

# **NON-ALCOHOLIC FATTY LIVER DISEASE: AN EXPANDING PROBLEM WITH LOW LEVELS OF AWARENESS IN DHAKA**

A dissertation submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the Degree of Bachelor of Pharmacy.

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## **Declaration by the Research Candidate**

I, **Shabbir Ahmed Robin**, hereby declare that this dissertation, entitled “**Non-Alcoholic Fatty Liver Disease: An Expanding Problem with Low Levels of Awareness in Dhaka**” submitted to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the degree of Bachelor of Pharmacy is a genuine & authentic research work carried out by me. The contents of this dissertation, in full or in parts, have not been submitted to any other institute or University for the award of any degree or Diploma of Fellowship.

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This is to certify that the dissertation, entitled “**Non-Alcoholic Fatty Liver Disease: An Expanding Problem with Low Levels of Awareness in Dhaka**” submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the degree of Bachelor of Pharmacy is a bona fide research work done by **Shabbir Ahmed Robin, ID: 2014-1-70-040** of his research in the Department of Pharmacy, East West University, under the supervision and guidance of me.

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## **Endorsement by The Chairperson**

This is to certify that the dissertation, entitled “**Non-Alcoholic Fatty Liver Disease: An Expanding Problem with Low Levels of Awareness in Dhaka**” submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the degree of Bachelor of Pharmacy is a bona fide research work done by **Shabbir Ahmed Robin, ID: 2014-1-70-040**.

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I express my sincere thankfulness to my family for guiding me all through my life, including that for my research project.

## *Dedication*

*This Thesis Paper is Dedicated to*

*My Beloved Parents,*

*Who are*

*My Biggest Inspiration...*

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## ABBREVIATIONS

<b>ALT</b>	Alanine Aminotransferase
<b>AST</b>	Aspartate Aminotransferase
<b>BMI</b>	Body Mass Index
<b>CT Scan</b>	Computed Tomography Scan
<b>FDA</b>	Food and Drug Administration
<b>HCC</b>	Hepatocellular Carcinoma
<b>HDL</b>	High Density Lipoprotein
<b>IDDM</b>	Insulin Dependent Diabetes Mellitus
<b>IR</b>	Insulin Resistance
<b>MetS</b>	Metabolic Syndrome
<b>MHO</b>	Metabolically Healthy Obesity
<b>NAFLD</b>	Non-Alcoholic Fatty Liver Disease
<b>NASH</b>	Non-Alcoholic Steatohepatitis
<b>NIDDM</b>	Non-Insulin-Dependent Diabetes Mellitus
<b>PT</b>	Prothrombin Time
<b>PTT</b>	Partial Thromboplastin Time
<b>RBC</b>	Red Blood Cells
<b>TG</b>	Triglyceride
<b>T2DM</b>	Type 2 Diabetes Mellitus

## ABSTRACT

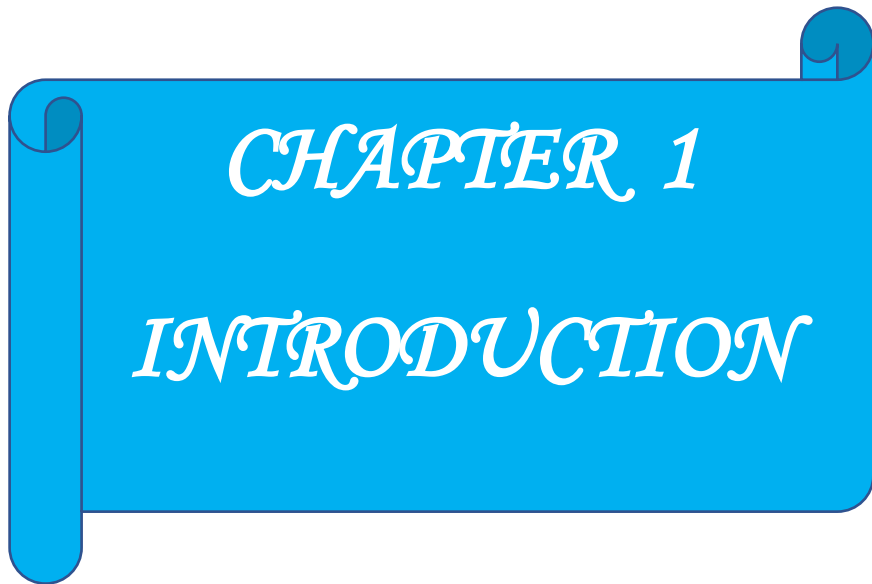
Non-alcoholic Fatty Liver Disease (NAFLD) is excessive buildup of fat mainly in the form of triglycerides in the liver tissue without any consumption of alcohol. NAFLD acts as a significant risk factor for the development of liver cirrhosis and hepatocellular carcinoma (HCC). With the modernization of the lifestyle and changing food habit of people and the rising prevalence of diabetes and obesity, NAFLD has become a serious problem in Dhaka. The purpose of this study was to find out about the knowledge and awareness of people in Dhaka about NAFLD.

The survey based study was carried out between July 2017 to December 2017 in different areas and hospitals in Dhaka among 165 participants. Participants were both male and female aged more than 18 years.

The result showed that 81% of the people have never come across the term “NAFLD”. Only 5.5% of the participants have been diagnosed with NAFLD among which 33.3% are pre-obese and 66.7% are overweight according to their BMI. 89% of the NAFLD patients also have diabetes which means diabetic people are in high risk for developing NAFLD. Knowledge about other lifestyle and food habit related diseases was also inadequate. Although 76% of the people are highly educated the knowledge and awareness of people about NAFLD is quite surprising.

The survey provided an inadequate knowledge and awareness about NAFLD among the people in Dhaka although having higher education level.

**Keywords:** NAFLD, HCC, Diabetes, BMI, Obese, Awareness.



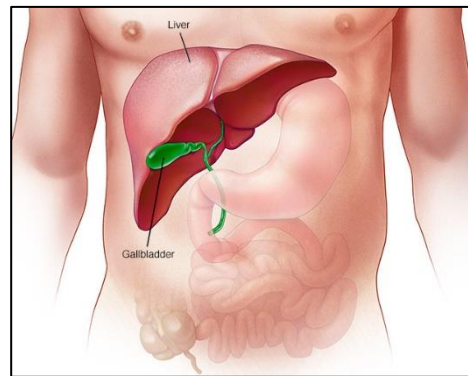
*CHAPTER 1*

*INTRODUCTION*

## 1. Introduction

### 1.1.1 Liver

The liver is the largest glandular organ. And it is located in the upper-right portion of the abdominal cavity under the diaphragm and to the right of the stomach. It's protected by the rib cage. The gallbladder sits under the liver, along with parts of the pancreas and intestines. The liver and these organs work together to digest, absorb, and process food (healthline.com 2017; webmd.com 2017).



**Figure 1.1.1:** Liver (Human anatomy)

An average adult liver weighs about three pounds. The liver is reddish-brown in color and feels rubbery to the touch. Liver performs multiple critical functions to keep the body pure of toxins and harmful substances. The main function of liver is to filter the blood coming from the digestive tract, before passing it to the rest of the body. The liver is considered a gland (an organ that secretes chemicals) because it produces bile (a substance needed to digest fats). Bile's salts break up fat into smaller pieces so it can be absorbed more easily in the small intestine (webmd.com 2017).

### 1.1.2 Functions of Liver

In addition to producing bile, the liver-

- Detoxifies the blood to rid it of harmful substances such as alcohol and drugs.
- Stores some vitamins and iron.
- Stores the sugar glucose.
- Produces proteins important for blood clotting.

