ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, SCHOOL OF MEDICINE, DEPARTMENT OF BIOCHEMISTRY

Glycemic Level and Lipid Profile Status in patients with Gastrointestinal Malignancy

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This is to certify that the dissertation prepared ByYitayal Mekuriaw, entitled:Glycemic Level and Lipid Profile Status of Gastrointestinal Malignant Patients, Attending at Tikur Anbessa Specializd Hospital of Addis Ababa, Ethiopia, 2018, and submitted for the partial fulfillment of the requirements of the degree "Master of Science in Biochemistry" in the Department of Medical Biochemistry complies with regulations of the university and meets the accepted standards with respect to originality and quality.

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Declaration

I declare that this research paper entitled: Glycemic Level and Lipid Profile Status of Gastrointestinal Malignant Patients, Attending at Tikur Anbessa Specializd Hospital of Addis Ababa, Ethiopia, 2018, is my original work and has not been presented for any degree in any other university and that all sources of materials used for the research have appropriately been acknowledged.

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Abbreviations

BMI Body Mass Index

CT Computerized Tomography

DM Diabetes Mellitus

DNA Deoxyribo Nucleic Acid

EUS Endoscopic Ultera Sonography

FBS Fasting Blood Sugar

FGL Fasting Glucose Level

GLOBOCAN Global Burden of Cancer

GI Gastrointestinal

HDL-C High Density Lipoprotein Cholesterol

HGL High Glucose Level

IFG Impaired Fasting Glucose

IGR Impaired Glucose Regulation

IGT Impaired Glucose Tolerance

LDL-C Low Density Lipoprotein Cholesterol

LPLs Lipid Profile Levels

MRI Magnetic Resonant Imaging

MS Metabolic Syndrome

NCEP-ATP National Cholesterol Education Program Adult Treatment Panel

NFG Normal Fasting Glucose

OGTT Oral Glucose Tolerance Test

TC Total Cholesterol

TG Triglycerids

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Abstract

Gastrointestinal malignancies including esophageal, gastric, colorectal, hepatocellular, pancreatic and gallbladder are responsible for more occurrence and more deaths than any other malignancies worldwide. On the otherhand, positive as well as negative associations of serum lipids and lipoproteins and glucose levels with different malignancies including gastrointestinal malignancy have been reported by many researches.Thus, the main goal of this study was to find the association of glycemic level and lipid profile status of gastrointestinal malignant patients.This was done through hospital based cross-sectional study in (70) GI malignant patients attending at Tikur Anbessa Specialized Hospital.The necessary data including serum fasting glucose and lipid profile levels were also collected and statistically analyzed and found the following results:The mean serum FGL was (107.81-mg/dL) and (27.1%) IFG and (21.4%) hyperglycemic patients were found. Besides, significantly different ($p<0.05$, $p=0.000$) FBS levels in esophageal (86.70±15.326), gastric (90.60±4.088), colonic (111.44± 22.225), rectal (114.82±28.505) and pancreatic (178.00±72.691) malignant patients were also found. Likewise, significantly higher FBS levels ($p<0.05$) in employed (121.41± 41.562), high economic status (121.20±46.194) alcohol drinkers (120.78±38.295) and cigarette smokers (174.50± 118.08) patients than unemployed (101.70±21.438) low economic status (101.67±20.140) none alcohol drinkers (99.48±20.646) and non cigarette smokers (105.82±24.605) patients were observed. Significantly different HDL-c levels ($p<0.05$) was also found in the age groups of (30-39yrs) (47.86±12.031) and (60-70yrs) (38.47± 9.125). Moreover,TG, HDL-C and LDL-C levels of overweight (173.33± 85.710, 49.50±12.818, 132.00±31.27) and underweight (122.24±45.772, 38.38± 11.995, 99.34± 31.839) patients were significantly different (P= 0.042, 0.049, 0.028, TG, HDL-C and LDL-C respectively). Furthermore, abnormal LDL-c, HDL-c, TC and TG levels above the respective cut off value were found in 50%, 47.1%, 24.3% and 20% of the patients respectively.From the results of this study we can generally concluded that gastrointestinal malignant patients were affected by both dysglycimia except gastric and dyslipidemia.Occurrence of dysglycemia and dyslipidemia were increasing with increasing BMI and socioeconomic status as well as in cigarette smokers and alcohol drinkers. Besides significantly inverse association of HDL-c levels with age of the patients was found. Moreover, the FBS levels of the patients were negatively correlated with lipid profile of TC, TG, HDL-c and LDL-c levels, though not stastically significant.

Key words: gastrointestinal malignancy, fasting blood glucose, Lipid profiles, sociodemographic characteristics, personal medical history, clinicopathological characteristics.

1.INTRODUCTION

Cancer is a complex disease involving uncontrolled growth of abnormal cells (neoplasia) and numerous changes in cell physiology which ultimately lead to malignant tumors (Hanahan and Weinberg, 2011). The damage to the deoxyribonucleic acid (DNA) due to mutation leads to the development of tumor cells. When the DNA is damaged, either cells repairs the damage or results in apoptosis, whereas the function of apoptosis does not occur in damaged DNA in tumor cells leading to abnormal cell growth(American Cancer Society, 2014).

Carcinogenesis is a complex processes, normal cells must undergo multiple genetic "hits" before the full neoplastic phenotype of growth, invasion and metastasis occurs. This process of malignant transformations can be divided into multiple steps: initiation (irreversible first step toward cancer), promotion (stimulation of the growth of initiated cells) and progression (development of a more aggressive phenotype of promoted cells). Factors that affect one or more steps of this pathway could be associated with cancer incidence or mortality (Giovannucci et al., 2010). Tumor cells are invasive in nature which spread to the surrounding tissues and distant organs, causing high rates of morbidity and mortality in most cancer patients (Yuan, 2013).

The incidence rate for all cancers combined is higher in more developed countries compared with less developed countries in both males and females but similar in increasing mortality rate in both developed and developing countries. Survival statistics vary greatly by cancer type and stage at diagnosis, most importantly, the types of cancer that occur, the stages at which cancers are diagnosed, and whether treatment is available (Genetic Home Reference, 2015).

The risk factors for cancer can be broadly categorized into four types, namely behavioral (tobacco use, harmful use of alcohol, unhealthy diet and physical inactivity), biological (overweight, obesity, age, sex of the individual), environmental (exposure to environmental carcinogens such as chemicals, radiation and infectious agents (including certain viruses)) and genetic/hereditary make up. Owing to its nature, cancer is difficult to treat and cannot be eradicated at population level. However, it is possible to significantly reduce the effects of cancer on society if effective measures are put in place to control risk factors associated with cancer, promote early detection and offer good care to those affected. According to GLOBOCAN2012 estimates about 40% of cancers are preventable (NCCP Ethiopia, 2015).

Researchers also revealed that metabolic activities are altered in cancer cells relative to normal cells, and that these alterations support the acquisition and maintenance of malignant properties.Likewise, cancer cells alter their metabolism in order to support their rapid proliferation and expansion across the body.Some altered metabolic features are observed quite generally across many types of cancer cells**,** most tumor cells rather than fueling glucose in the oxidative phosphorylation pathway, commonly use glucose for aerobic glycolysis(Hanahan and Weinberg,2011; Pavlova and Thompson, 2016).

On the other hand, abnormal glucose metabolism increases the incidence and mortality rates of cardiovascular and cerebrovascular diseases (Hu and Yand 2006; Liu et al., 2007). Abnormal glucose metabolism including diabetes mellitus and impaired glucose tolerance are also increasing cancer risk possibly because they are associated with high fat, high-energy diet and imbalance of insulin and insulin like growth factor related cell growth regulators.Diabetes and abnormal glucose metabolism increase the risk of several cancers and IGT in cancer patients also increases mortality (Saydah et al., 2003; Seow et al., 2006; Sieri et al.,2012).However, several researchers argue that no relationship exists between abnormal glucose metabolism and malignancy(Berster and Göke, 2008).This controversy may primarily be due to population selection, diagnostic criteria, methodological inconsistencies such as nonstandard OGTTs or the use of fasting blood glucose alone, and abnormal glucose metabolism diagnosis i.e., based only on fasting blood glucose without an OGTT. These factors cause a diagnostic error rate of 87.4% for IGR and 80.5% for diabetes (Colagiuri, 2004).

Research on biochemistry and molecular biology of lipids and lipoproteins realize that different classes of lipoproteins play fundamental roles in diseases such as cardiovascular diseases, obesity, diabetes, cancer and several neurodegenerative disorders. In the same taken, aberrant blood lipid profiles or dyslipidemia has been considered as the risk factor of cardiovascular diseases. Similarly, various research findings also revealed that dyslipidemia is associated with cancer (Allampallam et al., 2000; Patel et al., 2004; Halton et al., 1998; Muntoni et al., 2009; Usman et al., 2015). Equally, dyslipidemia is associated with increased human cancer mortality (Calle et al.,2003). It has also been reported that lipids play crucial role in tumor development and progression (Muntoni et al., 2009; Hsu and Sabatini, 2008), and the malignant cells manipulate and up-regulate their lipogenic and lipolytic pathways for acquisition of lipids (Swinnen et al., 2006; Menendez and Lupu ., 2007) for their development and progression. However, the association between abnormal levels of serum lipid

components as the main features of dyslipidemia and the risk of individual cancers is unclear (Tabuchi, 2006; Ulmer et al., 2009; Van Duijnhoven et al., 2011).

Moreover, the exact mechanisms by which lipids and lipoproteins may contribute to carcinogenesis are notclearly understood. Reports however suggest that the lipid peroxidation product, malondialdehyde, may cross-link DNA on the same and opposite strands (Summerfield and Tappel, 1983) *via* adenine and cytosine (Marnett et al., 1980). This may in theory contribute to carcinogenecity and mutagenecity in mammalian cells (Stepsenwol, 1966; Takatani et al., 1991).

Previous studies have also demonstrated that almost all cancers are affected by aberrant lipid levels (Allampallam et al.,2000;Patel et al.,2004;Halton et al.,1998).However, there are several discrepancies in the reports regarding the association of dyslipidemia with cancers (Usman et al., 2015).

1.1. Literature Reviews

1.1.1. Gastrointestinal Malignancy

Among all organ cancers, gastrointestinal cancers (GI cancers) present an interesting pattern in distribution over the world. GI cancer is a term for cancers that affect the digestive system including gastric cancer (GC), colorectal cancer (CRC), hepatocellular carcinoma (HCC), esophageal cancer (EC) and pancreatic cancer (PC) and gallbladder cancer (GBC). The GI cancers are responsible for more occurrence and more deaths than any other cancers and are responsible for an increasing burden (incidence and mortality) worldwide (Sung et al.,2012).Based on the GLOBOCAN2012 reports the highest 5-year prevalence for the cancers of colorectal(3,544,000),stomach(1,538,000),liver (633,000), and esophagus(464,000),whereas the highest incidence was found in colorectal (1,361,000), stomach (952,000), liver (782,000), and esophagus (456,000) cancers across the globe (IARC, 2014).

Malignancies of the colorectal, stomach, esophagus, pancreas and liver have been reported in various proportions by many studies while gastric cancer was the leading gastrointestinal malignancy in Iran and Togo(Mahmoud et al.,2014; Pourhoseingholi et al.,2015; Pourhoseingholi et al.,2009; Brown and Ahnen , 201;Patel et al., 2012. Keighley, 2003; Amegbor et al., 2008).

It has also reported, GI malignancies are disreputable and frequently progressing to advanced stages even in the absence of serious symptoms and leading to delayed diagnoses and miserable prognoses

(Mahmoud et al.,2014).Thus, secondary prevention of GI malignancies through early detection and treatment of cancer-precursor/premalignant lesions had been encouraged(Mahmoud et al., 2014).

Gastrointestinal malignancy risk factors vary with the types of GI malignancies including genetic abnormalities, familial polyposis syndromes, obesity, diabetes, alcohol, cigarette smoking, dietary factors and infections including hepatitis B virus (HBV), hepatitis C virus (HCV) and *Helicobacter pylori* have been widely implicated in their aetiopathogenesis. The pattern of primary GI cancer differs in different regions of the world depending upon the genetic, cultural, dietary and socioeconomic factors(Mahmoud et al., 2014; Rozen , 2004; Brown and Ahnen , 2014; Najafi et al., 2011; Patel et al., 2012; Atrkar-Roushan et al., 2013).Basically the risk factors can be divided into modifiable and non-modifiable factors. Most modifiable risk factors are environmental, behavioral, or diet-related, while non-modifiable risk factors include heredity, age, gender, and medical conditions especially those associated with inflammation (Beth et al., 2015).

Some risk factors of the GI malignancy like smoking can be changed and others like age or family history can't be changed. Changing the risk factors including diet and physical activities can reduce the incidence of gastrointestinal Cancer by up to 75%.Unfortunately many GI cancers do not show many symptoms until they are in a more advanced stage. Some general symptoms of gastrointestinal malignancies include abdominal pain, loss of appetite, bloody stool, noticeable increase in fatigue and/or weakness, unexplained weight loss, nausea and vomiting (IARC, 2014; Cancer home, 2017).

1.1.1.1. Staging, Diagnosis and Treatment of Gastrointestinal Malignancy

1.1.1.1.1. Staging of gastrointestinal malignancy

Staging describes the extent or spread of malignancy at the time of diagnosis. Proper staging is essential in determining the choice of therapy and in assessing prognosis. A malignancy's stage is based on the size or extent of the primary tumor and whether it has spread to nearby lymph nodes or other areas of the body. A number of different staging systems are used to classify malignancy. A system of summary staging is used for descriptive and statistical analysis of tumor registry data and is particularly useful for looking at trends over time. According to this system if malignant cells are present only in the layer of cells where they developed and have not spread, the stage is in situ. If malignant cells have penetrated beyond the original layer of tissue, the malignancy has become

invasive and is categorized as local, regional, or distant based on the extent of spread (Ozsaran and Alanyali, 2013).

Moreover, the TNM system assesses malignant growth and spread in 3 ways: extent of the primary tumor (T), absence or presence of regional lymph node involvement (N), and absence or presence of distant metastases (M). Once the T, N, and M categories are determined, a stage of 0, I, II, III, or IV is assigned, with stage 0 being in situ, stage I being early, and stage IV being the most advanced disease (Chiang and Massagué, 2008; American Cancer Society, 2015).

TNM system based on the America joint committee on cancer (AJCC)/union for international cancer control (UICC), 2009, staging system for cancer (7th edition) stated primary tumor (T): Tx – primary tumor cannot be evaluated; T0 – no signs of tumor; Tis – carcinoma in situ; T1,2,3,4,- describes size and/or extension of primary tumor. N – degree of spread to regional lymph nodes; Nx – lymph nodes cannot be evaluated; N0 – tumor cells absent from regional lymph nodes; N1 – 1–3 lymph nodes metastasis; N2 – more than 4 lymph nodes metastasis. Distant metastasis (M): M0 – no distant metastasis; M1 – distant metastasis. TNM classification staging standard: I – T1/T2, N0, M0; II – T3/ T4, N0,T3N1 M0; III – any T, N1~N2, M0; IV – any T, any N, M1(Edge and Compton, 2010).

1.1.1.1.2. Diagnosis of gastrointestinal malignancy

Cancer diagnosis calls for a combination of careful clinical assessment (signs and symptoms of cancer, family history) and diagnostic investigations and procedures such as CT scan, MRI, endoscopy and laparoscopy.Once a diagnosis is confirmed, it is necessary to ascertain cancer staging to evaluate the extension of the disease and be able to provide treatment accordingly. Cancer when diagnosed early is far more likely to be treatable and to respond to effective treatment. A high proportion of cancers including GI malignancy that are relatively curable in developed countries are detected only at advanced stages in developing countries. Therefore, increased awareness among physicians and associated health care workers, the general public in developing countries combined with early and effective therapy could have a major impact on the disease (Gebremichael et al., 2016).

Similarly, the management of patients with GI malignancy requires a precise diagnosis and accurate staging information.Traditionally diagnosis of GI malignancy is made through a tissue biopsy guided by conventional light endoscopy or radiological imaging. Although, histological diagnosis remains the gold standard, increasingly sophisticated endoscopic and radiological imaging may enable physicians

to diagnose the malignancy less invasively.The staging of GI malignancy is traditionally performed with cross-sectional imaging and is more recently performed with endoscopic ultrasonography (EUS). Recent enhancements in imaging have improved the ability to accurately determine the depth and loco regional invasion of early malignancy arising from hollow and solid organs of the GI tract including malignancies of the esophagus, stomach, pancreas, small intestine, liver, and colon.Advances in Radiological Imaging including improvements in computerized tomography and magnetic resonance technology have dramatically improved the quality of imaging of many GI malignancies.This technology is now being applied to the detection and staging of GI malignancies (Kumar et al., 2004).

1.1.1.1.3. Treatment of gastrointestinal malignancy

The principal methods of treatment of cancer including GI malignancy are surgery, radiotherapy, chemotherapy (including hormonal manipulation) and psychosocial support. Surgery and radiotherapy are suitable for local and regional disease, and may affect cures in the early stages of cancer, especially when there is an early detection policy while chemotherapy may be applied in advanced forms.

The main or primary goals of a treatment program are to cure or considerably prolong the life of cancer patients and to ensure the best possible quality of life to cancer survivors. Treatment services initially target all patients presenting with curable tumors. If more resources are available, the program extended to include patients with the common cancers that are treatable but not curable. Treatment involves not only managing all aspects of the cancer itself but also the psychosocial and rehabilitation needs of the patients and their families. Psychosocial support is particularly important because in many countries cancer is greatly feared and stigmatized (Gebremichael et al., 2016). Treatment plans for gastrointestinal malignancy include a combination of surgery, chemotherapy and palliative care by taking into account many factors like lifestyle, the type and stage of malignancy (Cancer home, 2017).

One major approach to reduce GI cancer mortality is through the implementation of prevention and/or early detection strategies. Recognition of environmental and hereditary factors that predispose to a GI malignancy necessary for the successful development and application of prevention and investigation approaches (Beth et al., 2015).

1.1.2. Serum Glucose and Lipid Profile Levels in Gastrointestinal Malignancy

1.1.2.1. Serum Glucose Level in Gastrointestinal Malignancy

The metabolism of cancer patients changes gradually and affecting all metabolic pathways. As for carbohydrate metabolism, tumors shows an excessive glucose consumption and causing glucose intolerance with peripheral insulin resistance (Ehrmann-Jósko et al., 2006; Farooki and Schneider, 2007).Altered glucose metabolism in cancer patients is characterized by increased whole-body glucose turnover rate, decreased glucose uptake and utilization due to insulin resistance and increased hepatic glucose synthesis or gluconeogenesis from substrates derived from proteolysis and lipolysis.Increased Cori cycle activity or glucose carbon recycling in patients with malignant disease is well documented by several studies (Eden et al., 1984; Lundholm,1982; Burt et al.,1982).Increased whole-body glucose turnover has been documented in gastrointestinal cancer patients and this increase was proportional to the extent of the disease(Kokal et al.,1983).

High blood glucose level or hyperglycemia is a condition in which an excessive amount of glucose circulates in the blood which develops when the body has too little insulin or when the body cannot use insulin properly. A number of medical conditions can cause hyperglycemia including diabetes mellitus(Dobbs et al., 1975), obesity (Martyn et al., 2008), pancreatitis(Fogar et al., 1998) chronic stress(Mechanick, 2006) and cancer.Interestingly epidemiological evidence indicated that all of these hyperglycemia-related conditions are likely to be associated with tumorigenesis or tumor progression Hyperglycemia may also contribute to a more malignant phenotype of cancer cells and lead to drug resistance.Therefore, controlling hyperglycemia may have important therapeutic implications in cancer patients(Kaiser,2013;Raimondi et al.,2010;Feng et al., 2012)

It is also stated that Impaired Glucose Tolerance is associated with increased cancer risk and both hyperglycemia and IGT are also characterized by hyperinsulinemia. Although much convincing evidence demonstrates an association between hyperglycemia and cancer, it has yet to be demonstrated that hyperglycemia by itself is an independent risk factor. Most diabetic patients are presented with both hyperglycemia and hyperinsulinemia. Thus, it is difficult to distinguish the specific role of each abnormality in increasing cancer risk (Dankner et al. 2007).

