, Addis Ababa, Ethiopia, 2018.
The majority (74.6%) of the study participants didn’t use non-steroidal anti-inflammatory drugs, didn’t smoke cigarette (88.9%) but (89.3%) drank coffee while those who drank alcohol had nearly equal proportion (51.6%) with that didn’t drank alcohol (48.6%). (Table 2)

**Table 2:** Percentage of use of NSAID, alcohol, cigarette and coffee among the study participants in TASH, Addis Ababa, Ethiopia, 2018

<table>
<thead>
<tr>
<th>Factors (N= 126)</th>
<th>Frequency</th>
<th>Percent (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of NSAID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>94</td>
<td>74.6</td>
</tr>
<tr>
<td>Yes</td>
<td>32</td>
<td>25.4</td>
</tr>
<tr>
<td>At least daily</td>
<td>21</td>
<td>16.6</td>
</tr>
<tr>
<td>Once a week</td>
<td>6</td>
<td>4.7</td>
</tr>
<tr>
<td>Three times a week</td>
<td>7</td>
<td>5.5</td>
</tr>
<tr>
<td>Drinking alcohol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>65</td>
<td>51.6</td>
</tr>
<tr>
<td>Yes</td>
<td>61</td>
<td>48.4</td>
</tr>
<tr>
<td>At least daily</td>
<td>15</td>
<td>11.9</td>
</tr>
<tr>
<td>Once a week</td>
<td>35</td>
<td>27.7</td>
</tr>
<tr>
<td>Three times a week</td>
<td>14</td>
<td>11.1</td>
</tr>
<tr>
<td>Smoking cigarette</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>112</td>
<td>88.9</td>
</tr>
<tr>
<td>Yes</td>
<td>14</td>
<td>11.1</td>
</tr>
<tr>
<td>At least daily</td>
<td>24</td>
<td>19.0</td>
</tr>
<tr>
<td>Once a week</td>
<td>4</td>
<td>3.1</td>
</tr>
<tr>
<td>Three times a week</td>
<td>4</td>
<td>3.1</td>
</tr>
<tr>
<td>Drinking Coffee</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>13</td>
<td>10.7</td>
</tr>
<tr>
<td>Yes</td>
<td>113</td>
<td>89.3</td>
</tr>
<tr>
<td>At least daily</td>
<td>15</td>
<td>11.9</td>
</tr>
<tr>
<td>Once a week</td>
<td>56</td>
<td>44.4</td>
</tr>
<tr>
<td>Three times a week</td>
<td>54</td>
<td>42.8</td>
</tr>
</tbody>
</table>
Factors associated with peptic ulcer disease

Bivariate logistic regression showed that there was statistically significant association between peptic ulcer disease and sex of the study participant, use of non-steroidal anti-inflammatory drugs and smoking cigarette but no significant association was found with drinking alcohol, drinking coffee, blood group and Rh factor. (Table 3)

Table 3: Bivariate analysis of factors associated with peptic ulcer disease in Tikur Anbessa specialized Hospital, Addis Ababa, Ethiopia, 2018

<table>
<thead>
<tr>
<th>Variables</th>
<th>Peptic Ulcer Disease</th>
<th>COR 95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>38</td>
<td>51</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>25</td>
<td>12</td>
</tr>
<tr>
<td>Use of NSAID</td>
<td>No</td>
<td>53</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td>Alcohol drinking</td>
<td>No</td>
<td>28</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>35</td>
<td>26</td>
</tr>
<tr>
<td>Smoking Cigarette</td>
<td>No</td>
<td>60</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>Drinking Coffee</td>
<td>No</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>60</td>
<td>53</td>
</tr>
<tr>
<td>Blood group</td>
<td>A</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>AB</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>O</td>
<td>24</td>
<td>32</td>
</tr>
<tr>
<td>Rh factor</td>
<td>Negative</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Positive</td>
<td>61</td>
<td>57</td>
</tr>
</tbody>
</table>
Multivariate logistic regression was done for those factors that were significantly associated in binary logistic regression. The analysis showed that there was statistically significant association between sex, use of NSAID, smoking cigarette and peptic ulcer disease. Accordingly being a male was four times risky \( p=0.001, \text{AOR (95\% CI) 4.21(3.30, 7.50)} \) for acquiring peptic ulcer disease than femaleness. In the same way those who smoke cigarette were approximately seven times more likely to have peptic ulcer disease than non-smokers \( p=0.014, \text{AOR (95\%) 7.32 (1.48, 36.03)} \). Even though blood group O was found to have higher distribution among peptic ulcer disease patients than in the control group, there is no statistically significant association between blood group and peptic ulcer disease. (Table 4)