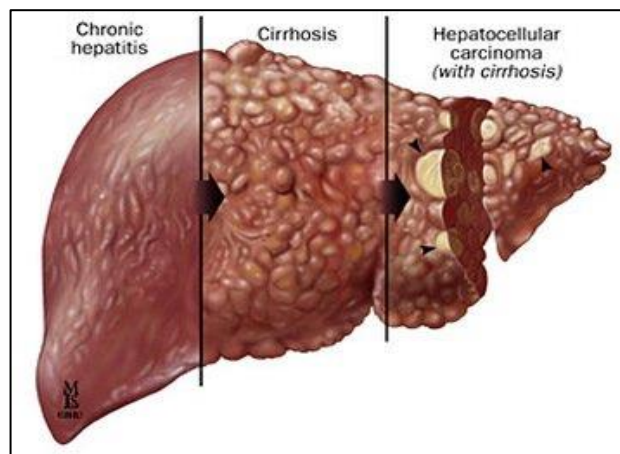
- Converts stored sugar to functional sugar when the body's sugar (glucose) levels fall below normal.
- Breaks down hemoglobin as well as insulin and other hormones.
- Converts ammonia to urea, which is vital in metabolism.
- Destroys old RBCs (Red Blood Cells) (healthline.com 2017).

### 1.1.3 Different Liver Diseases

A variety of illnesses can affect the liver, for example,

- **Hepatitis:**

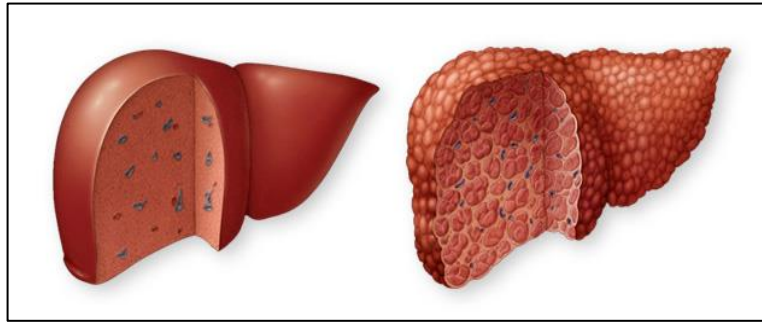
Inflammation of the liver, usually caused by viruses like hepatitis A, B, and C. Hepatitis can have non-infectious causes too, including heavy drinking, drugs, allergic reactions, or obesity (webmd.com 2017). Autoimmune hepatitis is a disease that occurs when your body makes antibodies against your liver tissue.



**Figure 1.1.2:** Chronic Hepatitis, Cirrhosis & Liver Cancer (hubpages.com 2015)

- **Cirrhosis:**

Long-term damage to the liver from any cause can lead to permanent scarring, called cirrhosis (webmd.com 2017). As cirrhosis becomes worse, the liver will have less healthy tissue. If cirrhosis is not treated, the liver will fail and will not be able to work well or at all (liverfoundation.org 2015).

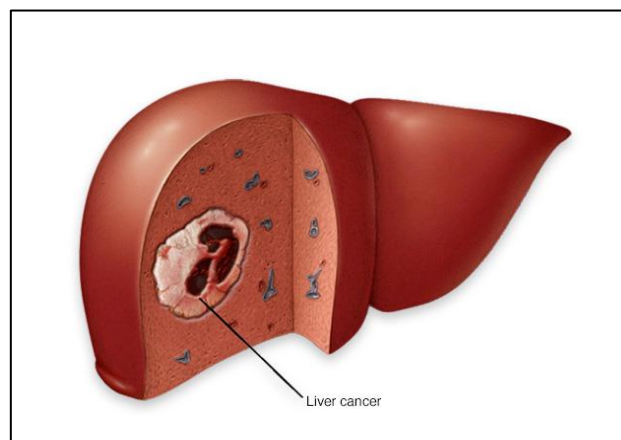


**Figure 1.1.3:** Normal liver vs. liver cirrhosis (mayoclinic.org 2017)

A normal liver (left) shows no signs of scarring. In cirrhosis (right), scar tissue replaces normal liver tissue.

- **Liver cancer:**

The most common type of liver cancer, hepatocellular carcinoma, almost always occurs after cirrhosis is present. It is one of the leading cause of death currently. The most common form of liver cancer begins in cells called hepatocytes and is called hepatocellular carcinoma (webmd.com 2017).



**Figure 1.1.4:** Liver Cancer (mayoclinic.org 2017)

- **Liver failure:**

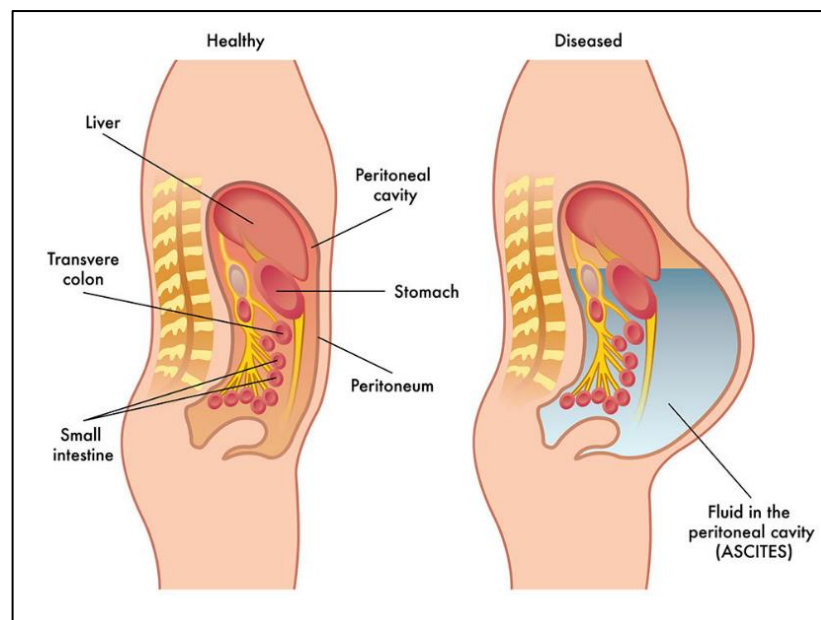
Liver failure occurs when large parts of the liver become damaged beyond repair and the liver is no longer able to function. Liver failure has many causes including infection, genetic diseases, and excessive alcohol (webmd.com 2017).



- **Ascites:**

As a result of Cirrhosis, the liver leaks fluid (ascites) into the belly, which becomes distended and heavy (webmd.com 2017).

In its early stages, ascites can usually be treated with medication (diuretics) and/or a salt-restricted diet. However, these treatments sometimes become ineffective or are no longer tolerated by the body. In such cases the ascites is described as 'refractory' to medical therapy and it is removed by paracentesis or sometimes by the placement of a shunt called TIPS. If the above treatments are ineffective, liver transplantation may be required (alfapump.com 2017).