Glucose is known to be a critical nutrient for proliferating cells. On the otherhand cellular energy metabolism is one of the main processes that are affected during the transition from normal to cancer

cells, particularly glucose metabolism is very often altered in tumor cells (Warburg, 1956; Hsu and Sabatini, 2008).

Glycolysis is a physiological response to hypoxia in normal tissues but cancer cells constitutively take up glucose and produce lactate regardless of oxygen availability, an observation that has been seen in many types of cancer cells and tumors (Koppenol et al., 2011). The increase in glycolytic change allows glycolytic intermediates to supply subsidiary pathways to fulfill the metabolic demands of proliferating cells (Lunt and Vander Heiden, 2011).Aerobic glycolysis appears to represent a selective advantage for tumor cells as they become more resistant to apoptosis and acquire increased growth and invasive properties. At present it is still unclear if the molecular mechanisms controlling the switch towards aerobic glycolysis are directly involved in the acquisition of apoptosis resistance or whether this resistance is a secondary adaptation to hypoxia of a subpopulation of transformed cells in precancerous lesions. Regardless of the mechanisms, glycolysis upregulation represents a clear advantage for cancers cells and at the same time a target for new anticancer therapies (Annibaldi and Widmann, 2010).

Researchers in the Me Can project also reported a significant increases in risk of fatal cancer per 1mmol/L (18 mg/dL) incremental in blood glucose level (Stocks et al., 2009). However, reducing hyperglycemia in individuals with type 2 diabetes has not been clearly associated with a decreased risk of developing cancer (Johnson and Bowker, 2011; Stefansdottir et al., 2011).Therefore, in obesity, diabetes, and the metabolic syndrome glucose may be playing a role in concert with hyperinsulinemia, inflammation, adipokines and altered estrogen levels(Gallagher and LeRoith, 2013).

Several prospective studies also reported an association of elevated blood glucose with increased overall cancer incidence. Impaired glucose tolerance, impaired fasting glucose and diabetes are some factors that determine various profiles of dysglycemia. Some of them postulated linear trend of increased blood glucose levels and cancer risks, even in glucose levels still within normal, prediabetes range. International study combined results from six European prospective cohorts, totaling 549,944 subjects (49% men), with mean age 45 years at baseline and a mean followup period of 11.3 years and most of presented data were adjusted for sex, age, BMI, and smoking status. The association between glucose level and cancer was approximately linear across full range of fasting glucose levels. An increase in 1 mmol/L of fasting plasma glucose (FPG) levels was associated with incidental cancer for all-site cancer incidence in men (excluding prostate cancer) and women (Stocks et al., 2009).

Moreover, the ten-year Korean prospective cohort study enrolling 1,298,385 subjects (64% men) showed a significant increase in all-cancer incidence for DM patients (Jee et al., 2005). After categorizing baseline FPG levels, linear trends in cancer incidence and mortality with increasing fasting serum glucose levels were observed in both sexes. Although, almost all cases of diabetes were expected to be type II, the Korean cohort study is noteworthy for low frequency of obesity in comparison to Western population (average BMI was 23.2 and only one-fourth of participants had BMI above 25). The actual relation between hyperglycemia and subsequent cancer risk may be difficult to assess, as there are appreciable intra-individual variations in post load and fasting glucose levels (Liu et al., 1982).

Also in a prospective study that included 1.3 million Koreans, Jee et al.,2004 reported, higher fasting blood sugar levels (140mg/dL and above) increased the risk of all types of cancer by up to 1.29 times. Specifically, they found that fasting blood sugar levels were highly associated with an increased risk of pancreatic cancer. Among men a higher fasting sugar level was strongly associated with a higher risk of cancer of the esophagus, liver, and colon/rectum, while women had a higher risk of liver and cervical cancer. The findings on the fasting blood sugar levels and cancer risk were the same for the groups with low and high BMIs. In the United States, 65% of the population is overweight and/or obese. Worldwide, obesity is in turn associated with diabetes. Findings that association of high fasting blood sugar levels and cancer risk were significant in Korea where there was no a high prevalence of obesity (Cooney and Gruber, 2005).

1.1.2.2. Serum Lipid Profile Levels in Gastrointestinal Malignancy

Lipids are major cell membrane components essential for various biological functions including cell growth and division of normal and malignant tissues (Raval et al.,2003). Lipid metabolism of cancer patients changes gradually and may cause inhibition of plasma lipoprotein lipase activity and leads to hyperlipidemia (Silva.,2006).An increased in lipolysis associated with lowered lipogenesis increased turnover of glycerol, free fatty acids and triacylglycerol which are depleted from the adipose tissues are all metabolic changes induced by advanced tumors and may be related to an increase in hormone sensitive lipase (HSL) and to the release of lipolytic tumor factors(Cerne et al., 2007).

In the body both endogenous and exogenous lipids are carried in plasma or serum in the form of lipoproteins which are water soluble particles consist of a nonpolar lipid core(triglycerides,cholesterol

esters**)** surrounded by an envelope composed of specific apolipoproteins (apo), phospholipids, and other polar lipids.Lipoproteins are commonly classified according to ultracentrifugation characteristics as HDL, LDL, intermediate-density (IDL) and very-low-density (VLDL) lipoproteins. Chylomicrons and VLDL serve as vehicles to transport triglycerides and cholesterol from the sites of absorption (intestine) and endogenous production (liver) to the sites of consumption **(**myocytes, steroidogenic glands, etc.**)** or storage (adipocyte), LDLs are responsible for the transportation of cholesterol from liver to the cells. In contrast, HDL serves as a vehicle to transport surplus cholesterol from peripheral tissues to the liver for disposal (Vaziri, 2006).

As lipoproteins are the distributors of both endogenous as well as exogenous lipids across the tissues therefore, it is suggested that deregulation of lipid metabolic pathways may affect plasma levels of lipoproteins including serum or plasma lipids of TC, HDL cholesterol, LDL cholesterol, very low-density lipoprotein cholesterol (VLDL) and TGs (Allampallam et al., 2000; Patel et al., 2004; Halton et al., 1998).

Lipid profile levels including cholesterol and triglycerides are affected by various Factors such as age, sex, genetics, certain aspects of lifestyle including diet, level of physical activity, smoking status, some medical conditions or others.These conditions can alter the lipid profile levels or may raise or lower cholesterol and triglyceride levels and caused dyslipidemia (Robert, 2013). .

Dyslipidemia is an elevation of LDL cholesterol level, low level of HDL cholesterol, high level of TC and/or elevated level of TG.Or a patient is considered to have dyslipidemia or abnormal lipid profile in the presence of the following abnormalities either singly or in combination. These include plasma TC $\geq$ 200mg/dL,TG levels $\geq$ 150 mg/dL, HDL-C (for men $\leq$ 40 mg/dL and women $\leq$ 50 mg/dl), LDL-C $\geq$ 100 mg/dL(Ogbera et al., 2009).Dyslipidemia is common in patients with obesity and type 2 diabetes.Obesity is associated with increased LDL cholesterol (Flock and Green,2011).Obese and diabetic patients also frequently have dyslipidemia with elevated circulating VLDL cholesterol and triglycerides, an increase in small dense LDL cholesterol and a decrease in HDL-C cholesterol (Chahil and Ginsberg, 2006).The Framingham Offspring cohort study showed an elevated cholesterol particularly elevated VLDL and low HDL cholesterol was associated with a greater risk of cancer (Mainous et al., 2005; Melvin et al., 2013).

In meta-analysis of study shown that an elevated total cholesterol (>6.5 mM) was associated with an 18% increased risk of cancer, elevated triglycerides (>1.71 mM) was associated with a 20% increased risk and decreased HDL cholesterol (<1.03 mM) was associated with a 15% increased risk.Studies have also reported that cholesterol-lowering therapy with 3-hydroxy-3-methyl-glutaryl-CoA (HMG CoA) reductase inhibitors is associated with a lower risk of overall cancer mortality (Nielsen et al., 2012), some studies again reporting a lowering risk of developing specific cancers including hepatocellular carcinoma (Singh et al., 2013).

The possible mechanism that the cholesterol directly contributes to cancer growth and progression is may be due to the LDL receptor (LDLR) which is widely expressed on cancer cells (Stranzl et al., 1997) and the LDLR is a major site of cholesterol uptake into cells from LDL, VLDL, and VLDL remnant (Chappell et al., 1993; Virgolini et al., 1995). In normal cells, cholesterol levels are tightly regulated by sterol regulatory element-binding protein-2 (SREBP-2) and liver X receptors (LXRs), which down regulate cholesterol uptake via the LDLR and increase cholesterol efflux (Jo and Debose-Boyd, 2010; Martini and Pallottini, 2007). In cancer cells, however, this downregulation of the LDLR does not occur and no increase in cholesterol efflux gene transcription occurs, resulting in increased intracellular cholesterol (Antalis et al.,2010;Zelcer et al.,2009).Cholesterol has been shown to increase phosphatidylinositol 3-kinase (PI3K)/Akt signaling in vitro in colon, breast, and prostate cancer cells and increased cell proliferation (Alikhani et al.,2013 ; Scheinman et al.,2013 ; Zhuang et al., 2002).

Many epidemiological studies also consistently linked the metabolic syndrome which is characterized by three or more components among abdominal obesity, high blood pressure, hyperglycemia, hypertriglyceridemia, and low HDL cholesterol (Agnoli,2014) as well as its separated components most importantly impaired glucose metabolism and obesity (dyslipidemia) with increased risk of cancer(Ahmed et al.,2006; Bjørge et al., 2010; Russo et al., 2008).Previous studies have demonstrated that almost all cancers are affected with aberrant serum or plasma lipid levels(Allampallam et al.,2000; Patel et al., 2004; Halton et al.,1998). However, there are several discrepancies in the reports regarding the association of dyslipidemia with cancers.The reasons for these inconsistencies in previous research reports might be observed due to the types of cancer or due to related confounding factors including, lifestyle, obesity (Usman et al., 2015) and effect of antineoplastic therapies (Alexopoulos et al.,1992). Also the reason for these contradictory reports could be the fact that various types of cancers exploit different modes for the acquisition of lipids that in turn affect the serum or plasma lipid profiles.For

gastrointestinal malignancies, a positive linear association has been reported between TG and risk of colon and rectal cancer (Tabuchi, 2006; Ulmer et al., 2009; Van Duijnhoven et al., 2011). In contrast, the role of TC in esophageal, stomach, colon, and rectal cancer development remains inconsistent in observational studies(Van Duijnhoven et al., 2011; Iso et al., 2009; Chyou et al., 1992). Little is known about how other specific lipid markers such as HDL cholesterol and LDL cholesterol and their components apolipoprotein A-I (apoA-I) and apolipoprotein B (apoB) affect cancer risk (Konradsen et al., 2008; Renehan et al., 2008). But some observational studies stated that low levels of serum HDL are associated with increased risk of all cancers. There are very few contradictory studies that showed that increased risk of cancer is associated with high levels of serum HDL. For instance it has been reported that women with breast cancer display high levels of HDL in comparison to the healthy women (Munir et al., 2014).To date the precise mechanism by which serum lipids contribute to the development of cancer is unknown. However, dyslipidemia enhances oxidative stress as well as chronic inflammation (Ahotupa et al., 2010; Erdelyi et al., 2009; Moustafa et al., 2012) and it is highly related to insulin resistance (Hsieh et al., 2008), all of which have been linked to carcinogenesis. Besides circulating lipids an experimental study has also shown that dietary lipids may induce local inflammation in an alimentary tract which is thought to enhance development of gastrointestinal malignancies (Ji et al., 2011). Nevertheless, evidence for a link between dietary fat and cholesterol in the development of esophageal, stomach, colon, and rectal cancer is still questionable (Mayne and Navarro, 2002; Järvinen et al., 2001; Lucenteforte et al., 2009).

However, whether lipids and lipoproteins cause these carcinogenesis processes or are intermediate or correlated or associated factors within these pathways is unknown. Similarly, dietary and lifestyle factors such as smoking (Craig etal., 1989), obesity (Lee et al., 2008), physical inactivity(Hardman, 1999) a high fat/low fiber diet (Kasim-Karakas et al., 2000) and higher alcohol consumption (Frohlich,1996) also influence lipid and lipoprotein concentrations unfavorably.Therefore, altered lipid and lipoprotein concentrations may be a consequence or corollary of an unhealthy lifestyle rather than a direct initial component cause in the chain of events leading to cancer (Fra¨nzel et al., 2011).

1.2. Statement of the problem

Cancer including GI imposes an enormous burden on society both in more and less economically developed countries.Besides almost all cancers are affected by dyslipidemia and dysglycemia (IGT and hyperglycemia) which are suggested to be associated with cancer development, progressions and mortality.Although, cancer problem including GI is a public health burden for Ethiopia and Sub-Saharan Africa at large because of aging and growth of the population as well as increased prevalence of risk factors, it is the most neglected and least prioritized health issue (Morhason-Bello et al., 2013; Stewart and Wild, 2014). Therefore, effective planning and evaluation of control measures including prevention, early detection, treatment and care of the patients require reliable and timely data in low income country like Ethiopia (Robai and Parkin, 2015).

Among all organ cancers gastrointestinal cancers (malignancies) are frequent cancers worldwide. According to GLOBOCAN 2012 report about 30% of all incident cases were attributable to GI malignancy and colorectal cancer contributed about 10% of all cancer cases which was nearly 1.4 million new cases. GI malignancy accounts for 37.0% of all cancer deaths with 9.1%, 8.8%, and 8.5%, liver, gastric, and colorectal cancers respectively, contributed after lung cancer, most to the total number of 8.2 million annual cancer deaths worldwide (Ferlay et al., 2015).

In Ethiopia the most common leading cancer among male cancers was colorectal which accounts about (19%, 1083) from the total of 5701 cancer cases registered from September 2011 to August 2014 (Assefa, 2014). Based on Addis Ababa cancer registry report, Tigeneh, 2015, reported that the prevalence of GI malignancy in Ethiopia from 1998 to 2010 was 16%, among this, 12% males and 4% females were recorded.

The above mentioned problems and despite of the problems, to the extent our knowledge, no other related studies in Ethiopia, initiates our study to evaluate and examine the glycemic level and lipid profile status in patients with GI malignancy of the study area and to give recommendations so as to minimize GI malignancy morbidities and mortalities.

1.3. Significance of the study

Based on the above mentioned problems determing fasting blood glucose level and lipid profile status of patients with GI malignancy and strategies to address and improve the evidence base for patients with dyslipidemia and hyperglycemia may important and leads to further development of clinical tools to assist in decision making,improve integration and coordination of health care, and skill development for clinicians to increase survival rate,recommend quality of life and affordable health costs of the GI malignant patients. It is also advisable to evaluate the risk factors of GI malignancy at early stage in order to design preventive actions because many causes of morbidity and mortality in relation to malignancy are controllable and manageable at an early stage.Hence, this study can some what increases pre-existing GI malignancy control knowledge of prevention, early detection, treatment, care and overall survival of the patients mainly in developing countries like Ethiopia. Thus, the people may be benefited from the result of this study. Moreover, cancer research in Ethiopia is not proportionate with the magnitude of the problem. Therefore, this study can be the base for further related studies.

2. Objective

2.1. General objective

To assess the association of glucose and lipid profile level of patients with gastrointestinal malignancy attending at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia.

2.2. Specific objectives

- To estimate the glucose and lipid profile levels of patients with GI malignancy.
- To evaluate the correlation between glycemic and lipid profile levels of patients with GI malignancy.
- To assess the associations of sociodemographic and clinicopathological characteristics with glucose and lipid profile levels of patients with GI malignancy.

3. Materials and Methods

3.1. Study Area

The study was conducted at TASH, Oncologic centre, at College of Health Science, Addis Ababa University, Addis Ababa, Ethiopia. TASH is one of the major referral and teaching hospital found in the capital and gives services for patients from every corner of the country.The oncology service in organized way was started in Tikur Anbessa Specialized Hospital since 1998 Ethiopian calendar.The hospital has 600 beds, of which 18 are allocated for cancer treatment. Annually around 2000 new cancer patients were visited the oncologic center and from 1998 to august-2014, a total of 19,151 new cancer patients were registerd and seen in the radiotherapy oncologic center of the hospital.

3.2. Study Period

The study was conducted from November 2017 to April 2018.

3.3. Study Design

The study design was hospital based cross-sectional study design.

3.4. Population

3.4.1. Source population

The source population was all patients with malignancy who visited TASH during the study period.

3.4.2. Study population

The study population was all patients with gastrointestinal malignancy, attending at TASH during the study period.

3.4.3. Study participants

The study participants were all patients with histologically confirmed gastrointestinal malignancy, attending at TASH during the study period and fulfilling the inclusion criteria.

3.5. Inclusion and exclusion criteria

3.5.1. Inclusion Criteria

- All patients with histologically confirmed gastrointestinal malignancy.
- All patients $\geq$ 18 years of age
- Patients who were willing to give consent.

3.5.2. Exclusion Criteria

- Patients with chronic diseases including **DM, HTN, TB, HIV, Thyroid disease** and others.
- Patients on lipid lowering medications.
- Patients with no informed consent

3.6. Sampling methods and sample size determinations

Purposive sampling technique was implemented to select the health care facility and simple random sampling technique from oncologic clinic ward was used to get the calculated number of study participants in the study period. By using semi-structured questionnaire, the patients were selected that include all pieces of information of patients needed for study variables.The sample size was determined using single population proportion formula with a confidence interval (CI) of 95%) and based on prevalence of gastrointestinal malignant patients(16%) in Ethiopia as reported by case based registry in Tikure Anbessa Specialized Hospital(Tignehe, 2015).

$$n = \frac{(Z1\text{-}\alpha/2)p(1\text{-}P)}{d^2} = 227$$

Where **n** is minimum sample size required; **Z1-α/2** is the standard normal variable at (1-α) % confidence level and α (level of significance), Usually 95% confidence level is used =1.96; **P** is estimate of the prevalence rate of gastrointestinal malignant patients in the population; **d** is the margin of sampling error tolerated, assume to be 0.05. Therefore, n after adjustment is approximately 227 patients but due to budget constraint and lack of well documented population based prevalence studies in Ethiopia, seventy (70) patients were selected and enrolled.

3.7. Study Variables

3.7.1. Independent Variables

- Sociodemographic characteristics of the patients
- BMI
- Personal medical and family history of malignancies
- Clinic-pathological characteristics of the patients

3.7.2. Dependent Variables

- Serum fasting glucose, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol and triglycerides levels in patients with GI malignancy.

3.8. Blood Sample and Data Collection Procedures

First, the study participants were asked for their consent to be interviewed and give blood sample. Five-mL of blood sample was withdrawn from the study participants who had fasted overnight by qualified health care professionals in the hospital, at the Oncologic clinic ward for the immediate laboratory analysis of the blood sample. The Blood that was collected in appropriate tubes, allowed to stand for 30 minutes at room temperature for complete clotting and clot retraction. Samples were then centrifuged at 3500 rpm (revolutions per minute) for 5 minutes in Hu Max human standardized centrifugation machine to extract serum.The extracted serum was then immediately used to determine the levels of FG, TC, HDL-c, LDL-c and TG.