**Table 4: Multivariate analysis of factors associated with Peptic Ulcer Disease among TASH patients, Addis Ababa, Ethiopia, 2018**

| Variables      | Peptic ulcer disease |  | COR 95\% CI     | AOR 95\% CI     |  
|----------------|----------------------|---|-----------------|-----------------|---
|                | No  | Yes |                |                 |  
| Sex            | Male | 38  | 51             | 2.79 [1.24, 6.26] | 4.21 [3.30, 7.53] | 0.001 |
|                | Female | 25  | 12             | 1               | 1               |  
| Using NSAID    | No  | 53  | 41             | 1               | 1               | 0.001 |
|                | Yes | 10  | 22             | 2.84 [1.21, 6.66] | 2.1 [0.41, 0.39] |  
| Alcohol        | No  | 28  | 37             | 1               | 1               | 0.028 |
|                | Yes | 35  | 26             | 1.77 [0.87, 3.60] | 2.78 [1.11, 6.97] |  
| Smoking        | No  | 60  | 52             | 1               | 1               | 0.014 |
|                | Yes | 3   | 10             | 4.23 [1.11, 15.98] | 7.32 [1.48, 36.03] |  
| Coffee         | No  | 3   | 10             | 1               | 1               | 0.063 |
|                | Yes | 60  | 53             | 3.77 [0.98, 14.44] | 4.78 [0.91, 24.96] |  
| Blood group    | A   | 16  | 12             | 0.560 [0.22, 1.40] | 0.29 [0.09, 0.94] | 0.040 |
|                | B   | 15  | 12             | 0.600 [0.23, 1.51] | 0.33 [0.10, 1.09] | 0.060 |
|                | AB  | 8   | 7              | 0.656 [0.20, 2.06] | 0.36 [0.08, 1.57] | 0.178 |
|                | O   | 24  | 32             | 1               | 1               |  
| Rh factor      | Negative | 2 | 6    | 1               |  
|                | Positive | 61 | 57    | 3.21 [0.62, 16.56] | 7.12 [0.96, 52.92] | 0.550 |
6. DISCUSSION

This study was conducted to assess the association between peptic ulcer disease and ABO/ Rh blood group including other associated factors. These associated factors include the use of non-steroidal anti-inflammatory Drugs (NSAIDs), drinking alcohol, smoking cigarette, drinking coffee, H. pylori infection, and socio-demographic factors. From these factors, use of Non-steroidal Anti-inflammatory Drugs (NSAIDs), drinking alcohol, smoking cigarette and being male were factors that were significantly associated with incidence of peptic ulcer disease (Table 4).

The findings of this study revealed that the ABO blood group distribution among Peptic Ulcer disease patients was 19.04% (12/63) for blood group A and B, 11.11% (7/63) for blood group AB and 50.79% (32/63) for blood group O while among control groups it was 25.39% (16/63) for blood group A, 23.80% (15/63) for blood group B, 12.69% (8/63) for blood group AB and 38.09% (24/63) for blood group O indicating higher percentage of peptic ulcer disease incidence among patient with O blood group than other blood group type (Figure 1).

This is consistent with a research done in Iraq (Abdulridha, 2013). It can be explained that this is because of the carbohydrate antigens that contributed for the susceptibility or resistance to infectious diseases. Especially the H antigen of blood group O expressed in gastric mucous membrane is suitable to the attachment of Helicobacter pylori which is identified to be the major cause of peptic ulcer disease (Amandeep et al., 2012; Mattos et al., 2004).