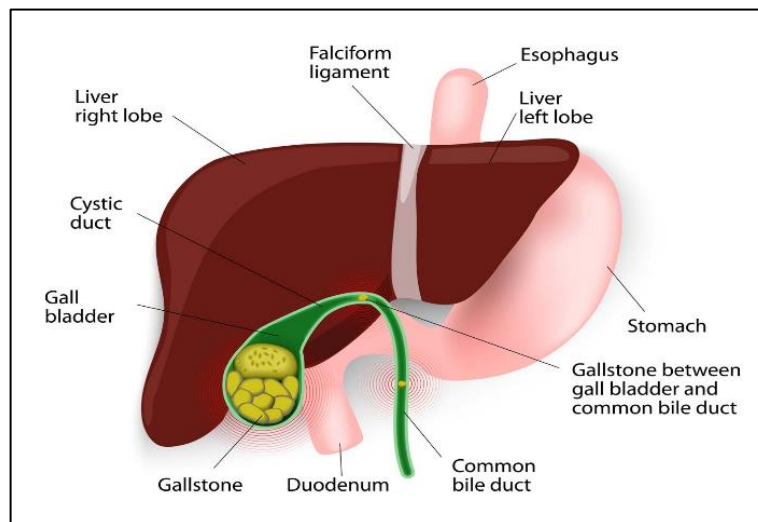


**Figure 1.1.5:** Normal liver vs. Ascites liver (alfapump.com 2017)

A normal liver (left) shows no signs of fluid leakage. In Ascites liver (right), liver leaks fluid into belly.

- **Gallstones:**

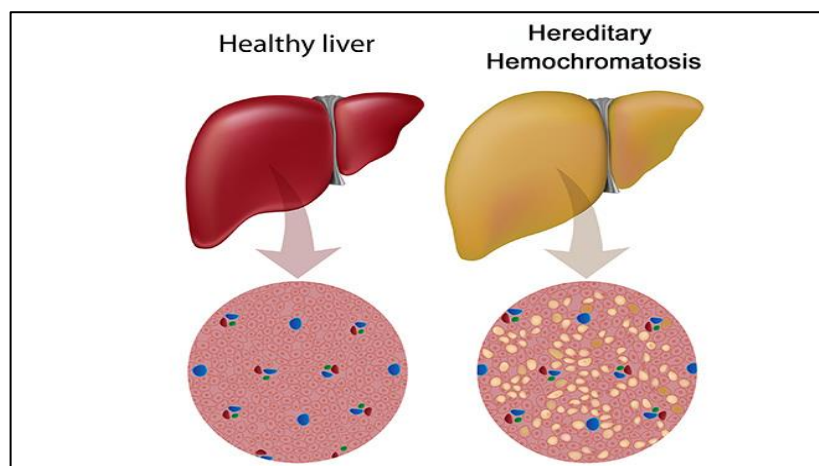
If a gallstone becomes stuck in the bile duct draining the liver, hepatitis and bile duct infection (cholangitis) can result (webmd.com 2017).



**Figure 1.1.6:** Gallstones (Grünhage et al. 2007)

- **Hemochromatosis:**

Hemochromatosis allows iron to deposit in the liver, damaging it. The iron also deposits throughout the body, causing multiple other health problems (webmd.com 2017).

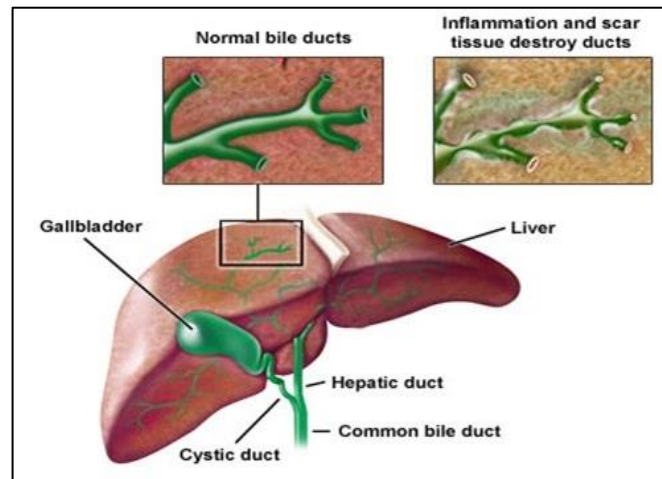


**Figure 1.1.7:** Normal liver vs. Hemochromatosis liver (Vineetha 2017)

A Healthy liver (left) shows no signs of iron deposition. In Hemochromatosis liver (right), iron is deposited.

- **Primary Sclerosing Cholangitis:**

A rare disease with unknown causes, primary sclerosing cholangitis causes inflammation and scarring in the bile ducts in the liver (webmd.com, 2017).

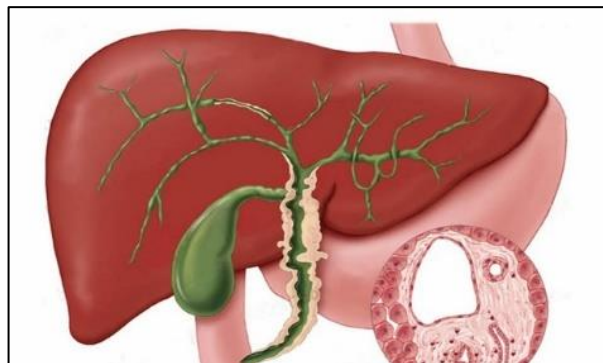


**Figure 1.1.8:** Normal liver vs. Primary Sclerosing Cholangitis (MedicalAssessment.com 2017)

Healthy bile duct (left) shows no signs of scarring. In Primary Sclerosing Cholangitis (right), inflammation and scarring of the bile ducts of the liver is seen.

- **Primary Biliary Cirrhosis:**

In this rare disorder, an unclear process slowly destroys the bile ducts in the liver. Permanent liver scarring (cirrhosis) eventually develops (webmd.com 2017).



**Figure 1.1.9:** Primary Biliary Cirrhosis (medlibes.com 2010)

- **Alcohol-related liver disease**

The liver is damaged after years of alcohol misuse, this can lead to cirrhosis (scarring of the liver) (nhs.uk 2017).

- **Non-alcoholic fatty liver disease (NAFLD)**

A build-up of fat within liver cells, usually seen in overweight people or those who are obese (nhs.uk 2017).

### **1.1.4 Symptoms of liver diseases**

Symptoms of liver disease can vary, but they often include-

- Swelling of the abdomen and legs
- Changes in the color of your stool and urine
- Weakness and fatigue
- Weight loss
- Nausea
- Vomiting, and
- Yellow discoloration of the skin (jaundice)

Sometimes there are no symptoms. Tests such as imaging tests and liver function tests can check for liver damage and help to diagnose liver diseases (medicinenet.com 2017).

### **1.1.5 Liver Tests**

#### **1.1.5.1 Blood Tests**

- **Liver function panel:**

A liver function panel checks how well the liver is working and consists of many different blood tests (webmd.com 2017).

- **ALT (Alanine Aminotransferase):**

An elevated ALT helps identify liver disease or damage from any number of causes, including hepatitis (webmd.com 2017).

- **AST (Aspartate Aminotransferase):**

Along with an elevated ALT, the AST checks for liver damage (webmd.com 2017).

- **ALP (Alkaline Phosphatase):**

Alkaline phosphatase is present in bile-secreting cells in the liver; it's also in bones. High levels often mean bile flow out of the liver is blocked (webmd.com 2017).

**Table 1.1.1:** Normal Range Values for Liver Function Blood Tests (jotscroll.com 2017)

Tests	Normal Range
Bilirubin	5-17 $\mu\text{mol l}^{-1}$
Alkaline Phosphatase (ALP)	35-130 $\text{IU l}^{-1}$
Aspartate Transaminase (AST)	5-40 $\text{IU l}^{-1}$
Alanine Transaminase (ALT)	5-40 $\text{IU l}^{-1}$
Albumin	35-50 $\text{g l}^{-1}$
Prothrombin time (PT)	12-16 s

- **Bilirubin:**

High bilirubin levels suggest a problem with the liver (webmd.com 2017).