3.9. Principlesof the Biochemical Laboratory Analysis

After fasting blood sample had been collected, centrifuged and sparate the serum.All the biochemical analytes ofserum glucose and lipid profile levels of the patients were analyzedusing commercially available human linear chemistry reagents and Mindri-2000 chemistry autoanalyzer machinewhich works on enzymatic spectrophotometric principle.The instructionsprovided by the manufacturer and/ or the standard procedure or protocol were strictly followed to minimize discrepancyof the analysis.

3.9.1. Principles of fasting blood glucose level measurement

Fastingblood glucose level was determined by usingthe glucose oxidase methodsand in principle the normal reaction of glucose oxidase is shown below:

$$\beta\text{-D- Glucose} + {}_{1/2}O_2 + H_2O \xrightarrow{\text{GOD}} \text{D-Gluconic acid} + H_2O_2$$

$$2H_2O_2 + \text{4-Aminoantipyrine} + \text{Phenol} \xrightarrow{\text{POD}} \text{Red quinoneimine dye} + 4H_2O\ (\text{water})$$

The glucose is oxidized to gluconic acid and hydrogen peroxide in the presence of glucose oxidase (GOD.) Hydrogen peroxide further reacts with phenol and 4-aminoantipyrine by the catalytic action of peroxidase (POD) to form a red-colored quinonemine dye complex. Intensity of the color formed is directly proportional to the amount of glucose present in the sample.

3.9.2. Principles of serum lipid profile status measurements

Lpid profile measurments of TC, TG, HDL-c and LDL-C were determined through enzymatic methods by using human commercial labteste reagents on a Minderi-2000 auto-analyser chemistery machine. Serum TC and TG were quantitatively determined by a colorimetric method and HDL and LDL were determined in a homogenous assay with a colorimetric end point. LDL-c level could also be obtained through the Friedewald equation from measurement of total and HDL cholesterol and triglycerides (Friedewald et al., 1972). The lipid profile assays employs wet chemistry and photometric technology to perform absorbance readings which measure the color of the sample. The absorbance is converted automatically into concentrations based on the standard calibration curves stored by the instrument's microprocessor (Sblendorio and Palmieri, 2008).

3.9.2.1. Serum total cholesterol level

Cholesterol wasmeasured in serum and in a series of coupled reactions that hydrolyze cholesteryl esters and oxidize the 3-OH group of cholesterol. In principle, one of the reactions by product, H2O2 is measured quantitatively in a peroxidase catalyzed reaction that produces a color. Absorbance is measured at 500 nm. The color intensity is proportional to cholesterol concentration. Desirable or normal cholesterol levels were considered to be those below 200 mg/dL. The reaction sequence is as follows:

Cholesterol esters in the sample are enzymatically cleaved by the cholesterol esterase (CHE) into free cholesterol and fatty acids. Further oxidation by cholesterol oxidase (CHO) origins cholest-4-ene-3-one and hydrogen peroxide (H2O2) which in presence of a peroxidase (POD) converts phenol and 4-aminophenazone (4-AP) into a red substance (quinoneamine). The intensity of the color of this substance is directly proportional to the cholesterol concentration. In the HDL test, VLDL and LDL fractions are precipitated with a polianionic buffer.There after enzymes react only on the HDL fraction present in the supernatant fraction obtained by centrifugation (Sblendorio and Palmieri, 2008).

Cholesterol ester → CHE→Cholesterol + Fatty acids

Cholesterol + O2 → CHO →4-Cholesten-3-one + H2O2

H2O2 + PhOH+ 4-AP → POD → QuinoneamineRED + H2O (water)

3.9.2.2. Serum triglycerides level

Triglyceride was alsomeasured in serum using a series of coupled reactions. Inprinciples, triglycerides are hydrolyzed to produce glycerol. Glycerol is then oxidized using glycerol oxidase, and H2O2, one of the reaction products, is measured as described above for cholesterol. Absorbance is measured at 500 nm. The reaction sequence is as follows:

Triglycerides are converted by lipoprotein lipase to fatty acids and glycerol. Glycerol then in the presence of glycerol kinase (GK), ATP and glycerol-oxidase (GPO) produces H2O2 and dihydroxy-acetonphosphate (DHAP). H2O2 in the presence of 4-AP and the sensitive chromogen subsequently produces a red phenolic derivative using POD. The intensity of the color of the red substance is directly proportional to the triglycerides concentration in the sample (Sblendorio and Palmieri, 2008):

Triglycerides + 3H2O → LIPASE → Glycerol + Fatty acids

Glycerol + ATP → GK → Glycerol-3-phosphate + ADP

Glycerol-3-phosphate + O2+H2O → GPO → DHAP + H2O2

2H2O2 + 4-AP + R-OH → POD → Complex (red) + H2O

3.9.2.3. High density lipoprotein (HDL) cholesterol level

HDL was measured directly in serum andthe basic principle of the method is as follows. The apoB containing lipoproteins in the specimen are reacted with a blocking reagent that renders them non-reactive with the enzymatic cholesterol reagent under conditions of the assay. The apoB containing lipoproteins are thus effectively excluded from the assay and only HDL-cholesterol is detected under the assay conditions.The method uses sulfated alpha-cyclodextrin in the presence of Mg+2, which forms complexes with apoB containing lipoproteins, and polyethylene glycol-coupled cholesteryl esterase and cholesterol oxidase for the HDL-cholesterol measurement. The reactions are as follows:

1. Apo-B containing lipoproteins + α-cyclodextrin + Mg^{+2} + dextran SO_4 gives soluble non-reactive complexes with apolipoprotein-B containing lipoproteins.

2. HDL-cholesteryl esters →PEG cholesteryl esterase→HDL-unesterified cholesterol + fatty acids.

3. Unesterified cholesterol + O_2 → PEG cholesterol oxidase→Cholestenon + H_2O_2.

4. H_2O_2 +5-aminophenazole + N-ethyl-N-(3-methylphenyl)-N' Succinyl ethylene diamine + H_2O + H^+ peroxidase →qunoneimine dve + H_2O.Absorbance is measured at 600 nm.

3.9.2.4. Low density lipoprotein (LDL) cholesterol level

LDL-cholesterol was measured directely and/or calculated from measured values of total cholesterol, triglycerides and HDL-cholesterol according to the relationship: LDL-cholesterol = Total cholesterol - HDL-cholesterol –(TG/5) where TG/5 is an estimate of VLDL-cholesterol and all values are expressed in mg/dL. Desirable levels of LDL-cholesterol are those below 100 mg/dl in adults.

The lipid profile test results were classified following the national cholesterol education program (NCEP) values, according to which, total cholesterol levels <200mg/dL are desirable; levels ranging from 200 to 239mg/dL are borderline high; and levels ≥240mg/dL are high.For triacylglycerols, values are considered normal when <150mg/dL; borderline when ranging from 150 to 199mg/dL; high when ranging from 200 to 499mg/dL; and very high when ≥500mg/dL.For HDL cholesterol, levels were considered low when<40mg/dL; normal when ranging from 40 to 59mg/dL; and high if ≥60mg/dL. For LDL cholesterol, values described as optimal were <100mg/dL; borderline optimal when ranging from 100 to 129mg/dL; borderline high when ranging from 130 and 159mg/dL; high when ranging from 160 to 189mg/dL; and very high if >190mg/dL (NCEP, 2002).

3.10. Body Mass Index Measurement.

The Body Mass Index (BMI) of the patients was measured and calculated from the body weight (kg) and height (meter): BMI =Weight (kg) / Height $(m)^2$ (Tambe *et al*.,2010). Based on the WHO classifications (WHO, 1997) four categories of BMI can be identified: underweight,<18.5 kg/m2; normal, >18.5–24.9 kg/m2; overweight, >25.0–29.9 kg/m2; and obesity, >30 kg/m2.

3.11. Data quality control and management

- The data collection questionnaire was well prepared and all variables were filled on the data extraction format daily.
- All the laboratory procedures were handled by professional laboratory technologists and all the tests were standardized and automated.

3.12. Data processing and analysis

After checking for completeness of the data, processing and analysis of the data obtained from questionnaires and laboratory analyses of the blood samples was performed by entering the data into SPSS software version 23.0 package and then the different variables were tested and analyzed. Simple descriptive statistics were used to present the sociodemographic, BMI, personal medical and family history of malignancy and clinic-pathological characteristics of the study subjects. Chi-square ($\chi 2$) tests were used to compare categorical variables while continuous variables were presented as mean ± standard deviation and were compared using the student t-tests for groups. Other associations were performed with Pearson's correlation coefficient as well as one way ANOVA test analysis. A p-value of <0.05 at 95% confidence interval was considered to be statistically significant in all the analyses.

3.13. Ethical consideration

Before starting data collection and preliminary study, ethical clearance letter was obtained from the Departmental Research and Ethics Review Committee, Department of Biochemistry, College of Health Sciences, Addis Ababa University. Besides collaboration letter for data collection was obtained from TASH.Moreover, the objective of the study was briefly clarified and explained for each participant before enrolling any of the eligible study participants. Samples and data were collected after informed consent had been obtained from the study participants, and were coded.

3.14. Operational definitions

Cancer differentiation grades refers to the graded classification of tumors, according to how differentiated the tumor is. Usually there are three or four grades.There are differences in cancer differentiation. A tumor that closely resembles the structure of the tissue it started in is described as very differentiated. Thus, the closer the structure of the cancer cell is to that of a normal cell structure, the better it is differentiated. A tumor that resembles the original tissue to a lesser extent is termed poorly differentiated, or anaplastic.When cancer cells are poorly differentiated, it can complicate identifying the tissue they started in and targeting treatment. Many tumors are divided into three grades of differentiation.

Well differentiated, Grade 1: Mostly resembles normal tissue and usually has a good prognosis

Moderately differentiated, Grade 2; Intermediate forms of tumor with both good and bad prognosis

Poorly differentiated, Grade 3 and undifferentiated, Grade 4: Tumors spread easier than other tumors, and their prognosis is a little worse than for others.

Tumors are classified by histological type: meaning according to the type of tissue in which the tumor starts because among other things, it affects the choice of treatment.

Adenocarcinoma: This is a type of carcinoma that starts in cells called "glandular cells." These cells make mucus and other fluids. The glandular cells are found in different organs in your body.Adenocarcinomas can occur in different parts of the body. Among GI adenocarcinoma is common in lower part of esophagus, gastric, colon and rectal aea.

Squamous cell carcinoma: Most people think of skin cancer when they hear the words "squamous cell carcinoma." And it is true that this type of carcinoma often shows up on the skin. But squamous cell carcinoma can also be found in other parts of the body, such as cells lining: squamous cell carcinomas (SCCs), also known as epidermoid carcinoma, comprise a number of different types of cancer that result from squamous cells. These cells form the surface of the skin and lining of hollow organs in the body and line the respiratory and digestive tracts.Among GI (SCC) is common especially in buccal mucosa, esophageal and anual area.

4. RESULTS

4.1. Sociodemographic characteristics and dependent variables of the GI patients

The present study enrolled 70 gastrointestinal malignant patients (44.3%) males and (55.7%) females. The mean age of the gastrointestinal malignant patient was 45.39 years which ranges from 18 to 70 years. There was a significance mean difference ($p<0.05$) in age of males (51.06±12.299, ranges from 29 to 69years) and females (40.87±12.649 ranges from 18 to 60 years). Majority of the patients were found within 40-70 years.The highest percentage of patients were coming from Oromia regions (35.7%) followed by Addis Ababa (31.4%), Amahara (17.1%) and Debub (11.4%). While higher percentage (74.3%) were Urban resident and married (74.3%). As far as educational, occupation and economic status of the patients is concerned (28.6%) illiterate, (28.6%) elementary or junior, (22.9%) high school and (20%) college and above; (57.14%) low economic status<1500 per month, (37.14%) high economic status (> or = 2917 per month) and the rest (20%) had medium economic status of from 1500 to <2917 per month were found. Moreover, (65.7%) unemployed, (61.4%) non alcohol drinkers, (95.7%) non smokers and (81.4%) without regular physical activity history while (38.6%) alcohol drinkers, (4.3%) cigarette smokers and (18.6%) with regular physical activity history were found.As compared to female patients more male drinkers, smokers and with regular physical activity history were observed (Table 1).

Table 1: Sociodemographic characteristics of the gastrointestinal malignant patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, November 2017 to April 2018.

Variables		Males (n=31)	Females (n=39)	Total (n=70)(%)
Age		51.06±12.299	40.87±12.649	45.39±13.412
Smoking status	Yes	3	0	3(4.3)
	No	28	39	67(95.7)
Alcohol consumption	Yes	18	9	27(38.6)
	No	13	30	43(61.4)
Physical exercise	Yes	8	5	13(18.6)
	No	23	34	57(81.4)

Variables		Males (n=31)	Females (n=39)	Total (n=70)(%)
Region	Oromia	13	12	25(35.7)
	Addis Ababa	13	9	22(31.4)
	Amhara	2	10	12(17.1)
	Debub	2	6	8(11.4)
	Others	1	2	3(4.3)
Residence	Rural	8	9	17(24.6)
	Urban	23	29	52(75.4)
Educational status	Illiterate	9	11	20(28.6)
	Elementary	5	6	11(15.7)
	Junior	4	5	9(12.9)
	High school	7	9	16(22.9)
	college	2	2	4(5.7)
	Above college	4	6	10(14.3)
Occupation	Employed	15	8	23(32.9)
	Unemployed	15	31	46(65.7)
Economic status Ref.(Lin et al.,2015)	Low<1500/month	17	20	37(52.9)
	Medium 1500 to 2917/month	3	10	13(18.6)
	High>2917/month	11	9	20(28.5)

Age, continuous variable, is expressed as mean ± standard deviation; for the rest of the variables, qualitative,expressed as percent.

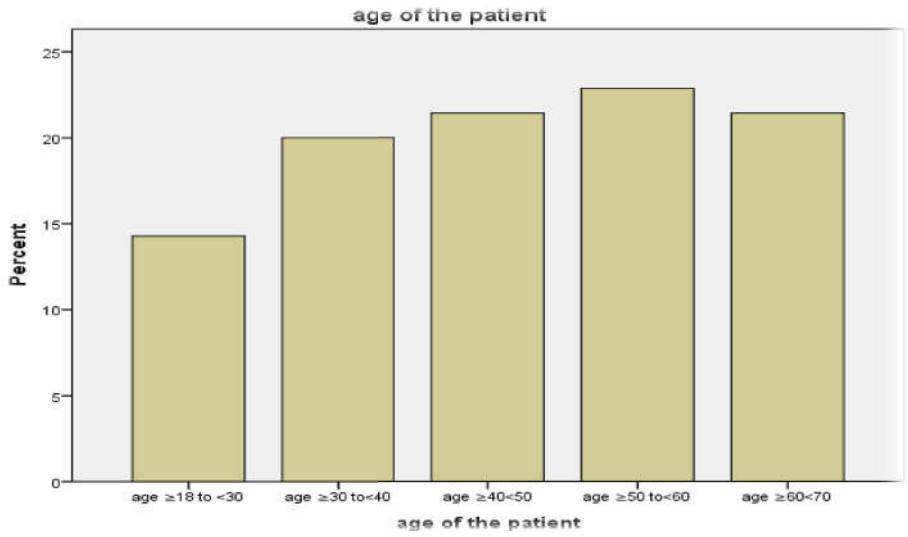


Figure 1: Age distributions of the gastrointestinal malignant patients in years.

The bivariate pearson correlation analysis exhibited that age was positively correlated with serum FBS (r= 0.136, p>0.05) and negatively correlated with lipid profile of TC, TG, HDL-C, LDL-C(r= -0.176 -0.084, -0.186 and -0.131, respectively, p>0.05).

The mean difference of FBS between different sex and age groups were insignificant. However, higher mean of FBS in males (115.63±37.646) than females (101.79±22.193), and the highest mean of FBS in the age of 40-49 years (116.67±33.07) and the least mean of FBS in the age of 18-29 years (93.80) were noted. On the other hand, higher mean lipid profiles in males than females were found. Besides, statistically insignificant mean difference of lipid profiles in different age groups except significant mean difference in HDL-C of the second (30-39years)(47.86± 12.031) and fifth(60-70 years) (38.47± 9.125) age subgroups were also found(Table 2).

Likewise, independent sample t- test analysis revealed insignificant mean difference of FBS and lipid profiles in patients who were and were not doing regular physical activities. Nevertheless, abnormally higher FBS,lower norma TC, TG and LDL-C and higher normal HDL-C levels in patients who were doing regular physical activities than patients who were not doing regular physical activities were observed. Patients who were not doing regular physical activities had abnormally high but lower FBS, abnormally higher LDL-C, lower normal HDL-C and higher normal TC and TG levels(Table 2).

In addition, the independent sample t- test revealed significance mean difference in the levels of FBS ($p<0.05$) and insignificance mean difference in the levels of lipid profiles ($p>0.05$) in patients of alcohol drinkers and cigarette smokers versus none alcohol drinkers and cigarette smokers. However, higher levels of FBS, TC, HDL-C, LDL-C, and lower levels of TG in alcohol drinkers, lower levels of lipids profile and higher levels of FBS in cigarette smoker patients were found. Overall, relatively, alcohol drinkers patients had abnormally higher FBS and LDL-C levels above the cut off value, higher normal HDL-C and lower normal levelsof TG than none alcohol drinkers patients and had lower normal FBS, HDL-C and LDL-C levels and high normal TG level. However, both alcohol drinkers and none alcohol drinkers patients had comparable level of TC. Likewise, cigarette smoker patients had abnormally higher FBS, abnormally lower HDL-C and lower normal TC,TG and LDL-C levels than none smokers who had abnormal and high FBS, LDL-C, and normal TC,TG and HDL-Clevels (Table- 2).

Furthermore, the FBS and lipids profile levels of the patients were evaluated by residents, educational background, occupation and economic status and the chi-square test, bivariate Pearson correlation analysis and independent sample t- test analysis revealed, no significant mean difference of FBS and lipids profile levels of the patients between urban and rural residents. However, higher FBS, HDL-C and almost equal but higher LDL-C and lower TC, TG levels in urban than rural residents were observed. Similarly, insignificant mean difference of FBS and lipid profile levels between different educational status was found. Nonetheless, abnormal and lower mean FBS in illiterate and elementary school patients than college and above college educations were noted. On the other hand, the mean TC levels of patients with college and above college educations were lower than patients with elementary school and illiterate educationas.Likewise, the meanTG levels of patients with college and junior school were lower than illiterate and elementary school educations.As compared to patients of above college, junior and high school educations, college and elementary school educational status patients had lower mean of HDL-C levels. Equally, the mean LDL-C levels of patients with illiterate and elementary school educations were abnormal and higher than junior and college educations (Table 2).

Moreover, the independent sample t-tests analysis exhibited significantly higher mean FBS levels of employed patients than unemployed (121.41 ± 41.562 versus 101.70 ± 21.438,($P<0.05$), respectively) While it exhibited statistically insignificant higher mean levels of (TC,TG and LDL-C) and lower

HDL-C in unemployed patients when compared to employed ones (TC; 170.80 v 157.52, TG; 128.80 v 109.13, HDL-C; 42.04 v 42.22, LDL-C; 106.72 v 95.22, respectively)

Furthermore, the mean FBS and lipid profiles showed insignificant difference in patients of different economic status subgroups except in FBS of patients with low and high economic status. As compared to low economc status, significantly higher mean FBS in high economic status patients was found. Likewise, relative to high economic status, low economic status patients had higher mean of TC, TG and lower mean HDL-C, LDL-C levels though, it was not statistical significant (Table 2).