The incidence of H. pylori infection among the ABO blood group were 56% (23/41) for blood group O, 14.6% (6/41) for blood group A, 19.5% (8/41) for blood group B and 9.7% (4/41) for blood group AB. Therefore when compared to other blood type, blood group O was found to have higher proportion of H. Pylori infection in this research (Figure 4). This result is also similar to study in Basrah that demonstrated significantly higher incidence of H. pylori among patients of blood group O (46.7%) as compared with A (20%), B (13.3%) and AB (3.3%) blood group (Baqir et al., 2016). Once again this might be because of the carbohydrate antigens especially the H antigen of blood group O expressed in gastric mucous membrane that might be suitable to the attachment of Helicobacter pylori bacteria (Mattos et al., 2004).

Despite the fact that there was an increasing trend in H. pylori infection among blood group O patients in this research, no significant association between ABO blood group and H. pylori infection was found (Table 4). This is supported by researches done in Kosovo (Zhubi et al., 2011), Gondar Ethiopia (Moges et al., 2006) and Hawassa, south Ethiopia (Tadesse et al., 2014) but it is inconsistent with a research done in Japan. The research in Japan indicate that the rate of H. pylori infection was significantly higher ($p=0.029$) for type O blood compared to other blood types. In
addition, the odds ratio of H. pylori infection adjusted for age, sex, and smoking and drinking habits was also significantly higher for type O blood compared to other blood types (Inoue et al., 2014). The difference might be because of study sample size.

Even though, blood group O was found to have higher distribution among peptic ulcer disease patients than in the control group when compared to other blood group types in this study but there is no significant association between ABO/ Rh blood group distribution and peptic ulcer with a p value of \( p=0.046, \text{AOR (95% CI) 0.29 (0.09, 0.94)} \) for blood group A, \( p=0.060, \text{AOR (95% CI) 0.33 (0.10, 1.09)} \) for blood group B, \( p=0.178, \text{AOR (95% CI) 0.36 (0.08, 1.57)} \) for blood group AB compared to blood group O (Table 4).

This result is inconsistent with a cohort research done in Stockholm Sweden, which states blood group O as a risk for peptic ulcer disease compared to other blood group type with the relative risk of 0.77 (95% CI: 0.64, 0.91) for those with blood group AB and 0.83 (95% CI: 0.73, 0.94) for blood group B to 0.91 (95% CI: 0.85, 0.99) for blood group A for gastric ulcers. For duodenal ulcers, the estimated relative risks were 0.85 (95% CI: 0.71, 1.00) for blood group AB, 0.75 (95% CI: 0.65, 0.85) for blood group B, and 0.81 (95% CI: 0.74, 0.87) for blood group A (Edgren et al., 2010). This inconsistency might be due to difference in sample size (63 vs. 1,073,584) and study design (crossectional vs. cohort).

Smoking cigarette increases the risk of having peptic ulcer disease seven times according to this research \( p=0.014, \text{AOR (95%) 7.32 (1.48, 36.03)} \) and this finding is consistent with a study in Iran (OR 2.3, 95% CI: 1.4-6.5) (Barazandeh et al., 2012) and Sweden (OR 3.12 (95% CI: 1.13, 8.64) (Aro et al., 2006). This might be because cigarette smoking stimulate basal gastric acid output (Debas et al., 1971). This increased gastric acid secretion is mediated through the stimulation of H2-receptor by histamine release and due to the increase of the functional parietal cell volume or secretory capacity in smokers (Maity et al., 2003).

Cigarette smoking also reduces the level of circulating epidermal growth factor (EGF) and decrease the secretion of EGF from the salivary gland, which are necessary for gastric mucosal cell renewal (L. Zhang et al., 2012). Therefore, cigarette smoke increases apoptosis but decreased cell proliferation, blood vessel formation (reduce angiogenesis in the gastric mucosa through inhibition of nitric oxide synthesis thereby arresting cell renewal process) and mucus synthesis in the GI mucosa. There is also a strong association between H. pylori infection and cigarette smoking; and smoking diminish the gastric mucosal defensive factors, or may provide a more favorable environment for H. pylori infection (Baltimore, 2013).
In the same way alcohol consumption was found to increase the risk of acquiring peptic ulcer disease about 3 folds (p=0.028, AOR (95%) 2.78 (1.11, 6.97)) in this study, similar to the study conducted in Nairobi Kenya that shows an association between alcohol consumption and peptic ulcer disease (p= 0.041) (Katunge, 2009). This might be because alcohol consumption increases H. pylori infection (OR = 9.05, 95% CI: 1.05–77.98) according to a research done in Sydney Australia (Li Zhang et al., 2010).