- **Albumin:**

As part of total protein levels, albumin helps determine how well the liver is working (webmd.com 2017).

- **Ammonia:**

Ammonia levels in the blood rise when the liver is not functioning properly (webmd.com 2017).

- **Hepatitis A tests:**

If hepatitis A is suspected, the doctor will test liver function as well as antibodies to detect the hepatitis A virus (webmd.com 2017).

- **Hepatitis B tests:**

Your doctor can test antibody levels to determine if you have been infected with the hepatitis B virus (webmd.com 2017).

- **Hepatitis C Tests:**

In addition to checking liver function, blood tests can determine if you have been infected with the hepatitis C virus (webmd.com 2017).

- **Prothrombin Time (PT):**

A prothrombin time, or PT, is commonly done to see if someone is taking the correct dose of the blood thinner warfarin (Coumadin). It also checks for blood clotting problems (webmd.com 2017).

- **Partial Thromboplastin Time (PTT):**

A PTT is done to check for blood clotting problems (webmd.com 2017).

### **1.1.5.2 Imaging Tests**

- **Ultrasound:**

An abdominal ultrasound can test for many liver conditions, including cancer, cirrhosis, or problems from gallstones (webmd.com 2017).

- **CT scan (computed tomography):**

A CT scan of the abdomen gives detailed pictures of the liver and other abdominal organs (webmd.com 2017).

- **Liver biopsy:**

A liver biopsy is most commonly done after another test, such as a blood test or ultrasound, indicates a possible liver problem (webmd.com 2017).

- **Liver and Spleen Scan:**

This nuclear scan uses radioactive material to help diagnose a number of conditions, including abscesses, tumors, and other liver function problems (webmd.com 2017).

### **1.2.1 Steatosis**

Fatty liver, or hepatic steatosis, is a term that describes the buildup of fat in the liver. It's normal to have some fat in the liver, but too much can become a health problem. Fatty liver is when fat accounts for more than 5-10% of the liver's weight (Calzadilla Bertot and Adams 2016).

When this progresses to become associated with inflammation, it is known as steatohepatitis.

Fatty liver disease is divided into:

- Alcohol-related fatty liver disease.
- Non-alcoholic fatty liver disease (NAFLD) (Bhala et al. 2009).

### **1.2.2 Non-alcoholic fatty liver disease (NAFLD)**

NAFLD is an umbrella term for a range of liver conditions affecting people who drink little to no alcohol. As the name implies, the main characteristic of NAFLD is too much fat stored in liver cells (Mayoclinic.org 2017).

NAFLD is defined as the presence of  $\geq 5\%$  hepatic steatosis without evidence of hepatocellular injury in the form of hepatocyte ballooning (Chalasani et al. 2017).

NAFLD is mainly associated with insulin resistance, type 2 diabetes mellitus, obesity, hypertriglyceridemia and hypertension; thus, it is regarded as a hepatic component of the metabolic syndrome, and an independent risk factor for cardiovascular disease (Ábel and Lengyel 2017).

Early-stage NAFLD doesn't usually cause any harm, but it can lead to serious liver damage, including cirrhosis, when it gets worse, associated with inflammation (nhs.uk 2016). Non-alcoholic steatohepatitis (NASH), a potentially serious form of the disease, is marked by liver inflammation, fibrosis associated with steatosis which may progress to scarring and irreversible damage. This damage is like the damage caused by heavy alcohol use. At its most severe, NASH can progress to cirrhosis and liver failure (mayoclinic.org 2017).

NAFLD is increasingly common around the world, especially in Western nations. In the United States, it is the most common form of chronic liver disease, affecting an estimated 80 to 100 million people. NAFLD occurs in every age group but especially in people in their 40s and 50s who are at high risk of heart disease because of such risk factors as obesity and type II diabetes. The condition is also closely linked to metabolic syndrome, which is a cluster of abnormalities including increased abdominal fat, poor ability to use the hormone insulin, high blood pressure and high blood levels of triglycerides, a type of fat (mayoclinic.org 2017).

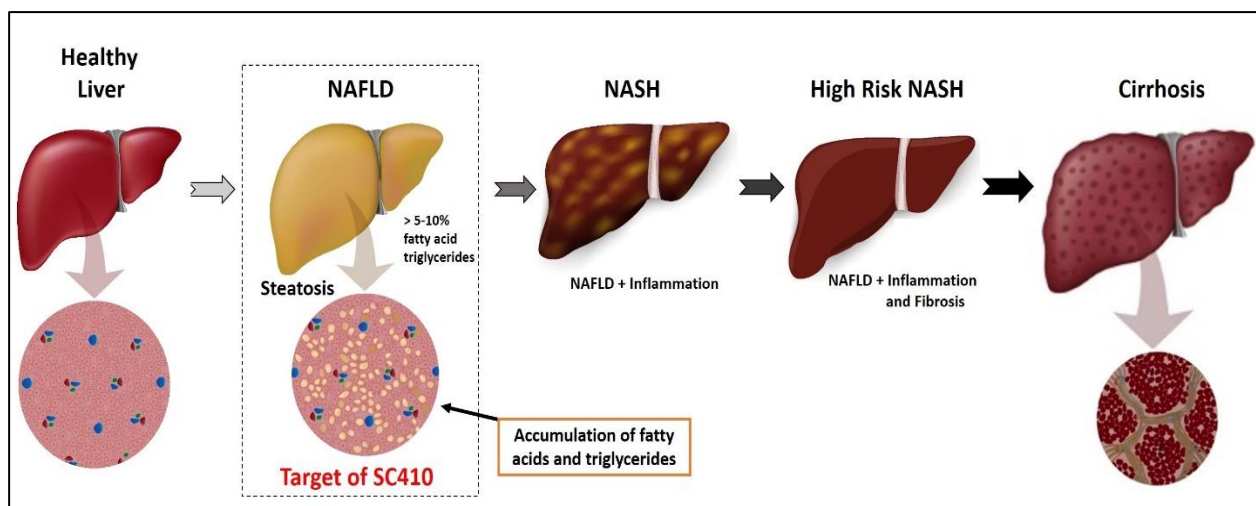
### 1.2.2.1 Stages of NAFLD

NAFLD develops in 4 main stages. Most people will only ever develop the first stage, usually without realizing it. In a small number of cases, it can progress and eventually lead to liver damage if not detected and managed (nhs.uk 2016).

The main stages of NAFLD are:

#### 1. Simple Fatty Liver (Steatosis)

A largely harmless build-up of fat in the liver cells that may only be diagnosed during tests carried out for another reason (nhs.uk 2016).



**Figure 1.2.1:** Overview of the Progression of NAFLD from a Healthy Liver to Cirrhosis (sancilio.com 2017)



## 2. Non-Alcoholic Steatohepatitis (NASH)

A more serious form of NAFLD, where the liver has become inflamed; ('Steato' means fat, and 'hepatitis' means inflammation of the liver) this is estimated to affect up to 5% of the UK population (nhs.uk 2016).

## 3. Fibrosis

Where persistent inflammation causes scar tissue around the liver and nearby blood vessels, but the liver is still able to function normally (nhs.uk 2016).

## 4. Cirrhosis

The most severe stage, occurs after years of inflammation. Here the liver shrinks and becomes scarred and lumpy. This damage is permanent and can lead to liver failure and liver cancer. It can take years for fibrosis or cirrhosis to develop (nhs.uk 2016).