Table-2: Fasting glucose and lipid profile levels of the GI malignant patients by sociodemographic characteristics.

Variable		FBS	TC	TG	HDL-C	LDL-C
sex	Male	115.63±37.646	159.03±38.890	112.68±48.934	41.77±10.016	94.97±24.020
	Female	101.79±22.193	172.54±46.525	129.13±60.287	42.41±12.839	109.36±47.11
	P-value	0.061	0.199	0.223	0.822	0.126
Age groups	18-29(10)	93.80±14.650	180.70±26.684	143.20±40.080	42.60±12.020	101.30±31.248
	30-39(14)	104.93±19.21	179.07±43.214	108.50±73.207	47.86±12.031	124.07±57.253
	40-49(15)	116.67±33.07	158.53±47.148	117.73±47.146	40.67±13.704	92.73±33.879
	50-59(16)	110.25±24.34	150.56±53.062	126.63±66.884	41.63±10.340	97.06±40.399
	60-70(15)	108.43±47.04	170.53±35.100	119.07±41.82	38.47±9.125	101.00±18.52
	Total(70)	107.81±30.45	166.56±43.535	121.84±55.77	42.13±11.597	102.99±39.048
	P –value	0.470	0.290	0.656	0.271	0.238
Residents	Rural(17)	99.82±24.267	170.82±35.804	135.94±57.855	41.12±12.888	101.47±27.139
	Urban(52)	110.22±32.276	164.81±46.327	116.81±55.285	42.15±11.161	101.98±41.360
	p-value	0.228	0.627	0.225	0.750	0.962

Variable		FBS	TC	TG	HDL-C	LDL-C
Educational Status	Illiterate (20)	100.74±22.600	180.80±41.591	128.90±58.967	41.40±11.900	112.40±49.181
	Elementary (11)	101.55±22.788	171.82±54.308	149.73±62.455	38.18±10.352	109.27±38.299
	Junior school(9)	108.78±57.008	159.67±29.343	100.44±37.125	44.11±11.688	97.89±19.323
	High school(16)	110.56±20.575	162.06±40.328	120.44±57.426	44.88±9.507	98.50±39.709
	College(4)	120.00±27.520	134.00±54.154	83.00±13.736	36.50±13.178	77.00±36.633
	Above College(10	118.00±34.817	158.70±45.174	114.10±55.933	44.00±15.085	99.40±30.409
	p-value	0.654	0.393	0.259	0.605	0.612
Occupations	Unemployed (46)	101.70±21.438	170.80±44.382	128.80±58.744	42.04±11.817	106.72±44.537
	Employe d (23)	121.41±41.562	157.52±42.252	109.13±48.903	42.22±11.662	95.22±25.107
	p-value	0.012	0.238	0.171	0.954	0.255
Economic status	Low(37)	101.67±20.140	167.97±45.922	128.78±53.763	40.81±11.257	100.73±44.014
	Medium (13)	104.23±16.361	166.31±35.778	100.77±37.524	45.38±11.080	105.85±36.157
	High (20)	121.20±46.194	164.10±45.481	122.70±67.317	42.45±12.651	105.30±31.934
	p-vale	0.061	0.951	0.300	0.475	0.880
Physical activity	No(57)	106.38±30.427	167.11±43.803	123.91±57.775	41.53±11.556	104.26±40.491
	Yes(13)	114.00±30.997	164.15±44.005	112.77±46.888	44.77±11.868	97.38±32.778
	P-value	0.420	0.827	0.520	0.367	0.570
Alcohol	No(43)	99.48±20.646	166.51±44.465	125.84±54.536	40.58±10.839	99.44±30.995
	Yes(27)	120.78±38.295	166.63±42.849	115.48±58.154	44.59±12.525	108.63±49.40
	p -value	0.004	0 .991	0.454	0.160	0.342
Smoking status	No(67)	105.82±24.605	166.99±43.94	122.37±56.84	42.58±11.586	103.63±39.793
	Yes(3)	174.50±118.08	157.00±38.974	110.00±21.071	32.00±7.000	88.67±5.033
	P-value	0.001	0.701	0.710	0.123	0.520

Data are expressed as Mean ±SD; P value ≤0.05 is statistically significant

4.2. BMI, Personal medical, family history, dependent variables of the GI patients

The present study revealed that the average BMI of the (67) study participants was low-normal (19.68 Kg/m2).Highest percentage of the patients (47.8%) had a body mass index from18.5 to < 25 kg /m2 or normal, (43.3%) less than 18.5kg/m2 which is underweight and few (8.9%) had more than 25 but<30 kg/m2 or overweight which showed obesity. As compared to female (5.9%) lesser percentage of male patients (2.9%) were affected by overweight. In the study 0% obese patients was found.

Besides significant mean difference of BMI (P<0.05) between site specific GI malignant patients of esophageal, gastric, colonic, rectal and pancreatic were observed.The BMI of colonic, rectal and pancreatic malignant patients were normal whereas, esophageal and gastric malignant patients' BMI were below normal and the lowest BMI was found in esophageal malignant patients. Furthermore, the patients in our study had no personal and family history of malignancy or cancer. Also from the (62) study participants equal percentages of patients (12.9%) had acute illness and surgical operation history within the past two months before the day of data collection were observed (Table 3).

Table 3: BMI, Personal medical and family history of the gastrointestinal malignant patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, November 2017 to April 2018.

Variables		Males (n=31)	Females (n=39)	Total (n=70)(%)
Personal history	No	30	38	68
	Yes	0	0	0
Family History	No	31	39	70
	Yes	0	0	0
Acute illness	No	26	36	62(88.6)
	Yes	5	3	8(11.4)
Surgery done	No	28	34	62(88.6)
	Yes	3	5	8(11.4)
BMI (M-30,F-37-67)	Mean and SD	20.507±3.195	19.0035±4.26865	19.6767±3.87181
	<18.5kg/m2	8	21	29(43.3)
	18.5 to<25kg/m2	20	12	32(47.8)
	25 to <30kg/m2	2	4	6(8.9)
	≥30kg/m2	0	0	0

Variable	Esophageal	Gastric	Colonic	Rectal	Pancreatic	p-value
BMI	15.91±2.02980	18.186±3.17	20.725±3.683	20.74±4.158	20.63± 5.4588	0.024

(Table 3)Continuous variable,is expressed as mean ± standard deviation; for the rest of the variables, qualitative, the numbers are in percent out of the total 70 patients.

The body mass index of the patients and its relationship with serum fasting glucose and lipids profile levels were assessed and pearson correlation analysis revealed that BMI was positively correlated with FBS and lipids profile levels of the patients (FBS, $r=0.332$, $p<0.05$; TC, TG, HDL-C, LDL-C: $r=$ 0.161, 0.154, 0.261, 0.190, respectively, $p>0.05$, with statistically significant positive correlation or association with HDL-C level, $p<0.05$).By the same token, BMI was positively correlated with FBS and lipids profile without statistical significe except HDL-C level. In addition the results of present study revealed the mean FBS level of patients with underweight BMI was normal.Whereas, the mean FBS levels of patients with overweight and normal weight BMI were abnormally high and within impaired fasting glucose level range.Similarly the mean lipids profile levels of overweight patients except HDL-C levels were abnormal and higher above the cut off value than underweight and normal weight patients while the HDL-C level was within higher normal range. Moreover a higher normal TG and abnormally lower HDL-C levels in underweight than normal weight patients were observed. Besides relatively the mean TG and HDL-C levels of patients with underweight, normal weight and overweight BMI were significantly different($p<0.05$).Likewise the mean difference of TG and LDL-C in overweight and underweight patients were significant($p<0.05$).Whereas the mean difference of FBS, TC and LDL-C in the three BMI subgroups were not statisticaly significant($p>0.05$). As compared to underweight, overweight patients had abnormal and higher meanTG and LDL-C levels (Table 4).

The mean FBS, TC, TG, HDL-C and LDL-C of the gastrointestinal malignant patients by presence and absence of acute illness and surgery within the past two months before the day of data collection were also assessed and the independent sample t_ test showed no statistically significant difference($p>0.05$). However, higher FBS and lower TG levels in patients with acute illness and surgery, lower HDL-C level in patients with acute illness, lower TC and LDL-C levels in patients with surgery were found. Overall, patients with acute illness and surgery had higher mean FBS and lower lipid profile levels except HDL-C, while the mean HDL-C level was comparable (Table 5).

Table 4: fasting glucose and lipid profile levels of the gastrointestinal malignant patients by BMI.

Variables		FBS	TC	TG	HDL-C	LDL-C
BMI groups	<18.5kg/m2(29)	99.04±22.754	163.14±42.308	122.24±45.772	38.38±11.995	99.34±31.839
	18.5 to <25(32)	113.25±33.47	163.41±43.783	110.28±55.169	44.69±10.443	102.69±45.83
	25-30kg/m2(6)	120.67±44.83	201.67±48.028	173.33±85.710	49.50±12.818	132.00±31.27
	Total(67)	107.89±31.09	166.72±44.232	121.10±56.394	42.39±11.787	103.87±39.65
	p-value(29,32,6)	0.120	0.127	0.040	0.032	0.182
	p-value(29,32)	0.063	0.981	0.363	0.032	0.744
	p-value(29,6)	0.089	0.055	0.042	0.049	0.028
	p-value(32,6)	0.639	0.061	0.024	0.323	0.144

Data are expressed as Mean ±SD; P value ≤0.05 is statistically significant

Table 5: Fasting glucose and lipid profile levels of the gastrointestinal malignant patients by acute illness and surgery within the previous two months of data collection date.

Variables		FBS	TC	TG	HDL-C	LDL-C
Acute illness < 2- months	No(62)	106.30±31.014	166.74±45.466	123.16±56.921	42.68±11.782	103.00±40.90
	Yes(8)	119.38±24.319	165.13±25.809	111.63±47.869	37.88±9.628	102.88±21.11
	p -value	0.256	0.922	0.586	0.273	0.993
Surgery done < 2-months	No(62)	107.64±32.013	168.76±44.752	123.65±58.308	42.06±11.701	104.73±39.05
	Yes(8)	109.13±14.913	149.50±29.228	107.88±27.956	42.63±11.501	89.50±38.789
	p -value	0.898	0.242	0.456	0.899	0.303

Data are expressed as Mean ±SD; P value ≤0.05 is statistically significant

4.3. Clinicopathological characteristics and dependent variables of the GI patients

Out of the study participans (14.3%) esophageal, (15.7%) gastric, (38.6%) colonic, (24.3%) rectal, (4.3%) pancreatic, (1.4%) hepatocellular and (1.4%) hepatoblastoma malignant patients were found. The male to female figures of site specific GI malignancies were: 2/8 esophageal, 6/5 gastric, 11/16

colonic, 10/7 rectal, 1/2 pancreatic malignant patients. Majority were affected by colonic followed by rectal, gastric and esophageal while least of them were affected by pancreatic, hepatocellular and hepatoblastoma malignancies. Higher proportion percentages of females were affected by esophageal, colonic and pancreatic while males were affected by gastric and rectal malignancies.

In addition, most of the patients (55.9%) had stages III (malignancy of lymph node involvement) (36.8%) stage IV (distance metastasis malignancy), least (7.4%) stage II malignancy and the rest (2.9%) missing stage.

Moreover, histological classification and type of differentiation of the malignancies were also assessed and found (86.4%) adenocarcinoma, (13.6%) squamous cell carcinoma. Most patients (56.1%) had also well differentiated malignancy followed by (24.2%) poorly differentiated and (19.7%) moderately differentiated malignancy, and the rest (5.7%) missing.

Furthermore, our result showed, (33.3%, M1) pathological evidence of metastasis, (59.4%, M0) no evidence of metastasis or without metastasisand and (7.2%, MX) presence of distant metastasis cannot be assessed or is unknown status. Clinically equivalent percentage of patients was diagnosed with lymph node involvement and distance metastasis of malignancy. Besides, (49.3%, NX) unknown lymph node involvement status,(40.6%, N1 and N2) pathological lymph node involvement and 7(10.1%, N0) nodes were assessed and there was no pathologic evidence of regional lymph node metastasis.As compared to (13.0%, N2(more than four lymph nodes involvement)), higher percentage of patients (27.5%) had N1(1-3 lymph node involvement of the malignancy).

As far as primary tumor size of the malignancy is concerned, (52.2%) T3, (31.9%) T4, (13.0%) T2 and (2.9%) TX (unknown primary tumor size of the malignancy) was distinguished.Where (T1-T4) describes an increasing size and/or local extent of the primary tumor.

In addition, the mean chemotherapy cycle of (51) patients was also considered and exhibited, 3.82 cycles, 3.76 cycles in males and 3.88 cycles in females. Most of the patients had taken less than or equal to 7 cycles of chemotherapy which accounts for (86.3%) valid value. Moreover, the mean duration of sign and symptoms or manifestations of the patients in months was 19.00 ±13.544 without significance difference between male and female patients **(**Table 6).

Table 6: Clinicopathological characteristics of the gastrointestinal malignant patients.

Variables		Males (n=31)	Females (n=39)	Total (n=70)(%)
Type of GI malignancy	Esophageal	2	8	10(14.3)
	Gastric	6	5	11(15.7)
	Colonic	11	16	27(38.6)
	Rectal	10	7	17(24.3)
	Hepatocellular	1	0	1(1.4)
	Hepatoblastoma	0	1	1(1.4)
	Pancreatic	1	2	3(4.3)
Stages of the GI malignancy	Stage II	2	3	5(7.4)
	Stage III	18	20	38(55.9)
	Stage IV	10	15	25(36.7)
Tumor size(T) Pathological	T2	2	7	9(13.0)
	T3	16	20	36(52.2)
	T4	11	11	22(31.9)
	TX	1	1	2(2.9)
Lymph node Involvemen(N) pathological	NO	1	6	7(10.1)
	Yes	12	16	28(40.6)
	NX	17	17	34(49.3)
	N1	9	10	19(27.5)
	N2	3	6	9(13.0)
Metastasis status (M) pathological	No	18	23	41(59.4)
	Yes	11	12	23(33.3)
	MX	1	4	5(7.2)
Histological classification	Adenocarcinoma	26	31	57(86.4)
	Squamous cell carcinoma	4	5	9(13.6)

Variables		Males (n=31)	Females (n=39)	Total (n=70)(%)
Types(differentiation)	Well differentiated	17	20	37(56.1)
	Moderatelydifferentiated	6	7	13(19.7)
	Poorly differentiated	7	9	16(24.2)
Number of cycles of chemotherapy	Cycles in months	3.76±3.153	3.88±3.637	3.82±3.375
	number of patient	25	26	51
Duration of sign and symptom	Duration in months	19.30±12.959	18.76±14.156	19.00±13.544
	number of patient	30	38	68

(Table 6)Continuous variables are expressed as mean ± standard deviations; for the rest of the variables, qualitative, expressed as percent.

The present study were also assessed the associations of mean serum fasting glucose and lipid profile levels of gastrointestinal malignant patients by specific anatomic sites, stages, type of differentiation and other clinicopathological characteristics of the patients(Table 7).

The results revealed that comparatively the mean FBS of esophageal, gastric, colonic, rectal and pancreatic malignant patients were significantly different ($p<0.05$), whereas, the mean difference of TC, TG, HDL-C and LDL-C were not significant ($p>0.05$). Besides, the mean FBS, TC, TG, and LDL-C except HDL-C of esophageal and pancreatic, FBS in esophageal and rectal and colonic,TC, TG and LDL-C in esophageal and gastric, FBS and HDL-C in gastric and pancreatic, FBS in gastric and rectal, FBS, TC, and HDL-C in colonic and pancreatic, FBS and TC in rectal and pancreatic malignant patients were significantly different ($p<0.05$) were observed (Table 7).

Table 7: Fasting glucose and lipid profile levels of the gastrointestinal malignant patients by Site specific gastrointestinal malignancies.

Variable	Esophageal	Gastric	Colonic	Rectal	Pancreatic	p-value
FBS	86.70±15.326	90.60±4.088	111.44±22.225	114.82±28.505	178.00±72.691	0.000
TC	181.40±24.766	144.91±39.325	175.48±45.497	168.76±43.066	110.33±49.541	0.072
TG	141.30±28.091	94.45±30.329	125.19±65.461	131.47±64.074	85.00±9.539	0.349
HDL-c	37.30±9.832	43.00±10.592	44.56±10.906	43.59±13.210	26.67±10.263	0.177
LDL-c	107.70±18.732	86.55±17.328	111.07±50.257	105.82±34.990	63.00±32.140	0.263

Data are expressed as Mean ±SD; P value ≤0.05 is statistically significant.

Moreover, abnormal FBS and lipid profiles by specific anatomic sites of gastrointestinal malignant patients were also evaluated and found that IFG: (4.3%) in esophageal, (10%) in colonic, (11.4%) in rectal, and (1.4%) in pancreatic malignant patients; diabetic hyperglycemia or hyperglycemia: (12.9%) in colonic, (5.7%) in rectal, and (2.9%) in pancreatic malignant patients. Relatively, higher percentage of colonic had diabetic hyperglycemia while lower percentage of colonic IFG than rectal malignant patients. Similarly, as compared to esophageal and pancreatic, higher percentage of colonic malignant patients had IFG and hyperglycemia. IFG and hyperglycemia were not found in gastric malignant patients. On the other hand, from the proportion percentages of specific site GI malignant patients, comparatively, higher proportion percentage of rectal had IFG than pancreatic, esophageal and colonic malignant patients. Moreover, higher proportion percentage of pancreatic had diabetic hyperglycemia than colonic and rectal malignant patients. Hyperglycemia in esophageal and both diabetic hyperglycemia and IFG in gastric malignant patients were not found.

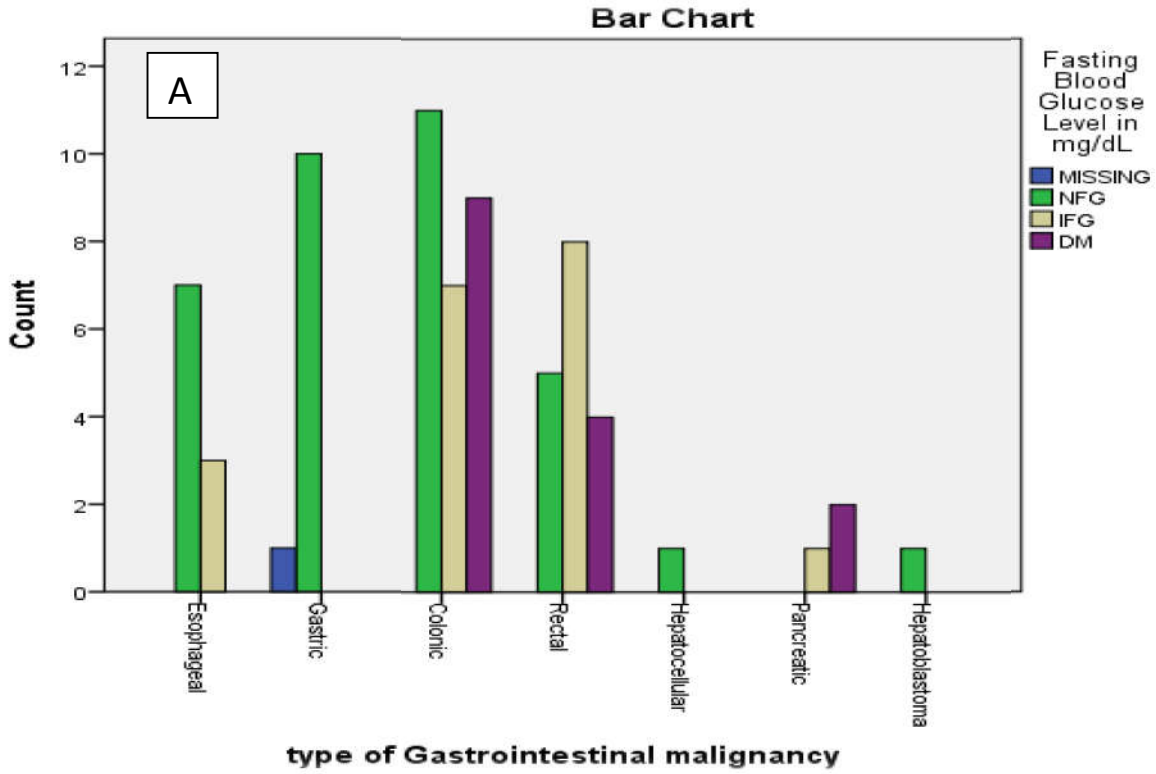
Similarly,abnormal lipid profiles of TC of borderline high was observed in (4.3%) esophageal, (8.6%) colonic and (7.1%) rectal malignant patients, while only (4.3%) colonic with high TC and no abnormal TC level in gastric and pancreatic malignant patients were observed .Relatively, from the total study patients, higher percentage of colonic (12.9%) had abnormally highTC level above the cut off value

than rectal (7.1%) and higher proportion percentage of colonic had also abnormally high TC level above the cut off value than esophageal and rectal malignant patients. Generally, abnormally high TC level above the cut off value was found in esophageal, colonic and rectal except gastric and pancreatic malignant patients.