Alcohol at low concentrations (5%) also may modestly stimulate gastric acid secretions but at a concentration of higher than 5% has no effect on gastric acid secretion (Baltimore, 2013). This capacity of producing gastric acid stimulation has been attributed to the presence of maleic and succinic acids, which are found in non-distilled beer and wine (Stermer, 2002). Alcohol consumption can cause mucosal inflammation, which may lead to mucosal damage and disruption of gastric mucosal barrier which increases the mucosal acid permeability (Zatorski, 2017).

Additionally according to this study males were four times prone to have peptic ulcer disease when compared to females (p=0.001, AOR (95% CI) 4.21(3.30, 7.50)) which is consistent with a research in Iran (OR 3.6, 95% CI: 1.2-5.8) (Barazandeh et al., 2012). This might because males are more exposed for health risk behaviors such as smoking and alcohol consumption than females which were stated to be risk factors for peptic ulcer disease (Levenstein, 2002). The rhythmic interplay in each month between the pituitary and the ovaries might also provide the protective mechanism for females (David et al., 1938). 

Non-steroidal anti-inflammatory drugs (NSAIDs) were found to have statistically significant association with incidence of peptic ulcer disease in this study (p= 0.001, AOR (95%) 2.1 (0.41, 0.39)) (Table 4). This is a similar result to the study conducted in Meshkinshahr, Iran (OR 2.8, 95% CI: 1.3-4.4) (Barazandeh et al., 2012). Non-steroidal anti-inflammatory drugs (NSAIDs) are known to initiate mucosal injury topically by their acidic properties and by diminishing the hydrophobicity of gastric mucus. As a consequence, endogenous gastric acid and pepsin may injure surface epithelium (Mustafa et al., 2015). NSAIDs also cause decreased synthesis of mucosal prostaglandin which were one of the protective factors that prevent peptic ulcer disease occurrence by increasing mucosal blood flow. Adequate blood flow in mucosal circulation will not be maintained when there is reduced prostaglandin production because of inhibitory effect of NSAIDs. This makes NSAIDs the second most common cause of peptic ulcer disease (Zatorski, 2017).
7. CONCLUSION AND RECOMMENDATION

7.1 Conclusion
Peptic ulcer disease was more prevalent among patients with blood group O than other blood group types. Similarly H.pylori infection have shown an increasing trend among blood group O patients than the rest ABO blood group types.

According to this research, peptic ulcer disease has statistically significant association with use of non-steroidal anti-inflammatory drugs, alcohol consumption, smoking cigarette and male sex but has no statistically significant association with ABO blood group type, Rh factors and drinking coffee.

7.2 Recommendation
Based on the results of this study, the following recommendations are made:

- Health care providers should give attention for risk factors of peptic ulcer disease and inform the risk factors for their clients to reduce recurrence of the disease.
- Because peptic ulcer disease is considered as totally non-communicable disease; there should be consumer education brochures and spot drama should be released on H.pylori transmission and other risk factors of peptic ulcer disease.
- Health risk behaviors such as smoking, drinking alcohol should be avoided by the society to stay healthy from peptic ulcer disease. Especially males and those with blood group O should avoid smoking and drinking alcohol to reduce their susceptibility for the disease.
- Large scale study is highly recommended to ascertain the association between blood group and peptic ulcer disease.
Strength of the study

This research has assessed the association between ABO/Rh blood group distribution and incidence of peptic ulcer disease for the first time in Ethiopia. During the analysis, the effect of confounding variables on the major independent variable were reduced using multivariate logistic regression analysis. Therefore, the level of association between dependent variable and major independent variable was determined with a great care.