### **1.2.2.2 Symptoms of NAFLD**

Nonalcoholic fatty liver disease usually causes no signs and symptoms. When it does, they may include:

- Enlarged liver
- Fatigue
- Pain in the upper right abdomen
- Abdominal swelling (ascites)
- Enlarged blood vessels just beneath the skin's surface
- Enlarged breasts in men
- Enlarged spleen
- Red palms
- Yellowing of the skin and eyes (jaundice) (Mayoclinic.org 2017).

### **1.2.2.3 Risk factors of NAFLD**

A wide range of diseases and conditions can increase risk of nonalcoholic fatty liver disease, including:

- High cholesterol
- High levels of triglycerides in the blood
- Metabolic syndrome
- Obesity, particularly when fat is concentrated in the abdomen
- Polycystic ovary syndrome
- Sleep apnea
- Type 2 diabetes
- Underactive thyroid (hypothyroidism)
- Underactive pituitary gland (hypopituitarism)

Nonalcoholic steatohepatitis is more likely in these groups:

- Older people
- People with diabetes

It is difficult to distinguish nonalcoholic fatty liver disease from nonalcoholic steatohepatitis without further testing (Mayoclinic.org 2017).

### **1.2.2.4 Incidence and Prevalence of NAFLD:**

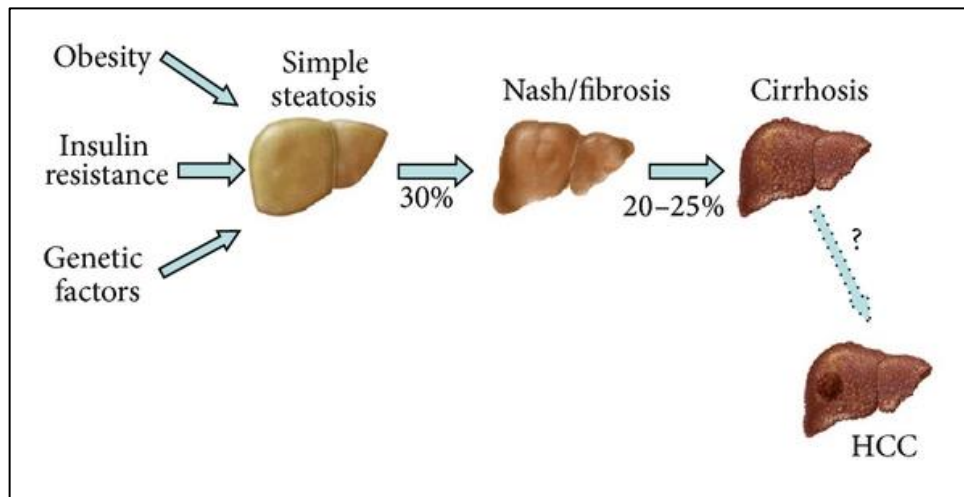
Nonalcoholic fatty liver disease (NAFLD) is a major cause of liver disease worldwide. In a study, the global prevalence of NAFLD is 25.24% with highest prevalence in the Middle East and South America and lowest in Africa. Metabolic comorbidities associated with NAFLD included obesity 51.34%, type 2 diabetes 22.51%, hyperlipidemia 69.16%, hypertension 39.34%, and metabolic syndrome 42.54%. Fibrosis progression proportion, and mean annual rate of progression in NASH were 40.76% (Younossi et al. 2016).

The prevalence of NAFLD in the general population of Western countries is 20-30%. About 2-3% of the general population is estimated to have NASH, which may progress to liver cirrhosis and hepato-carcinoma. As a rule, the prevalence of NAFLD is higher in males and increases with increasing age, and it is influenced by the diagnostic method and the characteristics of the population, especially lifestyle habits. Study have reported that 30% of the adults in the USA and 25% in Italy have NAFLD. The prevalence of NAFLD is 80-90% in obese adults, 30-50% in patients with diabetes and up to 90% in patients with hyperlipidemia. The prevalence of NAFLD among children is 3-10%, rising up to 40-70% among obese children. Moreover, pediatric NAFLD increased from about 3% a decade ago to 5% today, with a male-to-female ratio of 2:1 (Bellentani et al. 2010).

#### **1.2.2.5 Prevalence of NAFLD in High-Risk Groups**

Features of metabolic syndrome (MetS) are not only highly prevalent in patients with NAFLD, but components of MetS also increase the risk of developing NAFLD. This bidirectional association between NAFLD and components of MetS has been strongly established (Chalasani et al. 2017).

- **Obesity (excessive body mass index [BMI] and visceral obesity):** It is the most common and well-documented risk factor for NAFLD. In fact, the entire spectrum of obesity, ranging from overweight to obese and severely obese, is associated with NAFLD. In this context, the majority (>95%) of patients with severe obesity undergoing bariatric surgery will have NAFLD (Chalasani et al., 2017).
- **Type 2 diabetes mellitus (T2DM):** There is a very high prevalence of NAFLD in individuals with T2DM. In fact, some studies have suggested that around one third to two thirds of diabetic patients have NAFLD. It is also important to remember the importance of bidirectional association between NAFLD and T2DM. In this context, T2DM and NAFLD can develop almost simultaneously in a patient, which confounds the prevalence of NAFLD in patients with T2DM or the prevalence of T2DM in patients with NAFLD (Chalasani et al., 2017).



**Figure 1.2.2:** Obesity, Genetic Factors, and Insulin Resistance (IR) Contribute to Fat Deposition in the Liver (Oliveira et al., 2016)

- **Dyslipidemia:** High serum triglyceride (TG) levels and low serum high-density lipoprotein (HDL) levels are also common in patients with NAFLD. The prevalence of NAFLD in individuals with dyslipidemia attending lipid clinics has been estimated to be 50%. The overall prevalence rate of NAFLD was 53.76%; however, the NAFLD prevalence rate for those with the lowest total cholesterol to HDL-cholesterol and TG to HDL-cholesterol ratios was 33.41%, whereas the prevalence rate in the group with the highest ratios was 78.04% (Chalasani et al., 2017).
- **Age, sex, and ethnicity:** The prevalence of NAFLD may vary according to age, sex, and ethnicity. In fact, both the prevalence of NAFLD and stage of liver disease appear to increase with age (Chalasani et al., 2017).

### 1.3.1 Diabetes Mellitus

Diabetes mellitus is a syndrome of impaired carbohydrate, fat, and protein metabolism caused by either lack of insulin secretion or decreased sensitivity of the tissues to insulin (Guyton and Hall 2006).

There are two general types of diabetes mellitus:

**1. Type I diabetes**, also called insulin-dependent diabetes mellitus (IDDM), is caused by lack of insulin secretion (Guyton and Hall 2006).

**2. Type II diabetes**, also called non-insulin-dependent diabetes mellitus (NIDDM), is caused by decreased sensitivity of target tissues to the metabolic effect of insulin. This reduced sensitivity to insulin is often called insulin resistance (Guyton and Hall 2006).

In both types of diabetes mellitus, metabolism of all the main foodstuffs is altered. The basic effect of insulin lack or insulin resistance on glucose metabolism is to prevent the efficient uptake and utilization of glucose by most cells of the body, except those of the brain. As a result, blood glucose concentration increases, cell utilization of glucose falls increasingly lower, and utilization of fats and proteins increases (Guyton and Hall 2006).