Equally, (8.6%) colonic, (7.1%) rectal, (4.3%) esophageal malignant patients had abnormal TG levels above the cut-off value of ≥ 150mg/dL in descending percentage and abnormal TG level was not found in gastric and pancreatic malignant patients. Relatively, from the proportion percentage of specific site malignancy, higher proportion percentage of esophageal had abnormally high TG level above the cut off value than rectal and colonic malignant patients. Generally, colonic, esophageal and rectal were affected by abnormally high TG level above the cut off value, whereas gastric and pancreatic malignant patients were not.

Likewise, abnormally low HDL-C<40mg/dL was observed in (14.3%) colonic, (10%) esophageal, (8.6%) gastric and rectal each, (4.3%) pancreatic in lessening percentage of patients. Higher proportion of pancreatic malignant patients had abnormally low HDL-C levels below the cut off value than esophageal, gastric, colonic and rectal malignant patients. In the same token, all the pancreatic malignant patients were affected by abnormally low levels of HDL-C in a higher proportion than the other malignant patients of esophageal, gastric, colonic and rectal. Inclusively HDL-C levels below the normal cut off value or abnormally low level was observed in colonic, esophageal, rectal and gastric, and pancreatic malignant patients.

Similarly, LDL-C level ≥100mg/dl was observed in (2.9%) gastric, (10%) esophageal, (12.9%) rectal, (22.9%) colonic and no abnormal LDL-C level in pancreatic malignant patients. Relatively, higher proportion percentage of esophageal had higher LDL-C level above the cut off value than colonic, rectal and gastric malignant patients.Totally, gastric, esophageal, rectal and colonic malignant patients except pancreatic malignant patients were affected by abnormally high LDL-C level above the cut of value(Figure: 2(A,B,C)).


Bar Chart
A
Fasting Blood Glucose Level in mg/dL
MISSING
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IFG
DM
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Esophageal
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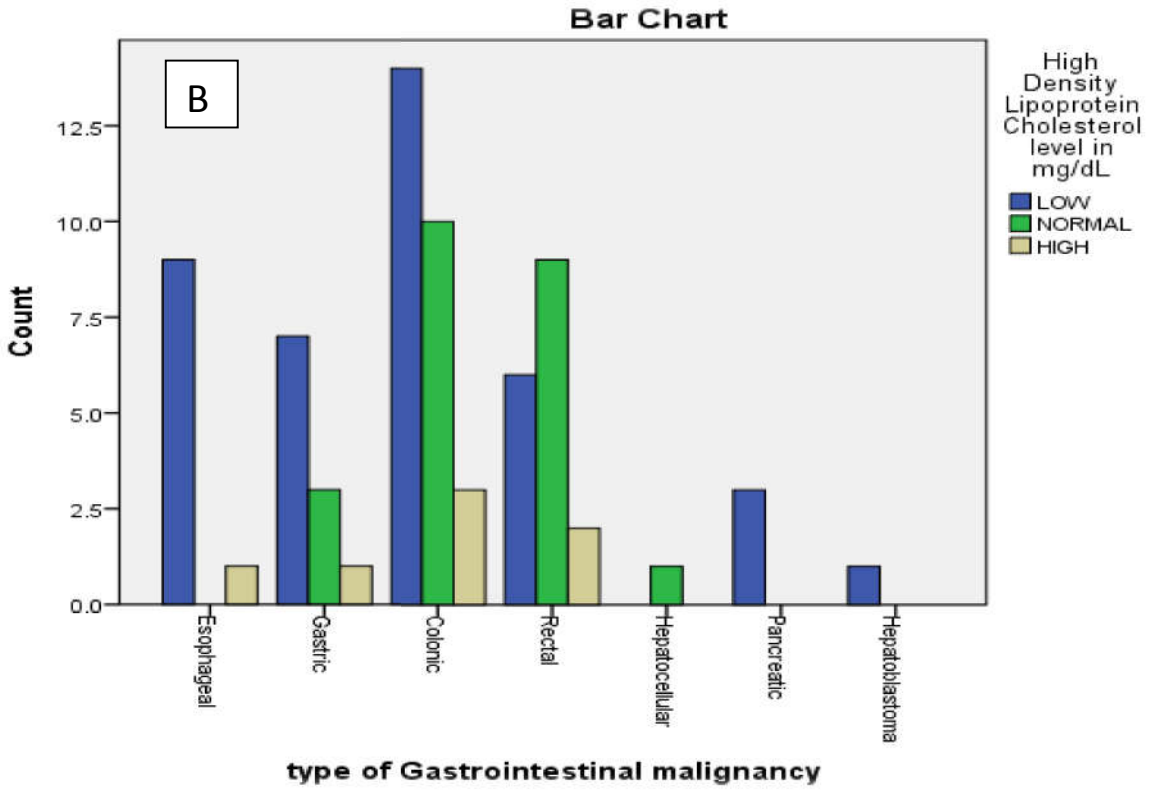
Colonic
Rectal
Hepatocellular
Pancreatic
Hepatoblastoma
type of Gastrointestinal malignancy


Bar Chart
B
High Density Lipoprotein Cholesterol level in mg/dL
LOW
NORMAL
HIGH
Count
12.5
10.0
7.5
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Esophageal
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Colonic
Rectal
Hepatocellular
Pancreatic
Hepatoblastoma
type of Gastrointestinal malignancy

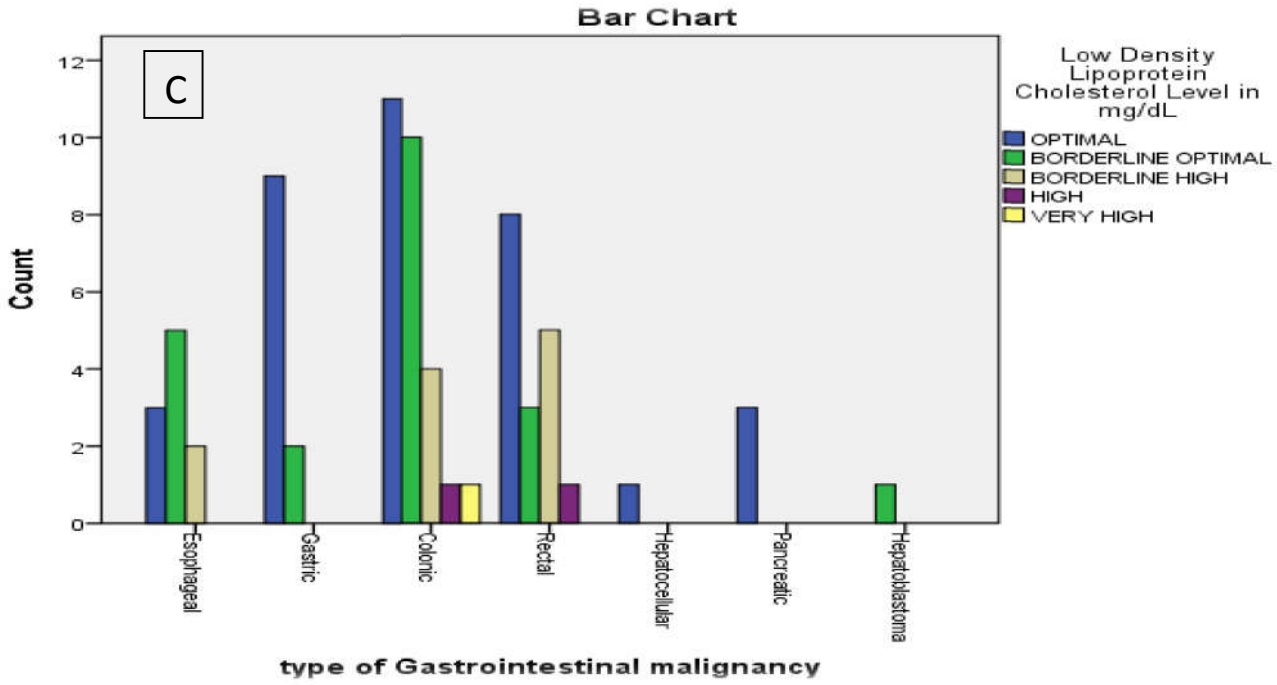

Figure 2: Counts of occurrence of abnormal serum glucose levels (A) and lipid profile levels of HDL-c (B) and LDL-c (C) respectively of site specific gastrointestinal malignant patients.

Furthermore, relatively,the assessment of the mean serum FBS and lipids profile levels of TC, TG, HDL-C, LDL-C of the patients according to stages, primary tumor size, presence or absence of lymph nodes involvement, presence or absence of distance metastasis, histological classification and type of differentiation of the malignancy shown no significant difference (Table 8, 9,10,11,12).

However,stage II Patients had lower normal FBS, TC and LDL-C and higher normal TG and HDL-C levels than stage IV malignant patients.While stage IV malignant patients had abnormally high FBS and LDL-C levels above the cut off value (Table 8).

In addition, squamous cell carcinoma patients had normal mean of FBS, TC, TG and abnormal LDL-C levels above the cut off value and lower HDL-C levels below the cut off value while adenocarcinoma patients had abnormal mean of FBS and LDL-C and normal TC,TG and HDL-C levels. Comparatively the mean FBS and HDL-C levels of adenocarcinoma patients were higher and the LDL-C level was lower than squamous cell carcinoma (Table 9).

Moreover, the mean FBS and LDL-C levels of patients with poorly differentiated malignancy were abnormally high above the cut off value and TG and HDL-C were normal, while well differentiated malignant patients' FBS, LDL-C were abnormally high above the cut off value and the TC, TG and HDL-C levels were normal.As compared to well differentiated, poorly differentiated malignant patients had lower FBS, TC and LDL-C and higher TG and HDL-C levels (Table 10).

Table 8: Serum fasting glucose and lipid profile levels of the GI malignant patients by stages of the malignancy.

Variables	Stage II(5)	Stage III(38)	Stage IV(25)	Total (68)	p-value
FBS	98.60±22.177	112.05±35.160	102.08±24.078	107.33±30.719	0.372
TC	166.00±32.917	162.53±45.632	173.72±43.771	166.90±43.922	0.372
TG	145.40±53.845	125.45±58.858	112.48±53.327	122.15±56.447	0.431
HDL-C	47.40±11.349	41.55±12.231	41.76±10.959	42.06±11.646	0.573
LDL-C	93.80±25.519	99.34±35.739	109.60±46.957	102.71±39.549	0.532

Data are expressed as Mean ±SD; P value ≤0.05 is statistically significant

Table 9: Serum fasting glucose and lipid profile levels of the gastrointestinal malignant patients by histological classification of the malignancy.

variable		FBS	TC	TG	HDL-C	LDL-C
Histological classification	ACC(57)	110.82±31.500	165.33±46.255	120.37±60.464	43.23±11.925	102.67±41.952
	SCC(9)	88.25±16.113	173.11±29.557	133.22±26.423	37.33±10.782	103.22±25.312
	P-value	0.052	0.628	0.534	0.168	0.969

Data are expressed as Mean ±SD; P value ≤0.05 is statistically significant; ACC:adenocarcinoma ; SCC:quamouscelcarcinoma.

Table-10: Fasting glucose and lipid profile levels of the GI malignant patients by type of differentiation of the malignancy.

Variables	Well differentiated (37)	Moderately differentiate (13)	Poorly differentiate (16)	Unknown Differentiation (4)	Total(70)	p-value
FBS	111.97±37.78	103.38±19.63	101.87±17.521	106.00±21.213	107.81±30.453	0.680
TC	167.35±50.605	157.62±39.01	173.06±28.501	162.25±45.916	166.56±43.535	0.818
TG	128.32±63.047	132.92±51.11	96.38±37.580	127.75±42.114	121.84±55.772	0.224
HDL-C	40.70±11.360	40.85±10.057	46.56±11.541	41.75±18.355	42.13±11.597	0.389
LDL-C	104.81±45.50	99.46±43.617	101.44±19.569	103.75±24.336	102.99±39.048	0.977

Data are expressed as Mean ±SD; P value ≤0.05 is statistically significant.

Furthermore, the mean FBS, LDL-C of (N2) malinant patients were abnormally high above the cut off value, while the TC, TG and HDL-C levels were normal. Relatively (N2) patients had higher FBS,TC, TG,LDL-C and lower HDL-C levels than (N0) malignant patients who had normal FBS,TC TG, HDL-C and abnormal LDL-C levels. In addition, (T4) malignant patients were higher in percentage and had abnormally higher (abnormal and higher) FBS and lower normal TC,TG, HDL-C and LDL-C levels than (T2) patients (Table 11).

Table 11: fasting glucose and lipid profile levels of the GI malignant patients by TNM classification of the malignancy.

variable		FBS	TC	TG	HDL-C	LDL-C
Tumor size(T) Pathological	T2(9)	102.44±15.899	176.56±32.315	137.33±64.796	50.22±13.507	103.78±23.926
	T3(36)	111.17±35.844	168.61±47.492	128.28±60.878	39.03±10.352	106.53±47.002
	T4(22)	105.38±25.837	164.23±42.560	108.73±43.684	44.64 ±11.631	99.00±30.739
	TX(2)	83.50±3.536	128.50±6.364	96.50±38.891	37.50±7.778	69.50 ±3.536
	Total(69)	107.81±30.453	166.56±43.535	121.84±55.772	42.13±11.597	102.99±39.048
	P-value	0.582	0.594	0.547	0.064	0.699

variables		FBS	TC	TG	HDL-C	LDL-C
Lymph node involvement	N0 (9)	89.50±16.776	178.56±29.018	127.78±38.935	42.22±12.498	104.00±26.358
	N1(23)	116.13±37.678	156.61±49.320	117.78±69.216	41.74±13.057	102.57±53.790
	N2 (8)	110.88±39.364	193.50±36.680	153.88±67.281	41.88±8.709	122.13±29.333
	NX(29)	104.48±22.042	164.55±42.375	115.48±44.044	42.72±11.470	97.03±30.237
	Total (69)	107.81±30.453	166.56±43.535	121.84±55.772	42.13±11.597	102.99±39.048
	P-value	0.212	0.222	0.478	0.977	0.592

Data are expressed as Mean ±SD; *P value ≤0.05 is statistically significant

Moreover, (61.4%) of the patients had malignancy without metastasis and (32.9%) with metastasis. Patients with distant metastasis malignancy had abnormally high but lower FBS, higher normal TC, lower normal TG and abnormally higher LDL-C levels than without metastasis and the HDL-c was normal and comparable (Table 12).

Table 12: fasting glucose and lipid profile levels of the GI malignant patients by distance metastasis of the malignancy.

variable		FBS	TC	TG	HDL-C	LDL-C
Distance metastasis	M0(43)	109.33±33.954	164.28±43.977	129.42±55.702	42.37±12.144	100.00±34.373
	M1(23)	103.70±24.356	174.26±45.369	111.87±55.546	42.57±10.987	109.78±48.687
	MX(3)	109.00±27.514	152.33±19.140	100.33±68.091	37.67±12.503	87.00±20.224
	Total(69)	107.81±30.453	166.56±43.535	121.84±55.772	42.13±11.597	102.99±39.048
	P –value(a	0.731	0.611	0.521	0.838	0.643

Data are expressed as Mean ±SD; P value ≤0.05 is statistically significant

4.4. Serum Fasting Glucose Level and Lipid Profile Status of the GI Patients

The present study evaluation of mean serum fasting glucose and lipid profile of the GI malignant patients revealed mean fasting glucose levels of 107.81±30.453 mg/dL which was impaired fasting glucose level or prediabetes.While the mean lipid profile levels of TC, TG, HDL-C and LDL-C were

166.56±43.535, 121.84±55.772, 42.13±11.597 and 102.99±39.048 mg/dL, respectively which were normal and less than optimal values except LDL-C of border line optimal.

The bivariate pearson correlation analysis also showed that the FBS level of GI malignant patients was negatively correlated with lipid profile levels of TC,TG,HDL-C,LDL-C(r= -0.123,-0.143,-0.133,-0.054, p>0.05).Whereas,total cholesterol level of the patients was positively correlated with TG, HDL-C, LDL-C levels(r=0 .477, 0.379, 0.810, p<0.05),while triglyceride level was negatively correlated with HDL-C(r=-0.158, p>0.05) and positively correlated with LDL-C (r=0.463, p<0.05). Besides, the HDL-C level of the patients was positively correlated with LDL-C (r=0.230, p>0.05).

Moreover, the distribution of occurrence of abnormal serum glucose and lipid profile levels of the patients were considered and found that (48.6%, HGL) among this, (27.1%, IFG) and (21.4%, hyperglycemia) were found. On the other hand, the distribution of occurrence of abnormal serum lipid profile levels of the patients shown that TC(4.3%, high) and (20.0%, borderline high);TG(20%, high ≥150mg/dl);HDL-C(47.1%, low<40mg/dL); LDL: (30.0%, borderline optimal), (15.7%, borderline high), (2.9%, high) and (1.4%, very high) levels were found. From the study participants (24.3%) had high TC levels (≥200mg/dl) and (50%) high LDL-C levels (≥100mg/dL) (Table 13).

Table 13: Prevalence of fasting glucose and lipid profile levels of the gastrointestinal malignant patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, November 2017 to April 2018.

Variable	Mean SD(70)	Male(31)	Female(39)	P-Value
FBS	107.81±30.453	115.63±37.646	101.79 22.193	0.061
NFG	35(50.0%)	12(34.3%)	23(65.7%)	
IFG	19(27.1%)	10(52.6%)	9(47.4%)	
DM	15(21.4%)	8(53.3%)	7(46.7%)	
TC	166.56±43.535	159.0338.890	172.54±46.525	0.199
Disirable	53(75.7%)	26(49.1%)	27(50.9%)	
Borderline high	14(20.0%)	4(28.6%)	10(71.4%)	
High	3(4.3%)	1(33.3%)	2(66.7%)	
TG	121.84±55.772	112.68±48.934	129.13±60.287	0.223
Normal	56(80.0%)	28(50.0%)	28(50.0%)	
Borderline high	6(8.6%)	0	6(100%	
High	8(11.4%)	3(37.5%)	5(62.5%)	
HDL-C	42.13±11.597	41.77±10.016	42.41±12.839	0.822
Low	33(47.1%)	12(36.4%)	21(63.6%)	
Normal	30(42.9%)	17(56.7%)	13(43.3%)	
High	7(10.0%)	2(28.6%)	5(71.4%)	
LDL-C	102.99±39.048	94.97±24.020	109.36±47.105	0.126
Optimal	35(50.0%)	19(54.3%)	16(45.7%)	
Bordeline optimal	21(30.0%)	9(42.9%)	12(57.1%)	
Borderline high	11(15.7%)	3(27.3%)	8(72.7%)	
High	2(2.9%)	0	2(100%)	
Very High	1(1.4%)	0	1(100%)	

Continuous variables are expressed as mean ± standard deviation; for the rest of the variables, qualitative, the numbers are in percent out of the total 70 patients. Data are expressed as Mean ±SD; P value ≤ 0.05 is statistically significant.