Limitation of the study

There were only 98 endoscopically confirmed peptic ulcer disease patients within the past two years which was the only number of electronically recorded PUD patients in TASH. This made difficult to get enough study subjects within the data collection period. Therefore, the main limitation of this research was small sample size.
8. REFERENCES


Sadiqque R. 2014. Prevalence of Peptic Ulcer Disease among the Patients with Abdominal Pain Attending the Department Of Medicine in Dhaka Medical College Hospital, Bangladesh. *IOSR Journal of Dental and Medical Sciences*, 13: 05-20.


Principal Investigator: Yonas Teshome

Addis Ababa University
College of Health Science
Department of Medical Physiology

Dear participant! Here, I, the undersigned, is an MSc student at Addis Ababa University College of Health Science, Department of Medical Physiology. Currently, I will be undertaking research on a topic entitled as the association between ABO/RH blood group and incidence of peptic ulcer disease among patients attending at Tikur Anbessa specialized hospital. For this study, you will be selected as a participant and before getting your consent, you need to know all necessary information related to the study which will be detailed as follows.

Introduction

Privacy is the state of being free from intrusion, and in the context of health care it concerns the responsibility of a care provider to protect a client from any disclosure (i.e., discovery by others), even unintentional, of personal health data, by providing security to the patient and the patient’s records. Confidentiality, in contrast, is the limiting of information to only those for whom it is appropriate. Therefore this information sheet briefly provides the necessary guide to be considered during the study.

Objective: The main aim of this study is to assess the association between ABO/RH blood group and incidence of peptic ulcer disease among patients attending at Tikur Anbessa specialized hospital during the study period.

Participants to be included: All peptic ulcer disease patients sampled by simple random sampling will be included in the study.

Risks and discomfort: Participant in this project will not cause more discomfort and no need of extra sample other than sample taken for diagnostic purpose. But, there could be minor pain and challenge in your finger during the blood drawing. The amount of blood taken from each volunteer throughout the study period is 01ml which will not affect your health. There is no major risk in participating in this research, as the whole procedure is carried out by health professionals following the standard good clinical practice.
**Benefits:** The immediate benefit in participating in this study is you will have the chance to know your blood group and whether your stomach is infected by H. pylori or not. In addition your participation will contribute in improving the health delivery system. Cost for blood collection and laboratory analysis will be covered by the project.

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

Confidentiality: The information that we will collect from this research project will be kept confidential. Information about you that will be collected from the study will be stored in a file, which will not have your name on it, but a code number assigned to it. Which number belongs to which name will be kept under lock and key, and it will not be revealed to anyone except the principal investigator.

**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.

**Persons to contact:**

If you have any question, you can ask at any time. If you have additional questions about the study, you can contact the:

Principal investigator: Yonas Teshome, cell phone-09 21 49 56 02, E-mail teshomeyonas16@yahoo.com

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.
Annex 2. Consent form (English Version)

Department of Medical Physiology, School of graduate studies, College of Health Sciences, Addis Ababa University, Consent form for the participation of the study participants in the research project

Name of the study participant ………………………

Code number……………………

I have clearly been informed about the research project that aims to assess the association between ABO/RH blood group distribution and incidence of peptic ulcer disease. I have understood that participation in this study is entirely voluntarily. I have been told that my answers to the questions will not be given to anyone else and no reports of this study ever identify me in any way. I have also been informed that my participation or non-participation or my refusal to answer questions will have no effect on me. I understood that participation in this study does not involve risks. I understood that Yonas Teshome is the contact person if I have questions about the study or about my rights as a study participant, I will be contacting the principal investigator.