### **1.3.1.1 Type I Diabetes: Lack of Insulin Production by Beta Cells of the Pancreas**

Injury to the beta cells of the pancreas or diseases that impair insulin production can lead to type I diabetes. Viral infections or autoimmune disorders may be involved in the destruction of beta cells in many patients with type I diabetes, although heredity also plays a major role in determining the susceptibility of the beta cells to destruction by these insults. In some instances, there may be a hereditary tendency for beta cell degeneration even without viral infections or autoimmune disorders (Guyton and Hall 2006).

The usual onset of type I diabetes occurs at about 14 years of age in the United States, and for this reason it is often called juvenile diabetes mellitus (Guyton and Hall 2006).

### **1.3.1.2 Type II Diabetes: Resistance to the Metabolic Effects of Insulin**

Type II diabetes is far more common than type I, accounting for about 90 per cent of all cases of diabetes mellitus. In most cases, the onset of type II diabetes occurs after age 30, often between the ages of 50 and 60 years, and the disease develops gradually. Therefore, this syndrome is often referred to as adult-onset diabetes. In recent years, however, there has been a steady increase in the number of younger individuals, some less than 20 years old, with type II diabetes. This trend appears to be related mainly to the increasing prevalence of obesity, the most important risk factor for type II diabetes in children as well as in adults (Guyton and Hall 2006).

### **1.3.2 Relation of NAFLD and Diabetes**

NAFLD and type 2 diabetes (T2DM) are common conditions that regularly co-exist and can act synergistically to drive adverse outcomes. The presence of both NAFLD and T2DM increases the likelihood of the development of complications of diabetes (including both macro- and micro-vascular complications) as well as augmenting the risk of more severe NAFLD, including cirrhosis, hepatocellular carcinoma and death (Hazlehurst et al. 2016).

NAFLD and diabetes usually co-exist and that there is significant amount of unrecognized advanced NAFLD within asymptomatic diabetic patients. Obesity and physical inactivity are interlinked risk factors for the development of diabetes and both are clearly implicated in an individual's risk of developing NAFLD. In a large cross-sectional study, an individual's sitting time was associated with NAFLD diagnosed using US and interestingly this association held true in those with a normal BMI. Obesity is well known to correlate with both NAFLD prevalence and severity. In a study of patients who had liver biopsies whilst undergoing elective abdominal surgery the BMI was strongly correlated with NASH and in a separate study intraabdominal fat was associated with NASH (Hazlehurst et al. 2016).

### **1.4.1 Obesity**

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health (WHO 2017).

Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. It is defined as a person's weight in kilograms divided by the square of his height in meters ( $\text{kg}/\text{m}^2$ ) (WHO 2017).

Below is the equation used for calculating BMI in the International System of Units (SI):

$$BMI = \frac{\text{Weight (Kg)}}{\text{Height}^2(\text{m}^2)}$$

The table below shows the BMI cut-off according to both WHO criteria and Asian criteria:

**Table 1.4.1: Nutritional Status Based on the WHO and Asian Criteria Values**

BMI	WHO Criteria	Asian Criteria
Underweight	<18.5	<18.5
Normal	18.5-24.9	18.5-22.9
Overweight	25-29.5	23-24.9
Pre-obese	-	25-29.9
Obese	≥30	≥30

### **1.4.2 Obesity and NAFLD**

Obesity is known to be an important risk factor for a whole range of noncommunicable diseases that include type 2 diabetes mellitus (T2DM), chronic obstructive sleep apnea, various types of cancers (for example, colorectal cancer, esophagus and breast cancer after the menopause) and NAFLD. Although the fact that obesity increases risk of certain diseases is well accepted by clinicians, evidence has shown that some individuals who are obese are also metabolically healthy: so-called metabolically healthy obesity (MHO). BMI categories are positively associated with an increased incidence of NAFLD, suggesting that the obese phenotype, regardless of metabolic abnormalities, might increase the risk of developing NAFLD (Targher and Byrne 2016).

In a retrospective cohort study involving metabolically healthy individuals, Chang *et al.* found that BMI categories are positively associated with an increased incidence of NAFLD, suggesting that the obese phenotype, regardless of metabolic abnormalities, might increase the risk of developing NAFLD.

### **1.5 Treatment of NAFLD:**

Treatment falls into two categories: targeting either the steatosis or the pathogenesis of progression. There are no FDA approved pharmacologic agents and, no FDA guidelines for such drugs (Tolman and Dalpiaz 2007).

### **1.5.1 Treatment of Steatosis/Insulin Resistance**

The treatment of steatosis is inexorably linked to obesity, insulin resistance and dyslipidemia. In general, factors that decrease steatosis consist of weight loss or pharmacologic therapy directed at insulin resistance or dyslipidemia. The treatment of steatohepatitis is directed at oxidative stress, inflammation and fibrosis. Factors that decrease oxidative stress and inflammation include antioxidants, probiotics, anti-cytokines and glutathione precursors. Anti-fibrotic therapy is in its infancy (Tolman and Dalpiaz 2007).

### **1.5.2 Weight loss**

Weight loss improves liver chemistries, steatosis, necroinflammatory changes and fibrosis. (Huang et al., 2005) Weight loss may be achieved through diet and exercise or bariatric surgery. Weight loss and regular exercise is significantly associated with improvement in serum ALT and increased the odds of ALT normalization, while starting smoking was significantly associated with deterioration in serum ALT. Reducing weight by at least 5% with subsequent weight control and exercising regularly may be beneficial in treating NAFLD. (Suzuki et al., 2005) Furthermore, gradual weight reduction has been shown to lower insulin levels and improve quality of life (Petersen et al. 2005).

### **1.5.3 Diet**

The ideal diet and rate of weight loss is yet to be determined although it is known that rapid weight loss may exacerbate disease (Andersen et al. 1991). The durability of weight loss on hepatic steatosis remains to be determined. Low fat diets should be avoided (Kang et al. 2006; Solga et al. 2004). Some have suggested that a Mediterranean diet (i.e., high consumption of complex carbohydrates and monounsaturated fat, low amounts of red meat, and low/moderate amounts of wine) is preferred (Musso et al. 2003).

### **1.5.4 Bariatric surgery**

Bariatric surgery, has proved successful in many studies. The formerly used ileal bypass surgery was, however, associated with fatty liver and even hepatic failure. The durability of bariatric surgery has yet to be determined but it seems likely to be the only therapy that will change the natural history of NASH (Angulo 2006).



### **1.5.5 Orlistat**

Orlistat is a lipase inhibitor that promotes weight loss by reduction of fat absorption. Orlistat decreased aminotransferase levels and reversed fatty liver as determined by ultrasound, although alkaline phosphatase levels increased during therapy. The side effects of gas, bloating and steatorrhea are problematic (Sabuncu et al. 2003).

### **1.5.6 Sibutramine**

Sibutramine, an appetite suppressant, is a serotonin reuptake antagonist approved for weight loss. It also has been studied in patients with NAFLD. It significantly improved aminotransferases in 13 of 13 patients and decreased evidence of hepatic steatosis on ultrasound in 11 of 13 patients in an open label, nonrandomized study. These patients were all obese and were diagnosed with NASH. Alkaline phosphatase levels increased during therapy (Sabuncu et al. 2003).