5. DISSCUSSIONS

Abnormal glucose level including impaired glucose tolerance and hyperglycemia are increasing several cancer risks and mortality in cancer patients.Similarly,abnormal lipid profile levels or dyslipidemias are associated with cancer and increases human cancer mortality.Moreover,almost all cancers are affected with aberrant serum lipid and glucose levels.The present study also evaluated and discusses the findings of the serum fasting glucose and lipid profilel levels abnormalities and other associated risk factors for increasing the above mentioned biochemical abnormalities as well as malignancy in ingastrointestinal malignancy.

The evaluation or assessment of this study revealed that age was positively correlated or associated with FBS levels and negatively with lipids profiles, even if the associations was not statistically significant ($p>0.05$). On the other hand, significantly higher mean of HDL-C in age of (30-39years, 47.86) and (60-70years, 38.47 mg/ dL) subgroups were found and shown significant associations. This result was supported by Eichholzer et al.,2000 and Schatzkin et al.,1987 report and reported a low plasma cholesterol was observed in the older age patients rather than the young study participants; this holds up the hypothesis of a “pre-existing cancer effect” i.e., the incidence of cancer is higher in older subjects; with the possible preclinical cancer at starting point in younger age. A study done byWang et al., 2004 similarly stated that cancer and diabetes (hyperglycemia) are more common in the elderly and the elderly generally have low glucose tolerance, which chemotherapy may turn into overt diabetes in cancer patients. In the other way round, the above mentioned studies reported the negative correlation of age and cholesterol and the positive correlations of age and glucose levels of the cancer patients, although not stastically significant, and are agreed with the present study.

Moreover, the result of occerence of lower FBS, higher LDL-c and lower mean of HDL-c in patients who were not doing regular physical activities than patients who were doing regular physical activities (106.38, 104.26, 41.53mg/dL Vs 114.00, 97.38 ,44.77 respectively) though the difference was not statistically significant, was in line with a study conducted by Myers et al.,1989, reported as exercise, regular forceful exercise affects plasma lipid levels and exercise lowers the concentration of triglycerides,VLDL cholesterol, and LDL cholesterol, and raises HDL cholesterol levels**.** In contrast to our study,the American Diabetes Association,2015, reported that more physical activity or exercise than usual makes the body more sensitive to insulin and can lower blood glucose.While the present study shown that the mean serum

FBS levels of patients who were doing regular physical activities was within impaired fasting glucose level and higher than patients who were not doing.This controversy may be due to other factors affecting serum glucose levels such as difference lifestyle parameters including smoking status, Socio-economic status, BMI difference and/or due to anticancer chemotherapy.

Furthermore, the incidence of significantly higher FBS and higher LDL-C, HDL-C and lower TG, though insignificant in alcohol drinker patients than non alcohol drinkers result was in accordance with a study done by Myers et al.,1989 which stated that alcohol consumption raises HDL, in contrast to this study Myers stated alcohol consumption raises TG levels. This maight be due to some other factors which may affects serum TG levels. According to the study this effect of increament in TG and HDL-c can last for 2 or 3 days after consuming the last drinks. Based on the Hannuksela et al.,2003, report the mechanism underlying the effects of alcohol on lipid metabolism is that alcohol consumption has been shown to increase the activity of lipoprotein lipase and decrease the activity of cholesteryl ester transfer protein resulting in elevation of HDL cholesterol. In addition a study done by Van de Wiel, 2012, reported the hypertriglyceridemia induced by excessive alcohol drinking may be mainly due to an increase in the synthesis of large VLDL particles in the liver. Systemic reviews by Baliunas et al.,2009 and Howard et al.,2004 also stated an inverse association between moderate drinking and the incidence of diabetes (hyperglycemia) although it is still under debate whether there is a causal relationship between alcohol and diabetes (diabetic hyperglycemia) and not matced with our study.Overall, patients with diabetes (hyperglycemia) are prone to have dyslipidemia such as high triglyceride levels, low HDL cholesterol levels, and a preponderance of small dense LDL particles (Mooradian, 2009; Dunn, 2010)

On the other hand, cigarette smoker patients' FBS was significantly higher and HDL-c, TC, TG, LDL-c was insignificantly lower than non smoker, Hence, cigarette smoking had a significant association with FBS levels while insignificant links with lipids profile of LDL-c and HDL-c levels of the patients.This result was supported by a study which reported as LDL as we know is increased in the smokers. However, Since LDL is more susceptible to oxidation its higher peroxidation occurs during oxidative stress which results in generation of free radicals leading to lipid peroxidation and mutagenicity. A study also added that an increased LDL activity in tumor cells may produce hypocholesterolemia.Therefore LDL can be used as a mediator between smoking and occurrence of cancer (Vikramsimha et al., 2016). Bose et al., 2012, as well explained the mechenasim of carcinogenesis caused by smoking and lipids interactions. According to the study clarifications it is believed that tobacco carcinogens induce generation of free

radicals and reactive oxygen species which are responsible for high rate of oxidation / peroxidation of polyunsaturated fatty acids. Lipid peroxidation further releases peroxide radicals. There is substantial evidence that the hydroxyl radical generated can destruct tissue by initiation and propagation of lipid peroxidation by abstracting hydrogen from unsaturated fatty acids. This affects essential constituents of the cell membrane and might be involved in carcinogenesis/tumorigenesis.

In addition significantly higher mean FBS in employed (121.41) patients than unemployed (101.70) and significantly higher FBS in high economic than low economic status ($P<0.05$) were found .This result shown that socioeconomic status of the patients had an impact and significant associations with FBS while insignificant relations with lipid profiles more specifically to LDL-C levels.Thus, special attentions should be given to those patients with high socioeconomic status in investigation of FBS and lipid profiles.

Dyslipidemia is tightly linked to obesity and the known link between obesity and cancer suggests an important interaction between the host lipid metabolism and tumorigenesis.Body mass index (BMI), the most commonly used marker for adiposity, but it may mask differences between lean and adipose tissue, or fat distribution, which varies across individuals, ethnicities, and stage in the lifespan.Thus,other measurements of weight gain in adulthood such as waist circumference and waist-to-hip ratio contribute information on adipose tissue distribution and insulin sensitivity (Elisa et al., 2016). However, as BMI is the most commonly used marker for adiposity in epidemiological studies, we prefered BMI to measure the associations of serum FBS and lipid profile levels of the patients.

In the present study, though the difference was not significant, overweight patients' mean FBS was higher than underweights. Besides, overweight patients' mean lipid profiles were higher than underweight with significant mean difference of TG, HDL-c between underweight, normal and overweight patients(122.24, 110.28, 173.33 and 38.38, 44.69, 49.50, ($p<0.05$), $p=0.040$ and $p=0.032$, respectively), in TG, HDL-C and LDL-C between overweight and underweight patients and in TG between normal and overweight patients ($p<0.05$)(122.24, 173.33, 38.38, 49.50 and 99.34, 132.00, $p=0.042$, 0.049, 0.028 and 110.28, 173.33, $p=0.024$, respectively). Results shown that the body mass index of the patients had significant associations with the lipid profile status of TG, HDL-C and LDL-C while BMI had an effect on and relations with FBS levels of the patients. Based on the findings of Kuchiba et al., 2012,this difference in lipid profile status of the patients with different BMI'subgroups might be due to different metabolic strategies adapted by the malignant patients having different body mass index. Kuchiba further clarified that this may due to the choice of lipid acquisition pathway which may depend on certain factors such as obesity and cellular

FASN (fatty acid synthase) status may determine a cell's dependence on energy balance status for malignant transformation.This maight inturn determine the FBS and lipid profile levels of the patients. Epidemiological studies on the other hand showed a positive correlation between increased risk and worst cancer outcome with respect to BMI and fat distribution (Fujihara et al., 2012; Calle et al., 2003). Calle et al.,2003, similarly showed the Pearson Correlation of glucose, TC, and TG were positively associated with BMI, with TG being most strongly linked to BMI ($r = 0 . 3 2$, P value < 0.0001) and glucose the weakest ($r = 0 . 1 9$, P value < 0.0001). Calle group also added that overweightness and obesity are responsible for 14% of cancer deaths in men and 20% of cancer deaths in women as well as obesity-related mortality is for gastrointestinal tumors in both sexes. As results of the present and perevious studies BMI, dyslipidemia and malignancy are related to each other and therefore, more attention should be given to overweigh and obes malignant patients. Evidences are: dyslipidemia is tightly linked to obesity and is characterized by high levels of triacylglycerol (TG) and low-density lipoprotein cholesterol (LDL-C) as well as low levels of high-density lipoprotein cholesterol (HDL-C) in the bloodstream.Dyslipidemia is also associated with increased human cancer mortality (Calle et al.,2003). This has been functionally validated in experimental models of diet-induced obesity (DIO) that showed poor cancer outcomes (Alikhani et al., 2013; Zhuang et al., 2005). Weight loss intervention has been suggested as an effective cancer prevention strategy and is supported by reductions in cancer incidence and mortality of patients who have had bariatric surgery and dramatic weight loss (Sjo¨ stro¨m et al., 2009). However, whether nonsurgical weight loss interventions achieved by calorie restriction, behavioral therapy, and/or pharmacotherapy could also have a beneficial impact on cancer incidence is still unclear.

Mechanistic investigations into this relationship have analyzed the potential roles of insulin, insulin-like growth factors (IGFs), sex hormones, and adipokines (e.g., leptin, tumor necrosis factor alpha (TNF-a), and adiponectin). Plasma concentrations of these are often abnormal in obesity (Al-Zoughbi et al., 2014). Bianchini et al., 2002 also explained that onset of insulin resistance and chronic inflammation resulting from excess lipid supply and adipose expansion can distort the normal balance between cell proliferation and differentiation and apoptosis which eventually contribute to obesity-induced cancer incidence. However, the precise cellular mechanisms that link obesity with cancer incidence, recurrence, progression and death remain largely unexplored. Furthermore, whether dyslipidemia in normal-weight subjects is correlated to tumor incidence is unknown.

Moreover the stressful situations of acute illness and surgery in malignant patients were found to have an impact on FBS and lipid profile levels.The FBS was higher in patients with acute illness and surgery than without acute illness and surgery while the lipid profile was lower except HDL-c in surgery, even though the difference was statistically insignificant. Based on Myers et al.,1989 report the reason for this difference in the levels of the analytes of patients with and without acute illness and surgery is that severe stress can cause a temporary increase in blood glucose and is usually of one or more of these factors: surgery, trauma and heart attack. Cholesterol levels are also lower for shorter periods in response to severe pain, surgery, and short term physical strain. Moreover Myers group also further explained that trauma and acute infection can decrease cholesterol levels and after severe trauma cholesterol levels can decrease by as much as 40% and remain depressed for several weeks.Therefore, further studies should be looked forward the stressful situations like acute illness and surgery to investigate and estimate blood glucose level and lipid profile status of the GI malignant patients.

The GI malignant patients'mean serum fasting glucose levels was abnormal and within impaired fasting glucose levels range and the patients developed prediabetes.From the total,almost half percentage (49%) of the patients had abnormally high fasting glucose levels and majority (27.1%) impaired fasting glucose levels and (21.4%) diabetic hyperglycemia. Moreover, the patients were affected by abnormal serum glucose levels in different proportion percentages.This result was supported by a study done by Glicksman and Rawson,1956, reported that approximately 37% of all patients with cancer had abnormal glucose tolerance. Although, esophageal, colonic, rectal and pancreatic except gastric malignant patients were affected by abnormally high serum fasting glucose levels including impaired fasting glucose and diabetic hyperglycemia**,** pancreatic, colonic and rectal were mostly affected. Besides, the mean FBS levels of esophageal, gastric, colonic, rectal and pancreatic malignant patients were significantly different ($p<0.05$). Furthermore, the mean FBS of stage IV and N2 malignant patients were higher than stage II and N0 malignant patients (102.08 and 110.88 mg/dl Vs 98.60 and 89.50, respectively).Thus, patients with advanced stages were more affected by abnormal glucose levels than early stages malignancy.The results were supported by Kokal et al.,1983 study which stated that gastrointestinal cancer patients increased whole-body glucose turnover has been documented and this increase was proportional to the extent of the disease.According to the report, this is due to altered glucose metabolism in cancer patients is characterized by an increased whole-body glucose turnover rate, decreased glucose uptake and utilization due to insulin resistance, and an increased in hepatic glucose synthesis or gluconeogenesis from the substrates derived from proteolysis and lipolysis.An increased in Cori cycle activity or glucose carbon

recycling in patients with malignant disease is also well documented by several studies (Eden et al., 1984;Ehrmann-Jósko et al., 2006; Farooki and Schneider, 2007).Glicksman and Rawson,1956 also stated that the decreased glucose metabolism or glucose clearance from the circulation resulted in both significantly decreased glucose storage and glucose oxidation and abnormal glucose tolerance in gastrointestinal (GI) and lung cancer patients. Many researchers as well as Dankner et al., 2007 reported, impaired glucose tolerance without diabetes (hyperglycemia) is associated with increased cancer risk and both these conditions are characterized by hyperinsulinemia. Hence impaired glucose tolerance can occur as a component of risk factors and/or increasing progression of the malignancy as well as mortality of malignant patients. Dai et al., 2009 also found and reported that abnormal blood glucose is common in cancer patients after chemotherapy especially after taxane containing regimens resulting in secondary DM (hyperglycemia). Based on the Dai group report this may because of chemotherapeutic drugs inhibit three major enzymes in glycolysis (hexokinase, phosphofructokinase, and acetone kinase) and thus decreases sugar consumption. Moreover the group further clarified that high-dose platinum-containing programs require furosemide, which increases blood sugar and thus causes IGT.

The underlying pathophysiological mechanisms of DM (hyperglycemia) related carcinogenesis are poorly understood. Nonetheless, they are probably multifactorial including hyperglycemia facilitating neoplastic proliferation (Vander et al., 2009), hyperinsulinemia promoting carcinogens is through its effects on insulin and/or IGF-I receptors(Pollak M., 2008; Zhang et al.,2007; Mardilovich et al., 2009; Giovannucci E.,2001) and inflammatory cytokines secreted by adipose tissue enhancing malignant progression (van Kruijsdijk et al., 2009). Since insulin is produced by pancreatic β-cells and then transported via the portal vein to the liver, long-term exposure of growth factor (insulin) may case the higher incidences of cancer in pancreas and liver (Giovannucci et al., 2010).In addition, the hyperinsulinemia state of diabetes, slower bowel transit time, and elevated fecal bile acid concentrations may facilitate the growth of colorectal cancer (Lee et al., 2012).

On the other hand the patients mean lipid profiles of TC, TG, HDL-C were lower normal and lower than optimal values except LDL-C which was within the border line optimal range (166.56, 121.84, 42.13and 102.99 mg/dL, respectively). Hence, the patients were affected by low lipid profile levels except LDL-C The result was equally in accordance with the study conducted by (Acharya et al.,2016; Garg et al.,2014; Li et al.,2016; Lohe et al.,2010; Kumar et al., 2012 ;Ghosh et al.,2011; Patel et al.2004) and showed that the cancer patients showed a decrease in cholesterol, TGs, HDL, and VLDL with an increase in LDL

compared to control group. According to the studies, this can be due to- as the cell membrane is made up of lipoproteins, the body lipids are used for the biogenesis of the cell membranes of the newly forming neoplastic cells and this causes a decrease in the cholesterols, TGs, and lipoproteins in the cancer patients (Vikramsimha et al., 2016; Williams et al., 1981).On the other hand, Munir et al.,2014 reported that serum lipid levels of cancer patients also fluctuate during chemotherapy. According to Munir group study, it has been shown that cancer patients display a significant increase in serum cholesterol and LDL levels. Previous works point out serum lipids of cancer patients may go back to the normal levels after effective treatment.These observations corroborate the correlation between abnormal serum lipid profile and disease activity and patients that responded positively to chemotherapy demonstrated a significant increase in serum Chlolesterol, TG and LDL levels.

Moreover, occurrences of lipid profile abnormalities or dyslipidemias on patients were found and patients were affected by different lipid profile abnormalities. Our study clearly demonstrated that the malignant patients exhibited irregular serum lipid patterns. From the components of lipid profile, abnormally high LDL-C level above the cut off value was the most frequently occurring serum lipid profile abnormality followed by abnormally low HDL-C level below the cut off value, abnormally high TC and TG levels above the respective cut off value,found in 50%, 47.1%, 24.3% and 20% of the patients respectively.The results were in lines with the studies done by Tabuchi,2006; Ulmer et al.,2009;Van Duijnhoven et al.,2011, according to the studies one of the reasons for these varying levels of lipid profile of the patients might be due to the fact that various types of cancers may exploit different modes for the acquisition of lipids that in turn affect the plasma lipid profiles.Besides the mean LDL-c levels of stage IV, N2 and patients with distance metastasis malignancy was higher than that of stage II, N0 and without distance metastasis (109.60, 122.13 and 109.78 mg/Dl, repectively Vs 93.80, 104.00 and 100.00 mg/dL respetively). Accordingly advanced stage malignant patients were more affected by high LDL-c than early stage malignant patients.The result was supported by Vedavyas and reported a direct association between high LDL level and increased risk for lymph nodes metastasis. According to the report as angiogenesis is a key factor for growing cancer and metastasis, the growth of tumor and metastasis can be stopped by inhibiting angiogenesis and metastasis (Vedavyas, 2013). Farahnaz et al., 2015 also reported that only serum LDL greater than 110mg/ dL could predict cancer metastasis to lymph nodes ($p=0.007$).

A study in contrast reported that TC, LDL-C, HDL-C, TG and BMI were significantly lower in patients with metastatic than in patients with non-metastatic solid tumor.The study also reported, the significant

difference in LDL-c and serum TGs between patients with metastatic and non-metastatic cancer was lost when lipoprotein cholesterol and serum triglyceride levels were adjusted for nutritional variables. Moreover the study also added that the lipid profile levels of cancer patients as a whole is characterized by low LDL-c, low HDL-c and relatively high serum TGs. The abnormality is a common feature of both hematological and solid tumors and is not entirely explained by poor nutrition (Fiorenza et al., 2000).

Budd and Ginsberg,1986, likwise reported, lipid metabolism in malignant cells is accomplished by either from circulation by synthesis through the metabolism or from degradation of major lipoprotein fractions such as VLDL, LDL or HDL.Thus,changes in serum cholesterol levels may occur before the manifestation or detection of cancer and may be the result of the cancer process. Hence, Hypolipidemia may result due to the direct lipid lowering effect of tumor cells or some secondary malfunction of the lipid metabolism or secondary to antioxidant vitamins.

Munir et al., 2010; Rysman et al., 2010 similarly reported that as lipoproteins are the distributors of both endogenous as well as exogenous lipids across the tissues. It is therefore plausible that lipoproteins play a fundamental role in cancer progression via supplying lipids to malignant cells and tumors, hence, hypolipidemia may occur in patients because rapidly proliferating cancer cells require a constant supply of lipids for membrane biogenesis and protein modifications, also the cancer cells that are not rapidly proliferating require increased amounts of lipids for enhanced signaling and resistance against apoptosis.