Respondent’s signature__________________________________

Interviewer name_________________ signature ___________ date__________
Annex 3. Questionnaire (English Version)

Read and fill the following format correctly. Use “√” sign for the box

Section I: Sociodemographic characteristics:

1. Card No. _______________ Age _____________ Sex : Male ☐ Female ☐
2. What is your religion?
   A. Orthodox ☐ C. Protestant ☐
   B. B. Muslim ☐ D. Others specify -------
3. What is your ethnicity?
   A. Amhara ☐ C. Tigre ☐
   B. Oromo ☐ D. Others specify -------
4. Marital status
   a) Married ☐ C. Divorced ☐
   b) Single ☐ D. Widowed/ Widower ☐
5. School: Illiterate ☐
   a. Primary school ☐ C. College/ University ☐
   b. Secondary school ☐ D. Graduate school ☐
6. Average Income _________birr/month

Part II, Peptic ulcer disease related questions

7. Do you have any health problem or medical condition not related with peptic ulcer disease?
   A. Yes ☐
   B. No ☐
   If yes tell more_______________________________________
8. Are you taking any medication? Yes ☐ No ☐
   If yes tell me more_______________________________________
9. Do you use anti-pain /anti-inflammatory drugs (such as Ibuprofen, Diclofenac, Indomethacin and Aspirin) regularly? Yes ☐ No ☐
10. If yes how often?
    A. At least daily ☐ C. 3 times a week ☐
    B. Once a week ☐ D. Once a month ☐
11. Do you drink alcohol? Yes ☐ No ☐
12. If yes how often
   A. At least daily  
   B. Once a week  
   C. 3 times a week 
   D. Once a month 

13. Is there anybody who smoke cigarette around you? Yes  No 

14. If yes how often you are exposed?
   A. At least daily  
   B. Once a week  
   C. 3 times a week 
   D. Once a month 

15. Do you smoke cigarette? Yes  No 

16. If yes how often
   A. At least daily  
   B. Once a week  
   C. 3 times a week 
   D. Once a month 

17. Do you drink coffee? Yes  No 

18. If yes how often
   A. At least daily  
   B. Once a week  
   C. 3 times a week 
   D. Once a month 

I thank you
Annex 4. Subject Information sheet (Amharic version):

የተሳታፊዎች ለፈቃደኝነትና መተማመኛ መረጃ መስጫ እኔ ምን ለመበል ይችላሉ፡፡

ስሆን የመመረጋ ሰአትን ለጥቁር ለጠይሳስ ለሆስፒታል ይነካ ይችላሉ፡፡

ማይገኝ ወረቀት ይችላሉ፡፡

እርስዎ የተመረጋ ለሚወስዳቸው ቤት ይወስዳቸው ለማንኛዉም መረጃወች ለሚስጥራዊነት ያሉ

አለመስማማት እንዲያረጋግጡ ለትህትና እጠይቃለሁ፡፡

መግቢያ ከጥናቱ ከእርሶ የሚወስዳቸው ታህን የሆነ ይገኝ የተዛማቹ የብወቅ ወስነን:

የጥናቱ በሚያደርጉት ይሳትፎ ይሆኑ የሚል ይርእስ ይበ ይኘ፡፡

አለመስማማት ይሆኑ ይልማ ይነካ ይችላሉ፡፡

እርሶ የሚል ይብለዉ ይርካ ይስ ይስ ይሳትፎ ይሚለስ ይክፈል ይወያን ይኖራቸው ይሆኑ

ማቊረጥ ይችላሉ፡፡

እርሶ የሚል ይእኑ ይታርጉ ይህ ይታኝ ይኽላሉ፡፡

አለመሳተፍም ለሆነ የማንኛዉም ለስአት የተሳትፎዎን ይጠጥን ይሆኑ:

አለመአማኝነት ከወይም በወይም ይውስጥ ይችላሉ፡፡

አለመስማማት ይህ ይልማ ይነካ ይችላሉ፡፡

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አለመውስጥ ይህ ይን ይስ ይስ ይሳትፎ ይሚለስ ይክፈል ይወያን ይክፈል ይሆኑ