*CHAPTER 2*

*LITERATURE*

*REVIEW*

## 2. Literature Review

1. **Adams et al.** in 2005 reported about *the natural history of nonalcoholic fatty liver disease*.
2. **Andersen et al.** in 1991 reported the *Hepatic effects of dietary weight loss in morbidly obese subjects*.
3. **Angulo** in 2006 reported about *NAFLD, Obesity, and Bariatric Surgery*.
4. **Bellentani et al.** in 2010 reported about the *Epidemiology of Non-Alcoholic Fatty Liver Disease*.
5. **Calzadilla et al.** in 2016. *The Natural Course of Non-Alcoholic Fatty Liver Disease*.
6. **Chalasani et al.** in 2017 reported that *The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases*. *Hepatology*.
7. **Della Pepa et al.** in 2017 reported *Isocaloric Dietary Changes and Non-Alcoholic Fatty Liver Disease in High Cardiometabolic Risk Individuals*.
8. **Grünhage et al.** in 2007 about the *Increased gallstone risk in humans conferred by common variant of hepatic ATP-binding cassette transporter for cholesterol*.
9. **Huang et al.** in 2005 in a *pilot study of one-year Intense Nutritional Counseling Results in Histological Improvement in Patients with Non-Alcoholic Steatohepatitis*.
10. **Vernon et al.** in 2011 reported in a *Systematic review about the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults*.



*CHAPTER 3*  
*METHODOLOGY*

### **3. METHODOLOGY**

#### **3.1 Type of Study:**

The study was performed to find out about the knowledge and awareness of people of Dhaka city about Non-Alcoholic Fatty Liver Disease (NAFLD) and how lifestyle related diseases are also a risk factor for the progression of NAFLD.

#### **3.2 Study Area:**

BIRDEM General Hospital, NHN Hospital, East West University, Bangladesh University of Professionals and, Bashabo area.

#### **3.3 Study Population:**

In this study, a total number of 165 people were surveyed with a questionnaire to assess the knowledge, perception about NAFLD in people around Dhaka city. Only the participants who agreed to join the study were interviewed and provided the required information for the studies.

#### **3.4 Study Duration:**

The duration of the study was about six months starting from July to December in 2017.

#### **3.5 Questionnaire Development:**

The questionnaire was specially designed to collect the simple background data and the needed information. The questionnaire was written in simple English to avoid unnecessary semantic misunderstanding.

#### **3.6 Sampling Technique:**

In this study, purposive sampling technique was followed.

#### **3.7 BMI Calculation:**

Below is the equation used for calculating BMI in the International System of Units (SI):

**S.I. Units:**

$$BMI = \frac{Weight (Kg)}{Height^2 (m^2)}$$

### **3.8 Data Analysis:**

After collecting, the data were checked and analyzed with the help of Microsoft Excel 2016. The result was shown in pie and column chart and calculated the percentage of the results.

### 3.9 Sample Question

#### Demographic Information:

**Name:**

**Gender:**  Male  Female

**Height:**

**Age:**

**Weight:**

**Education:**  S.S.C  H.S.C  Graduate  Others:

**Occupation:**

**Marital Status:**  Single  Married  Widowed  Divorced

1. Do you perform any exercise?
  - Yes  No
  - \*If yes, what type of exercise do you perform?
    - Walking/Running  Swimming  Heavy exercises  Light exercises
    - Others, \_\_\_\_\_
2. What do you prefer to use?  Elevators  Stairs
3. Do you have breakfast every day?  Yes  No
4. How long do you take to have dinner?
  - ≤15 minutes  ≤30 minutes  ≥30 minutes
5. How many plates of rice or number of ruti do you eat at dinner?  
-
6. How many times per week do you eat meat dishes?
  - Never  Several Times  Occasionally
7. How many times do you eat out?
  - Never  Several Times  Occasionally
8. How many times per week do you eat fast food?
  - Never  Several Times  Occasionally
9. How many times per week do you eat fried items? (Fried rice, Fried chicken, Puri etc.)
  - Never  Several Times  Occasionally
10. How many times per week do you eat sweets?
  - Never  Several Times  Occasionally
11. Do you smoke?  Yes  No
12. Do you know following diseases are related to your lifestyle or food habit?

Disease Name	Yes	No
Diabetes		
Arthritis		
Fatty Liver Disease		
Obesity		
Heart Disease		
Stroke		
Liver Cirrhosis		

13. Do you have diabetes?

- Yes                       No

14. How long do you have diabetes? \_\_\_\_\_

15. Do you have a family history of diabetes?

- Yes                       No

\*If Yes, what is the relation with him/her? \_\_\_\_\_

16. Do you take insulin?

- Yes                       No

\*If yes, since when you started taking insulin?

- From the beginning of diagnosis     After a while

17. Do you take other medication for lowering blood glucose level (Oral hypoglycemic)?

- Yes                       No

\*If yes, name of the medication: \_\_\_\_\_

18. Have you heard the name of NAFLD (Non-Alcoholic Fatty Liver Disease)?

- Yes                       No

19. Have you ever been diagnosed with the following liver diseases? (Give ✓ marks)

Disease	Yes	NO
Hepatitis B		
Hepatitis C		
Liver Cirrhosis		
Fatty Liver		

20. Do you have high cholesterol level?

- Yes                       No

\*If yes, what are the medications you take for lowering cholesterol?

-

21. Have you been diagnosed with high blood pressure?

- Yes                       No

\*If yes, what are the medications you take for lowering blood pressure?

-





*CHAPTER 4*  
*RESULT*

## 4. Result

### 4.1 Gender

In the study, percentage of male and female participants were 42% and 58% respectively.

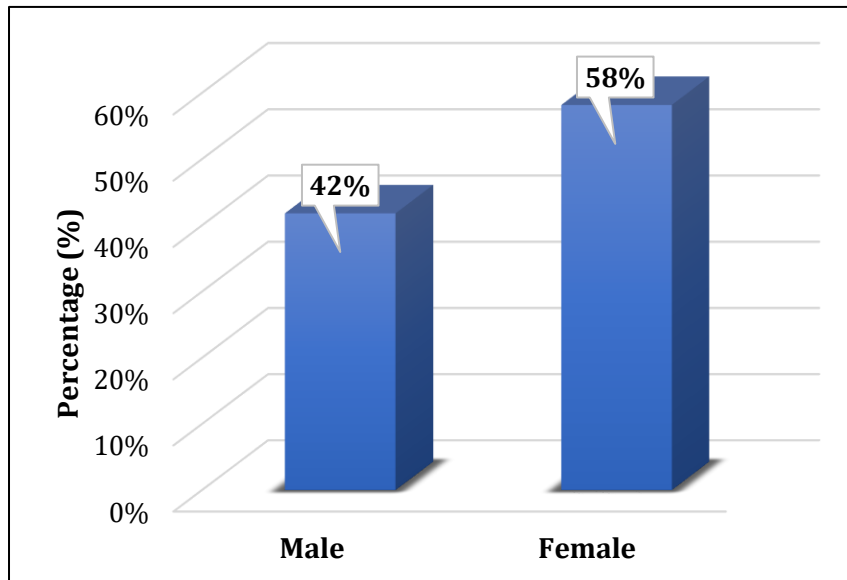


Figure 4.1: Gender Percentage of the Participants

### 4.2 Age Range

38% of the participants age were between 15-30 years, 25% of the participants were between 31-45 years, 28% of the participants age were between 46-60 years and 8% of participants age were 60+ age.