Although Hegele, 2009 sumerrized and reported that relatively the most common and consistent trend of lipid profile abnormality is a significant decrease in serum levels of cholesterol, HDL and LDL, and a significant elevation in the levels of serum TG. There are certain discrepant reports that presented opposite trends in overall cancers.This may because of several environmental and genetic factors that are known to influence human plasma lipid profile. Therefore, it is important to ascertain whether the association between levels of different lipid fractions and cancer is biologically significant or merely confounded by other risk factors that were overlooked during the analyses.

As mentioned above previous works including our study have shown that cancer patients exhibit aberrant serum lipid profiles. However, the underlying mechanism for these irregularities is not clearly understood. Moreover, the possible role of plasma lipids and lipoproteins in carcinogenesis is not clear. Nonetheless a number of speculations have been made by researchers working in this area and most of them suggested that an aberrant lipid profile in cancer patients is a consequence of cancer. The cancer cells are known to

exploit various pathways for acquisition of lipids.Endogenous lipogenesis has historically been considered as the principal source of fatty acids (FAs) in cancer cells as (Menendez and Lupu, 2007) stated above. Similarly Brusselmans et al.,2007; Freeman et al.,2010 further stated that up-regulation of the mevalonate pathway for acquisition of cholesterol has also been observed in various types of cancer.This deregulation of lipid synthesis/ acquisition pathways in tumor cells could be partly responsible for aberrant serum lipid profiles in the cancer patients.

Several studies in addition reported and shown that various types of cancer cells have been revealed to have higher uptake of LDL that is mediated by higher expression and activity of LDL-R(Tatidis et al.,2002; Rudling et al.,1990; Vitols et al.,1996).It has been suggested that this increased uptake of LDL may cause modification of cell membrane composition that would eventually affect the passive diffusion of anticancer drugs across the cell membrane(Tatidis et al.,2002).Thus, it can be speculated that increased uptake of LDL by cancer cells may affect its clearance from circulation and results in decreased serum LDL levels in the cancer patients. Some earlier research reports suggested that decrease in serum lipoproteins levels of cancer patients is closely associated with the presence of autoantibody against lipoproteins.The HDL concentration in the sera of cancer patients was significantly lower when the antibody was present (Riesen et al., 1975).These observations suggest that autoimmune mechanisms might be responsible for the decreased HDL serum levels in cancer patients. Previous studies have also shown that HDL is incorporated in the cell cycle via mitogen activated proteins kinase dependent pathway and significantly influences the cell cycle (Nofer et al., 2001; McGrowder et al., 2011). Hence, higher consumption of HDL by rapidly proliferating cancer cells may affect its serum levels.

Das et al., 2011, as well reported that an elevated intracellular lipolysis is a key factor behind adipose cachexia in weight-losing cancer patients**.** It has been again suggested bySantos and Schulze, 2012, that tumor load promotes this intracellular lipolysis in adipose tissues, though the underlying mechanisms are just beginning to be elucidated. On the other hand Kuemmerle et al., 2011 demonsterated lipoprotein lipase (LPL) which hydrolyzes TG within chylomicrons (CM) and very lowdensity lipoprotein (VLDL) was found to be critical for cancer cells to acquire FA from culture medium. Mori et al.,1991 also publicized that the tumor secretes an inhibitor of adipose LPL termed leukemia-inhibitory factor, causing inhibition of extracellular lipolysis and depletion of adipose stores.This increased intracellular lipolysis displayed by adipose tissues of the cachectic patients may affect the levels of circulating lipids. In fact

metabolic changes such as elevated levels of circulating FFAs, monoacylglycerides and diacylglycerides have been observed in these patients as explained by (Gercel-Taylor et al.,1996).

Currie et al., 2013 likewise revealed that rapidly proliferating tumor cells generally require high amounts of fatty acids (FAs) and cholesterol. Numerous studies have confirmed hyperactivation of de novo lipogenesis in various types of neoplasia.Targeting lipogenesis by inhibiting fatty acid synthase (FASN), stearoyl-CoA desaturase-1 (SCD1), ATP-citrate lyase (ACLY) or sterol regulatory element-binding protein-1 (SREBP1) was effective in tumor suppression. This study shown the hyperlipidemic effects of cancer and cancer proliferation can be suppressed by inhibiting its hyperlipidemic effects of cancer.

Furthermore, the patients results shown that the FBS levels of the patients were negatively correlated with lipid profiles, although not statisticaly significant ($p>0.05$).This maight be due to that most patients in our study had advanced stages of malignancy and may lost weight. Based on Lattermann et al., 2003 report, the body needs plenty of energy but glucose metabolism is inefficient and thus increases protein breakdown and fat mobilization to provide adenosine triphosphate.These events cause weight loss and a negative protein and fat balance. This trend worsens as the disease progress.

In the contrary a study reported that abnormal glucose metabolism exists in patients with malignant tumors and lipid changes in patients with malignant tumor and DM or IGR are more complicated than increases in blood lipids in diabetes. Based on the study, total cholesterol and triglycerides in the IGT and DM groups increased. However, this increase was not statistically significant possibly because the patients in the study mostly had advanced cancer and lost weight (Berster and Göke, 2008)**.** Another study similarly reported that diabetes (hyperglycemia) and IGT are significantly increased after chemotherapy, especially after multicycle chemotherapy (Wang et al., 2004). It is also known that metabolic syndrome (MS) is a heterogeneous disease of unclear etiology caused by genetic, infectious, or environmental factors and that develops on the basis of insulin resistance (IR). Dyslipidemia which is a component of MS is a good indicator of IR. As dyslipidemia is a good indicator of insulin resistance and dysglycemia, the FBS and lipid profile levels of the patients were most probably be positively correlated, though not significantly correlated. Thus, besed on our study, this correlation maight be due to the effects of chemotherapeutic drugs of the patients or it may due to the weight losing and the negative protein and fat balance of the patients or some other risk factors of dys-glycemia and dyslipidemia.

6. CONCLUSIONS

From the results of this study, we can concluded that abnormally high blood glucose levels including impaired fasting glucose level and diabetic hyperglycemia were seen and identified in gastrointestinal malignant patients of esophageal, colonic, rectal and pancreatic malignancies.

Besides, the mean FBS levels was significantly influenced by the types of GI malignancy.The highest mean FBS in pancreatic and the least in esophageal were found.

Abnormally high LDL-C level was the most frequently occurring or prevalent lipid profile abnormality followed by low HDL-C, high TC and TG levels respectively. Moreover, esophageal, gastric, colonic, rectal and pancreatic malignant patients were commonly affected by low HDL-C and the lowest mean HDL-C was found in pancreatic.

Furthermore, patients with advanced stages of malignancy of lymph node involvment and distance metastasis were found to be more affected by abnormally high FBS and LDL-C levels than patients without lymph node involvment and distance metastasis of malignancy.

BMI, as well was found to be significantly associationated with TG, HDL-c and LDL-c levels while alcohol drinking and cigarette smoking were with FBS levels. Besides significant inverse association of HDL-c level with age of the patients was found. As a whole occurrence of dysglycemia and dyslipidemia were increasing with increasing BMI and socioeconomic status as well as among in cigarette smokers and alcohol drinkers.

Overall, gastrointestinal malignant patients were affected by both dysglycimia except gastric and dyslipidemia.And the FBS levels of the patients were negatively correlated with lipid profile of TC, TG, HDL-c and LDL-c levels, though not stastically significant. As, previous studies have also reported that both dysglycemia and dyslipidemia in cancer patients are shown to be associated with cancer risk, development, progression and mortality incident. Investigation of the blood glucose and lipid profile levels, and other associated risk factors which may cause dysglycemia, dyslipidemia as well as malignancy are important in decreasing risks, progressions, mortality and in increasing survival and quality of life of the GI malignant patients.

7. STRENGTHS AND LIMITATIONS

Thisstudy had the succeeding major strengths despite its drawbacks

- The present study tried to investigate and analysis the FBS and lipid profile levels by considering the sociodemographic, BMI and clinicopathological characteristics that can affects the FBS and lipid profile levels of the patients.
- The study also incorporated esophageal, gastric and pancreatic malignancies which were not studied before.
- As, there was no similar studies before, the present study can serve as a baseline study.

Inspite of the streangths, the study had also the subsequent drawbacks or limitations.

- The numbers of site specific gastrointestinal malignancies were not equivalent and comparison of the study variables may be pitiable.
- The sample size was low and failed to use the same sample size as the calculated once which may not the representative sample of the study.
- Also, since the study design was cross-sectional, cause and effect relationship study of fasting glucose and lipid profile levels as well as other associated risk factors which cause alterations of the levels were restricted.

8. RECOMMENDATIONS

For further study of the blood glucose and lipid profile levels of the gastrointestinal malignant patients, the succeeding recommendations are specified.

- Using representative sample size and equivalent numbers of site specific GI malignant patients that are not on anticancer chemotherapy as well as studying anticancer chemotherapy in detail are important for advance elucidation and comparisons of the results.
- Further prospective or retrospective case control study should be conducted for enhanced analysis of the cause and effect relationship of dysglycemia, dyslipidemia as well as malignancy and for better readings of FBS and lipid profiles.
- Furthermore, routine investigation of fasting blood glucose with OGTT and lipid profile levels and treat the patients accordingly is essential for better implementation of treatment in improving the survival and quality of life of the patients.
- Last not least, for risk reduction, providing enhanced health education regarding overweightness, cigarette smoking, excessive alcohol consumption and other associated risk factors that increases incidence of abnormal blood glucose and lipid profile levels as well as malignancy is vital.

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10.ANNEXES

10.1. Annex 1: Information sheet (English and Amharic Version)

Research Project: glycemic level and lipid profile status of gastrointestinal malignant patients attending at Tikur Anbessa Specialized Hospital.

Sponsoring Organization: Department of Medical Biochemistry, School of Graduate Studies, College of Health Sciences, Addis Ababa University.

Investigator: Yitayal Mekuriaw (Bsc, MSc in biochemistry candidate)

Advisors: Dr.Daniel Seifu(PhD),

Dr.Wondimagegnhu Tigeneh (Oncologist)

Introduction

Dear participants you are kindly requested to take part in this research project as a study participant voluntarily. Read the information provided in this sheet carefully and then respond freely and voluntarily to what the investigator interviews you.

Objective Of The Research Project

This information sheet is prepared by the investigator and the advisors at AAU for a project with the objective of evaluation of glycemic level and lipid profile status of gastrointestinal malignant patients.

Procedures

If you agree to take part in the study, the investigator or a health worker will give you verbal and/or written information about the study and you will be given the consent form to sign, the physician or health professional will ask you some questions about your general health and perform a complete medical examination and assess whether you qualify to participate in the study. If you are fit for the study about 5 ml of blood samples will also be collected for only the laboratory examination of fasting blood glucose, HDL, LDL-C, total cholesterol, triglycerides and face to face interview for additional questions.

Discomforts and risks and benefits from participation

The degree of discomfort you may encounter in giving the sample is no more than when one does in his/her routine examination. But, there could be cases in which minor pain and change in color of your skin following the blood drawing occur transiently. The blood will be withdrawn by licensed health care professionals in the hospital and appropriate care will also be taken. You will not be provided with any direct incentives for your participation in the research. But the cost for general medical examination will be covered by the project. In addition, based on the results obtained from the research you will be cared accordingly or the results may serve you as a baseline data. In addition, the result of the study will be

beneficial for the better prevention and care of gastrointestinal malignant patients than before. Hence, you are indirectly benefiting other patients and the society in this aspect.

Confidentiality

All pieces of information about the patients will be kept confidential. Log books used in the laboratory will have no names but codes. The information sheet that links the coded number to patient name will be locked inside a box and it will not be revealed to anyone except your physician and the principal investigator. You have full right to withdraw from participating in this study at any time before and after consent even without explaining the reason. Your decision will not affect your right to get health service you are supposed to get otherwise.

Contact information: If you have any questions contact:

Yitayal Mekuriaw: 0920519571

Information sheet (Amharic version)

የተሳታፊዎችየፈቃደኝነትናመተማመኛመረጃመስጫቅፅ

በአዲስአበባዩኒቨርሲቲየጤናሳይንስኮሌጅየሕክምናባዮኬሚስትሪትምሕርትክፍል፡ጥናቱንስፖንሰርያደረገዉተቋምአዲስአበባዩኒቨርሲቲጤናሣይንስኮሌጅነው፡፡

መረጃመስጫቅፅ

በአዲስአበባዩኒቨርሲቲጤናሳይንስኮሌጅየሕክምናባዮኬሚስትሪት/ክፍልሁለተኛዲግሪተማሪየመመረቂያጥናትጽሁፍላይእዲሳተፉተጋብዘዋል፡፡እባክዎበዚህጥናት ለመሳተፍከመስማማትዎበፊትከዚህቀጥሎየሚገኘዉንምንባብበጥሞናያንብቡናግልጽያልሆነልዎትንማንኛዉንምሃሳብይጠይቁ፡፡

Glycemic level and lipid profile status of gastrointestinal malignant patients attended at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. የጥናቱ ርእስ ሲሆን አላማውም የጉሮሮ የጨጓራ፣ እና የአንጀት የካንሰርታካሚዎችነው፡፡የጨጓራ እና የአንጀት ካንሰር ስንል ከዚህ በታች የተዘረዘሩትን ማለትም (የጉሮሮ (የምግብ መውረጃትቦ)፣ የጨጓራ፣ አየንጀት(ትልቁ)፣ የፊንጢጣ፣ የጉበት፣ የቆሽት፣ የሀሞትከረጢት ካንሰርንያለባቸውታካሚዎች ያጠቃልላል) በደማቸው ውስጥ ያለውን የስኳር፣ የቅባት መጠንና እንዲሁም ሌሎች ከጉሮሮ፣ ጨጓራ እና የአንጀት ካንሰር ጋር ግንኙነት ያላቸውን ነገሮች መጠንና ሁኔታ መለካትነው፡፡ የጥናቱ ውጤት ለታካሚው ብሎም ለሌላው ማህበረሰብ የሚጠቅምና የተሻለ የጤና እንክብካቤ እንዲኖር የሚያደርግ ነው፡፡ እናም እርስዎ በዚህጥናት ለመሳተፍ ጠቃሚ ና ምቹ ሆነው ተመርጠዋል፡፡ የእርስዎ በዚህ ጥናት ላይ የሚያደርጉት ተሳትፎ ሙሉ በሙሉ በበጎ ፈቃደኝነት ላይ የተመሰረተ ነዉ፡፡

በጥናቱ ከተሳተፉ ለናሙና ይሆን ዘንድ 5 ሚሊሊትር ያህል ደም በሆስፒታሉ ጤና ባለሙያዎች የሚሰጡ ሲሆን የደም ናሙናውን በሚሰጡበትም ሰአት ሁል ጊዜ ለምርመራ ከሚሰጡበት የተለየ ህመምና አለመመቸት የለውም ለምናልባት ቢኖር ተገቢውን የጤና እንክብካቤ የሚያገኙ ይሆናል፡፡ በዚህጥናት ዉስጥ ላለመሳተፍ ወይም ለመሳተፍ ከወሰኑ በጎላለ ማቋረጥ የሚወስኑ ቢሆንም እንኩዋን በዚህ ሆስፒታል የሚሰጠዎ ማንኛዉም አገልግሎት ላይ ተጽዕኖ የለውም፡፡ በጥናቱ ለመሳተፍ የሚስማሙ ከሆነ የስምምነት ቅጹ ላይ በጽሁፍ ወይም በጣት ፊርማ ማስቀመጥ ይጠበቅበዎታል፡

ግልጽያልሆነልዎጥያቄካለ

ሞባል፡ 0920519571: Yitayal Mekuriaw

10.2.Annex 2: Informed consent (English and Amharic version)

Department of medical Biochemistry, 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 it aims to evaluate and correlate serum fasting glucose level and lipid profile status of gastrointestinal malignant patients. The objectives of the research project have clearly been explained to me and I have been told that the results obtained from me will help me as well as the community for better management of the disease. I had been also informed about the confidentiality of this research project. Moreover, I have also been well informed of my right to keep hold of information, decline to cooperate and make myself withdraw from the study. Therefore, with full understanding of the importance of the study, I agreed voluntarily to provide the requested samples and my benefit will be only from the free laboratory investigation result/s.

I _____ hereby give my consent for providing the

requested information and blood sample as the doctors find best for me.

Signature_____

Informed consent (Amharic version)

የተሳታፊዎችስምምነትማረጋገጫቅጽ

የሚስጥርቁጥር ----------

የተሳታፊዉስም ----------

እኔስሜከላይየተገለጸዉግለሰብየተፈለኩትበዚህጥናትእንድሳተፍሲሆንየጉሮሮ (የምግብመውረጃትቦ) ፣የጨጓራ፣አየንጀት (ትልቁ) ፣የፊንጢጣ፣የጉበት፣የቆሽት፣የሀሞትከረጢት፣ካንሰርያለባቸውታካሚዎችበደማቸውውስጥያለውንየስኳር፣የቅባትመጠንናእንዲሁምሌሎችከጉሮሮ፣ጨጓራአ ናየአንጀትካንሰርጋርግንኙነትያላቸውንነገሮችመጠንናሁኔታመለካትነውየሚለውጥናትአላማናጥቅምተገልፆልኛል፡፡ስለዚህለዚህጥናትመረጃናየስምምነትቃሌ ንየምሰጠዉበአጠቃላይየጥናቱንአላማናጥቅምበመረዳትናበፍጹምፈቃደኝነትነው፡፡በመጠይቁላይየምሰጠዉየእኔመረጃእንደማይባክንእንደሚያዝምተነግሮኛ ል፡፡በተጨማሪምጥናቱዉስጥላለመሳተፍከፈለኩኝመብቴየተጠበቀእንደሆነናበማንኛዉምጊዜከጥናቱበራሴዉሳኔመዉጣትጭምርመብቴመሆኑንናከጥናቱበ መዉጣቴምንምአይነትችግርእንደማይደርስብኝበሚገባተገልጾልኛል፡፡

ስለሆነምሁኔታዉንበሚገባበማጤንበፈቃደኝነትበምርምሩላይለመሳተፍፈቃደኝነቴንሰጥቻለሁ፡፡በተጨማሪምየምሰጠዉየደምናሙናለስኳር፣የቅባትመጠን ምርመራዎችብቻእንደሚዉልተነግሮኝተስማምቻለሁ፡፡ማንኛዉንምያልገባኝንነገርየመጠየቅእድልተሰጥቶኝበሚገባኝቋንቋመልስአግኝቻለሁ፡፡

በተጨማሪምየሁሉምየላብራቶሪምርመራዉጤቶችበጊዜዉለሀኪሜእንደሚሰጥልኝእናዉጤቱንማወቅከፈለኩማግኘትእንደምችልተነግሮኛል፡፡በአጠቃላይእኔ ከላይበመተማመኛቅፅየተጠቀሱትንሁሉበሚገባናበተረጋጋመንፈስአንብቤአለሁ፡፡ስለዚህበዚህጥናትለመሳተፍፈቃደኛመሆኔንበፊርማዬአረጋግጣለሁ፡፡

እኔየተባልኩትግለሰብይህንሁሉ

በማገናዘብበምርምሩላይስለኔመረጃእናየደምናሙናለመስጠትተስማምቻለሁ፡፡

የተሳታፊፊርማ _____ ቀን_____

_____

10.3. Questionnaire (English and Amharic versions)

Questionnaire (English version)

Dear respondents, you are kindly requested to give correct information accordingly.Thank you for your time and kindness.