አለመውስጥ ይህ ይን ይስ ይስ ይሳትፎ ይሚለስ ይክፈል ይወያን ይክፈል ይሆኑ

አለመውስጥ ይህ ይን ይስ ይስ ይሳትፎ ይሚለስ ይክፈል ይወያን ይክፈል ይሆኑ

አለመውስጥ ይህ ይን ይስ ይስ ይሳትፎ ይሚለስ ይክፈል ይወያን ይክፈል ይሆኑ

አለመውስጥ ይህ ይን ይስ ይስ ይሳትፎ ይሚለስ ይክፈል ይወያን ይክፈል ይሆኑ

አለመውስጥ ይህ ይን ይስ ይስ ይሳትፎ ይሚለስ ይክፈል ይወያን ይክፈል ይሆኑ

አለመውስጥ ይህ ይን ይስ ይስ ይሳትፎ ይሚለስ ይክፈል ይወያን ይክፈል ይሆኑ

አለመውስጥ ይህ ይን ይስ ይስ ይሳትፎ ይሚለስ ይክፈል ይወያን ይክፈል ይሆኑ

አለመውስግን እኔ መስማማት!!!
Annex 5: Informed consent (Amharic version)

የተሳታፊ ያስምምነት ማረጋገጫ ከቅጽ

የሚስጥር ማስጥር

አኔ ተደም እና በየጨጉራ ሊላጥ ለመም ሊከከል ይላውን

ግንኙነትና ተዛማጅነት ይላቸው ከገሮችን ወለማወቅ ወለሚሰራዉ ይስጥን እና ይለስቱ ያስርቘን ተሳሰፍ

የተሳታፊ ያርማ

ቀን-------

የተሳታፊ ያርማ ያስርቃውት ከበርማ ከአረጋግጣለሁ፡፡

የተሳታፊ ያርማ

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Amharic version questioner

ንወቻት ከታስወቻት ገጆና ይችላሉ ይጋገሩ። በጎን በት ያን ይህ ያለት ቍል ም“√” ይመስራሉ።

እስራት ይጋገር። የሆን በታች ይፋስወቻዎች ከታስወቻዎች ያታጨምር ያለው።

1. እርሬ ቀቅ ጋዜ ከታ ማን በት ማን
2. በሚፋስወቻ ይሚታው የው?
   ስ. እርወ ይ芝加哥 ማን በት ማን
   እ. ማወቻ ይጋኅ ማን በት ማን
   ያ. ማወቻ ይጋኅ ማን በት ማን

3. ከሌም ይሚታው የው?
   በ. እርወ ይጋኅ ማን በት ማን
   እ. ማወቻ ይጋኅ ማን በት ማን
   ያ. ማወቻ ይጋኅ ማን በት ማን

4. ያለው ቀን ግ የው?
   በ. እርወ ይጋኅ ማን በት ማን
   እ. ማወቻ ይጋኅ ማን በት ማን
   ያ. ማወቻ ይጋኅ ማን በት ማን

5. ያለው ይሚፋስወቻ ይሚታው የው?
   በ. እርወ ይጋኅ ማን በት ማን
   እ. ማወቻ ይጋኅ ማን በት ማን
   ያ. ማወቻ ይጋኅ ማን በት ማን

6. ያለው ይሚፋስወቻ ይሚታው ይሚፋስወቻ ያሉዎች ያላችሉ ያላችሉ?
   በ. እርወ ይጋኅ ማን በት ማን
   እ. ማወቻ ይጋኅ ማን በት ማን
   ያ. ማወቻ ይጋኅ ማን በት ማን

7. ያለው ይሚፋስወቻ ይሚታው የው ያላችሉ ያላችሉ?

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8. ከአገራዊ ዝርዝር ያላል በማድረስ ወስን ከተለያዩ ከአሰራር ከሚያስ-
እርስ ማስታትዎች?

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18. የአንዴ በሳምንት ከም እና ከይ የእ የገኝ ይታኋሉ።?

19. ከም ከስንት የወር ከም ይገኝ ከም ይታኋሉ።?
    ይ. ከስንት ከው ይገኝ ይታኋሉ።
    አ. ከስንት ከው ይገኝ ይታኋሉ።
    ዑ. ከስንት ከው ይገኝ ይታኋሉ።
    ም. ከስንት ከው ይገኝ ይታኋሉ።
Declaration

I, the undersigned, hereby declare that this MSc thesis is my original work and has not been presented for a degree in any other university, and that all sources of materials used for the thesis have been duly acknowledged.

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Prof. Fikre Enkusillasie (PhD)