Please answer every question in the questionnaire by marking "X" in the space or filling the necessary information. Thank you for taking time to complete this questionnaire.

Code N$^{o.}$_____ Card No._____

Part 1: Socio-Demographic Characteristics

I. Personal information

1.1. Age (Year)_____

1.2.Gender: □Male_____ □ Female _____

1.3.Region_____

1.4.Residence area (X): □ Rural_____ □Urban_____

1.5.Education level (X): □Illiterate ____□high school or less _____

□college or above_____

1.6.occoupation_____

1.7.Socioeconomic status (X): □ High(≥ 2917/month)

□Middle (1,500_2917/month)

□Low(< 1,500/month)

1.8.Marital status (X): □Single_____ □Married _____

□Widowed _____□divorced_____

II.Body Mass Index

1. Weight (in Kg) _____
2. Height (m)_____

3. BMI_____

III.Physical Activity

1. Do you perform physical exercise?

□Yes □No

2. If Yes, how often per week?

□Occasionally □ 4days □ 3days □ 2days □other____

IV. Alcohol consumption

1. Do you consume alcohol?

□ Yes □ No

2. Type of alcohol consume?.

□ traditional (locally) made alcohol □fabricated alcohol

3.If you say locally made alcohol, how often?.

□occasional □ 1 cup alcohol daily □2-5 cups of alcohol daily □other__

4. If you say fabricated alcohol, how often?

□Occasionally □1 Bottle alcohol daily □ 2-5 Bottle alcohol daily □other__

5. Is alcohol consumption status

□ Past □ present

V. Smoking

1. Do you smoke?

□Yes □No

2. If yes, how often?

□Occasionally □1 cigar daily □ 1 pack per day □ other____

3.how many packet/year please specify_____

4. Is smoking status

□ Past □ present

Part II: Personal Medical history

2.1 . Any of chronic condition(s)(X) :

□Diabetes type 1 _____ □Diabetes type 2____ □ High cholesterol___

□Hypertension_____ □Cardiovascular diseases other than hypertension

□Chronic obstructive pulmonary diseases(COPD) □Chronic renal diseases □Other chronic condition Specify_____

2.2. □ If DM, duration of diabetes (in months)_____

□If high cholesterol, Duration of high cholesterol(in months)_____

□If Hypertension, duration of hypertension(in months)_____

□If Cardiovascular diseases other than hypertension, duration (in months)__

□ If Chronic obstructive pulmonary diseases(COPD), duration (in months)___

□If Chronic renal diseases, duration (in months)___

□ If any other chronic conditions specify the duration in months_____

2. 3. Any drugs taking for diabetes(X):

□Yes_____ □ No_____

□ If**yes** specify the name(s) of the anti-diabetic drugs_____

□ And Duration (in months)_____

2.4. Any drugs taking for high cholesterol(X): Yes_____ No_____

□ If**yes** specify the name of the drugs_____

□ And Duration (in months)_____

2. 5. Any drugs taking for hypertension(X): Yes_____ No_____

□If **yes** specify the name of the anti-hypertensive drug(s)_____

□And duration (in months)_____

2.6. Any drugs taking for Cardiovascular diseases other than hypertension (X):

Yes_____ No_____

□If **yes** specify the name of the drug(s)_____

□And duration (in months)_____

2.7. Any drugs taking for Chronic obstructive pulmonary diseases(COPD)(X):

Yes_____ No_____

□If **yes** specify the name of the drug(s)_____

□And duration (in months)_____

2.8. Any drugs taking for Chronic renal diseases(X):

Yes_____ No_____

□If **yes** specify the name of the drug(s)_____

□And duration (in months)_____

2.9. Any drug(s) taking for other chronic conditions(X): Yes____ No____

□ If**yes** specify the name of the drug(s)_____

□And Duration (in months)_____

2.10. Any drugs taking for cancer(X): Yes_____ No_____

□If **Yes**What is the name(s)of drug specify_____

□ And Duration (in months)_____

2. 11. Any surgical operation done with in these two months before now(X)?.

□ Yes_____ □ No_____

□ If**yes** please specify the type of operation done_____

2.12. Any acute infection(s) encountered with in these two months before now(X)

□Yes_____ □ No_____

□ If**yes** please specify the name of the infection(s)_____

□ And the name of the drug(s) taken/taking if any_____

□And also duration of taking_____

Part III: Personal and Family history gastrointestinal malignancy

3.1. Have you ever had certain gastrointestinal malignancy conditions before?

□Yes_____ □No_____

□ If**yes** specify the type of gastrointestinal malignancy_____

3.2. Have you ever had certain cancer conditions other than gastrointestinal

Malignancy?. □ Yes _____ □ No: _____

□If **yes** specify the type of cancer_____

3.3. Family history of gastrointestinal malignancy (X) : □ Yes __□ No: ___

□ If **yes** (X), □1st degree relative _____ □ 2nd degree relative _____

□ 3rd degree relative _____

3.4.Family history of the specified gastrointestinal malignancy type (X):

□Yes _____ □ No_____

□If **yes** (X), □ 1st degree relative _____ □2nd degree relative _____

□ 3rd degree relative _____

3.5. Family history of other type of Cancer other than gastrointestinal (X) :

□Ovarian cancer____ □Endometrial cancer _____

□Breast cancer_____

□Other cancers Please specify _____

□ If **specified** (X), the specified cancer occur in:

□ 1st degree relative ____ □ 2nd degree relative __

□3rd degree relative _____

Part IV: Clinico-pathological characteristics

4.1. Type of gastrointestinal malignancy _____

4.1.1.Duration of illness (in months) _____

4.1.2. Specific Site of the gastrointestinal malignancy specify_____

4.2. How was the malignancy found (X)

4.2.1. As part of regular physical examination _____

4.2.2. Endoscopy (Colonoscopy) _____

4.2.3. Laparoscopy and laparoscopic _____

4.2.4.Image ultrasonography, CT Scan /MRI_____

4.2.5. Occult Blood_____

4.2.6 Others please specify_____

4.3. Sign and Symptom at presentation (X)

4.3.1.Abdominal pain_____

4.3.2. Appetite loss_____

4.3.3.Blood in stool(Tarry stool, Occult bllod)_____

4.3.4.Noticeable increase in fatigue and/or weakness_____

4.3.5.Unexplained weight loss_____

4.3.6.Nausea_____

4.3.7.Vomiting_____

4.3.8. Long standing constipation_____

4.3.9.Partial/complete intestinal obstruction_____

4.3.10.Others please specify_____

4.4. Stage of disease at diagnosis (X): I_____II _____ III _____ IV _____

4.5. TNM Classification of the tumor(Pathological):

4.5.1.Tumour size (X):

4.5.1.1.Tx_____

4.5.1.2. T1_____

4.5.1.3.T2_____

4.5.1.4.T3_____

4.5.1.5.T4_____

4.5.1.6.Tumor Size unspecified_____

4.5.2. Lymph node involvement (X):

4.5.2.1.Nx_____

4.5.2.2.N0_____

4.5.2.3.N1_____

4.5.2.4.N2_____

4.5.2.5.Lymph node status unspecified _____

4.5.3. Distant Metastasis (X):

4.5.3.1.M0 _____

4.5.3.2.M1_____

4.5.3.3.Distant Metastasis Unspecified_____

4.6.TNM Classification of the tumor(Clinical):

4.6.1. Tumour size (X):

4.6.1.1. TX -

4.6.1.2. T0 -

4.6.1.3.Tis -

4.6.1.4. T1, T2, T3, T4 –

4.6.2.Lymph node involvement (X):

4.6.2.1.NX -

4.6.2.2.N0 -

4.6.2.3.N1, N2, N3 –

4.6.3.Distant Metastasis (X):

4.6.3.1. MX -

4.6.3.2.M0 -

4.6.3.3.M1 -

4.7. Histology of the cancer (X):

4.7.1. Type of histological finding please specify_____

4.8.Degree of differentiation (X):

4.8.1. Well _____

4.8.2. Moderately _____

4.8.3.poorly _____

Questionnaire (Amharic version)

መጠይቅ

ውድተሳታፊቀጥሎያለውንመጠይቅለመሙላትስለተባበሩንእናመሰግናለን፡፡

ካርድቁጥር

መጠይቅ፡-

- መጠየቁንስትሞሉየ“X” ምልክትበክፍትቦታውላይበማስቀመጥእንድትሞሉበአክብሮትእንጠይቃለን፡፡

ክፍልአንድ

የታካሚዎችየአናኗርሁኔታ

1. **የታካሚውማንነት**

1.1 እድሜ (በአመት) .....

1.2 ፆታ ☐ወንድ ☐ት

1.3 ክልል .....

1.4 የመኖሪያአካባቢ ☐ከር ☐ማ

1.5 የትምህርትደረጃ

☐የልተማረ ☐ደኖደረጃ ☐ከተኖሁለተኖደረጃ

☐ኮሌጅናበላይ

1.6 .ስራ .....

1.7 . የአኮኖሚደረጃ ☐ከፍተኛገቢያለው≥2917/ወር

☐ከለያገቢያለውከ1500-2917/ወር

☐ዝተኛገቢያለው< 1500/ወር

1.8 .የጋብቻሁኔታ

☐የላገባ ☐ባ

☐ልወይምሚስትበህይወትየሌላው(ላት) ☐ግብታ(ቶ) የፈታ(ች)

2. <u>የታካሚውአካላዊሁኔታ</u>

1. ክብደትወይምግዝፈት (በኪሎግራም) .....
2. ቁመት (በሜትር) .....
3. የግዝፈትቁመትትስስር (በኪሎግራም /ሜ^2) .....

3. <u>የአካልብቃትእንቅስቃሴሁኔታ</u>

1. የአካልብቃትእንቅስቃሴያደረጋሉ

☐አዎ ☐አደርግም

አዎካሉበሳምንትስንትቀናትያደርጋሉ

☐አልፎአልፎአልታወቀቀናት
☐በሳምንትአራትቀናት
☐በሳምንትሶስትቀናት
☐በሳምንትሁለትቀናት
☐ሌላ.....

4. <u>የአልኮልመጠጥይወስዳሉ (ይጠቀማሉ) ?</u>

1. የአልኮልመጠጥይወስዳሉ

☐አዎ ☐አልወስድም

2. **አዎ**ካሉምንአይነትየአልኮልመጠት

☐ህላዊ (በዘልማድ) የተዘጋጀነው? አይነቱይግለፁ.....
☐ፋብሪካየወጣነው? ዓይነቱይግለፁ .....

3. ባህላዊ (በዘልማድየተዘጋጀ) ከሆነ (ነውካሉመጠኑምንያህልነው) በመለኪያይግለፁ.....

☐ልፎአልፎ ☐ለትእስከአምስትበቀን(መለኪያ)
☐ንድመለኪያበቀን ☐ከሆነምይጥቀሱ.....

4. የፋብሪካየአልኮልመጠጥከሆነመጠኑንበቀንውስጥምንያህልነው

☐ አልፎአልፎ

☐ አንድጠርሙስበቀን

☐ ሁለትእስከአምስትበቀን (ጠርሙስ)

☐ አላከሆነምይጥቀሱ.....

5. <u>ያጨሳሉ(ትንባሆ) (ሲጋራ)</u>

1. ያጨሳሉ (አጫሰውያውቃሉ)?

☐ አዎ ☐ ኩሽኤላውቅም

2. **አዎ**ካሉበቀንምንያህል

☐ አልፎአልፎላልታወቀጊዜ

☐ አንድሲጋራበቀን

☐ አንድፓኬትበቀን

☐ አላከሆነይጥቀሱ .....

3. **አዎ**ካሉበአመትስንትፓኬትያጨሳሉይጥቀሱ .....

4. ያጨሱበትወቅት

☐ ሁንጊዜነው

☐ ለፈጊዜነው

<u>ክፍልሁለት</u>

<u>የታካሚውየጤናሁኔታታሪክ</u>

2.1 .ከዚህበታችየተዘረዘሩትስርየሰደዱየጤናእግሮችአለቦት

☐ ስኳርህመም (አንደናው) አይነት

☐ ስኳርህመም (ሁለተኛው) አይነት

ከፍተኛየሆነየኮንስትሮል (የቅባት) መጠንአለቦት?

የደምግፊትህመም

ልብናተያያዥየሆኑህመሞአለቦት

የሳንባናሌሎችተያያዥየሆኑየመተንፈሻአካልህመምአለብዎት

ርየሰደደየኩላሊትችግርአለብዎት

ሌላካለይጠቁ----------

2.2 . ስኳርካሉእንዳለብዎትካወቁምንያህልጊዜሆነዎት?(በወራት/በአመት) ይጥቀሱ.....

ፍተኛየሆነየኮሎስትሮልመጠን(የሰብ)ቅባትመጠንካሉካወቁምንያህልጊዜሆነዎት (በወራት/በአመት) ይጥቀሱ

የደምፍፊትአለብኝካሉአንዳለብዎትካወቁምንያህልጊዜሆነዎት(በወራትወይምአመት) ይጥቀሱ.....

የልብናተያያዥየሆኑችግሮችአለብኝካሉካወቁምንያህልጊዜሆነዎትየአመት/በወር) ይጥቀሱ.....

ስርየሰደዱየሳንባናሌሎችተዛማጅየሆኑየመተንፈሻአካልህመምአለብኝካሉካወቁምንይህልጊዜሆነዎት (በወራት/ በአመ) ይጥቀሱ.

ስርየሰደደየኩላሊትችግርነውካሉአይነቱንናከወቁምንያህልጊዜእንደሆነዎት (በወራት) አመትይጥቀሱ.....

ሌላሰርሰደደየቆየየጤናችግርካለቦት(ነው) ካሉካወቁምንያህልጊዜእንደሆነዎት (በወራት)በዓመትይጥቀሱ፤

2.3 .**የስኳርህመም**አለብኝካሉለስኳናየሚመስዱትመድኃድኒትአለ

ኝዎ አልወስድም

ወስዳለሁካሉየስኳርህመምየመድኃኒቱንአይነትይጥቀሱ_____

ዎየስኳርህመምመድኃኒትእወስደለውካሉለምንያህልየጊዜእንደወሰዱ (በወራት) አመት) ይጥቀሱ…

2.4 .ከፍተኛየሆነየኮልስትሮል /ሰብ/ቅባትችግርአለብኝካሉለችግሩየሚመስዱትመድኃኑትአለ

ዎእወስዳለሁ ወስድም

ኣዎእወስደለሁካሉየመድሃኒቱንአይነትይጥቀሱ .....

መድሃኒቱንለምንያህልጊዜወሰዱት(በወር)በአመት) ይጥቀሱ.....

2.5 .የደምግፊትነውካሉለደምግፊቱየሚወስዱትመድሃኑትአለ

☐አዎእወስዳለሁ ☐አልወስድም

☐አዎእወስዳለሁካሉየመድሃኒቱንአይነትይጥቀሱ_____

☐የደምግፊትመድሃኒቱንለምንያህልጊዜወሰዱት(በወራት/በአመት) ይጥቀሱ .....

2.6 .ስርየሰደደየሳንባናሌሎችተዛማጅየሆኑየመተንፈሻአካልችግርአለብኝካሉለችግሩየሚወስዱትመድሃኒትአለ

☐አዎእወስዳለሁ ☐አልወስድም

☐አዎእወስዳለውካሉየመድሃኒቱንአይነትይጥቀሱ.....

☐መድሃኒቱንለምንህልጊዜወሰዱበወራት/በአመትይጥቀሱ.....

2.7 .ላለብዎየካንሰርህመምየሚወስዱትመድሃኒትአለ?

☐አዎእወስዳለሁ ☐ድም

☐አዎእወስዳለሁካሉየመድሃኒቱንአይነትይጥቀሱ .....

☐መድሃኒቱንለምንያህልጊዜወሰዱት(ለወደፊት/በአመትይጥቀሱ).....

2.8 .በዚህሁለትወራትውስጥቀዶጥገናአድርገውያውቃሉ፤

☐አዎ ☐ኧረኩም

☐አዎአደርጌአለሁካሉያደረጉትንየቀዶጥገናአይነትይጥቀሱ .....

☐ደረጉምንያህልጊዜሆነዎትበቀናትይጥቀሱ .....

2.9 .በዚህባሳለፍነው 2 ወራትውስጥአጣዳፊየሆነየጤናችግርአጋጥሞዎትያውቃል::

☐አዎ ☐ምኝአያውቅም

☐አዎአጋጥሞኛልካሉያጋጠመሞትንአጣዳፊየጤናችግርይግለፁ.....

☐ጤናችግርከጋጠመዎትምንያህልጊዜሆኖዎት(በቀናት) ይጥቀሱ.....

ክፍል 3

3.1 የታካሚውናየቤተሰብስላለባቸውየካንሰርችግርሁኔታ

3.1.1 ከአሁንበፊትአሁንያለበዎትየካንሰርችግርወይንምተዛማጅየሆኑ(GIT) ካንሰርችግርታካሚያውቃሉ

☐ ዎ ☐ ም

☐ ዎካሉየነበረቦትንየካንሰርአይነትይጥቀሱ_____

3.1.2 ከአሁንበፊትአሁንያላለቦዎትወይምተዛማጅከሁኑ (GIT) ካንሰርልላየካንሰርአይነትተመውያውቃሉ

☐ ዎ ☐ ም

☐ ዎካሉየካንሰሩንአይነትይጥቀሱ_____

3.1.3 በቤተሰብዎ /በዝምድዋ/ ላይ አሁን ያለበዎት ካንሰር አይነት ወይንም ተዛማጅ የሆነ (GIT) ካንሰር ተመመ ወይም ታመው የሚያውቁት አለ?

☐ ዎ ☐ ም

☐ ዎካሉከዚህበታችከተዘረዘሩትምልከቶች

☐ ናት/አባት/ልጅ

☐ ያት፣ወንድም፣እህት፣የልጅልጅ

☐ ድመአያት፣የወንድም (የእህትልጅ)፣የልጅልጆች፣አክስት፣አጎት

☐ ሌላካለይጥቀሱ.....

3.1.4 በቤተሰብዎ /በዘመድዎ/ አሁን ካለብዎት የካንሰር አይነት ጋር ተመሳሳይ የሆነ የካንሰር አይነት ታሞየሚያውቁ ወይንም ታመመ አለ?

☐ ዎ ☐ ም

☐ ዎካሉከዚህበታችየተዘረዘሩትውስጥምልከትያድረጉ

☐ ናት፣አባት፣ልጅ

☐ ያት፣ወንድም፣እህት፣የልጅልጅ

☐ ድመአያት፣የወንድም (የእህትልጅ)፣የልጅልጆች፣አክስት፣አጎት

☐ ሌላካለይጥቀሱ.....

3.1.5 በቤተሰብዎ/በዘመድዎ/ አሁንካለብዎት (ተዛማጅ) ከሆኑ (GIT) ካንሰር ሌላ ከዚህ በታች ከተዘረዘሩት ውስጥ ወይም ሌላ ካለ ይጥቀሱ

☐ የዘርፍሬከረጢት (ኦቨሪ) ካንሰር

☐ የማህፀንውስጠኛውቅናሽካንሰር (endometrial cancer)

☐ የጡትካንሰር

☐ ሌላካለይጥቀሱ .....

☐ ከላይከተዘረዘሩትየካንሰርአይነቶችሌላከጠቀሱካንሰሩየተከሰተውከዚህበታችከተዘረዘሩትውስጥማንላይነውይጥቀሱ .....

☐ እናት፣አባት፣ልጅ

☐ አያት፣ወንድም፣እህት፣የልጅልጅ

☐ ጓደመአያት፣የወንድም(የእህትልጅ)፣የልጅልጆች፣አክስት፣አጎት

☐ ሌላካለይጥቀሱ.....