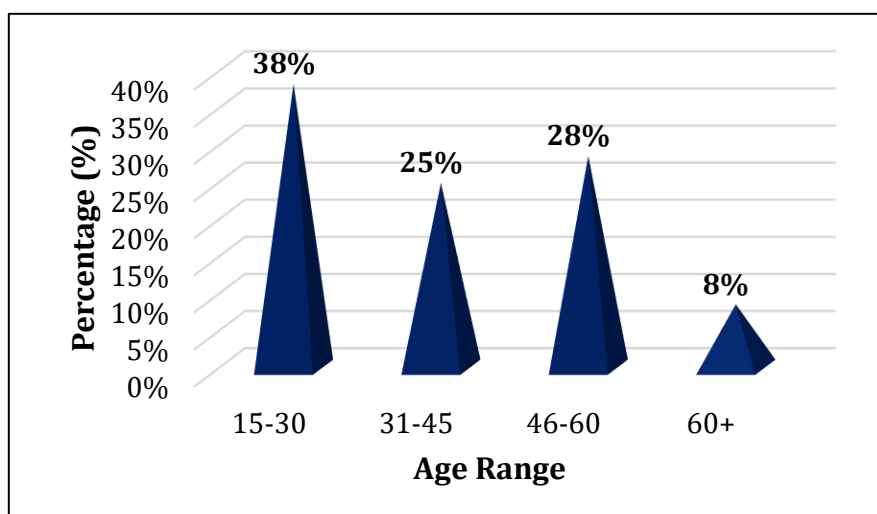


Figure 4.2: Age Range of the Participants

### 4.3 Level of Education

In the study, participants level of education was found that 16% have education level below S.S.C, 8% have passed S.S.C, 19% have passed H.S.C, and 57% are graduated and post graduated.

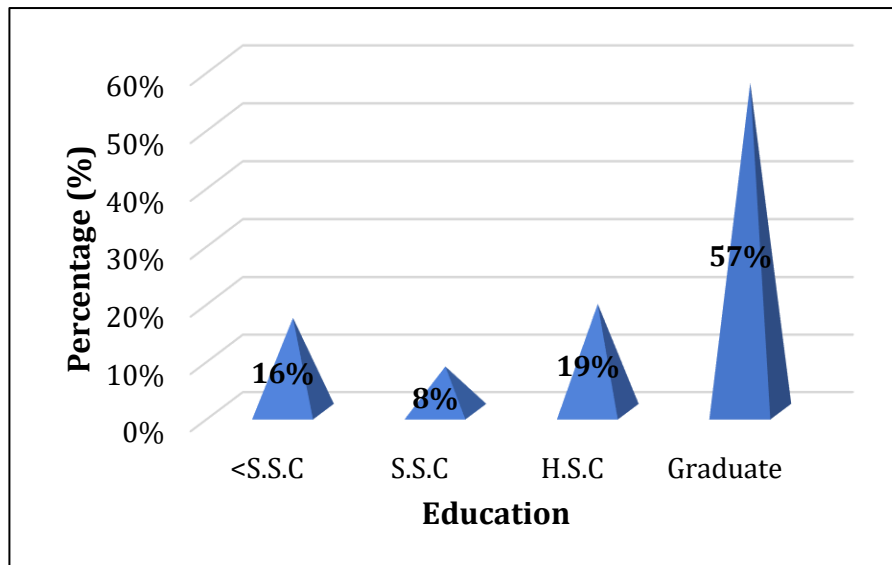


Figure 4.3: Education Level Percentage of the Participants

### 4.4 BMI of the Participants:

BMI percentage of normal, overweight, pre-obese and, obese people among the total are respectively 14%, 26%, 42% and, 17.0%.

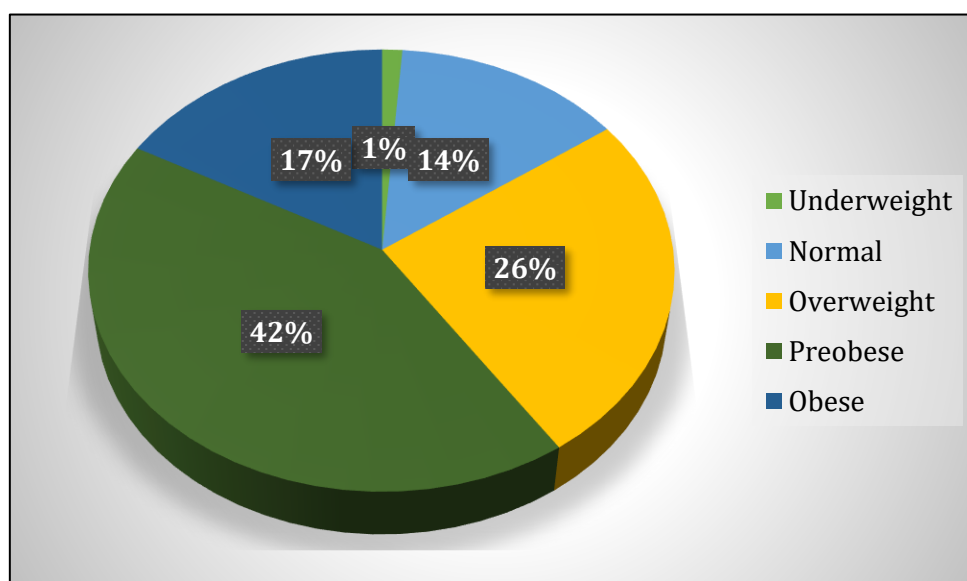


Figure 4.4: BMI Percentage of the Participants

#### 4.5 Respondents Performing Exercise

Percentage of participants who perform exercise were 65.5% and 34.5% of people don't perform any exercise.

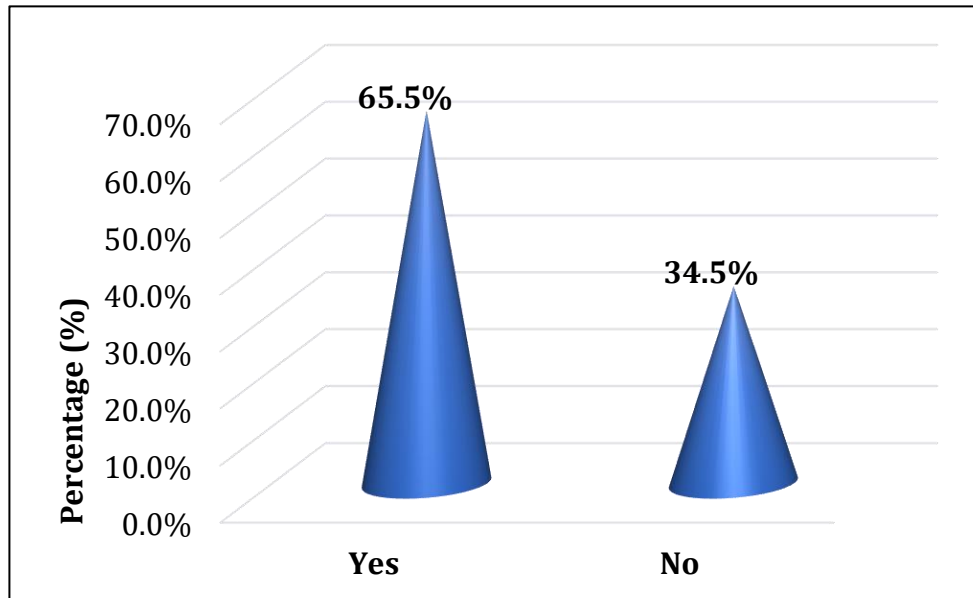


Figure 4.5: Percentage of Respondents Performing Exercise

#### 4.6 Respondents Performing Different Types of Exercise

In the graph, we can see the percentage of people performing different types of exercise.

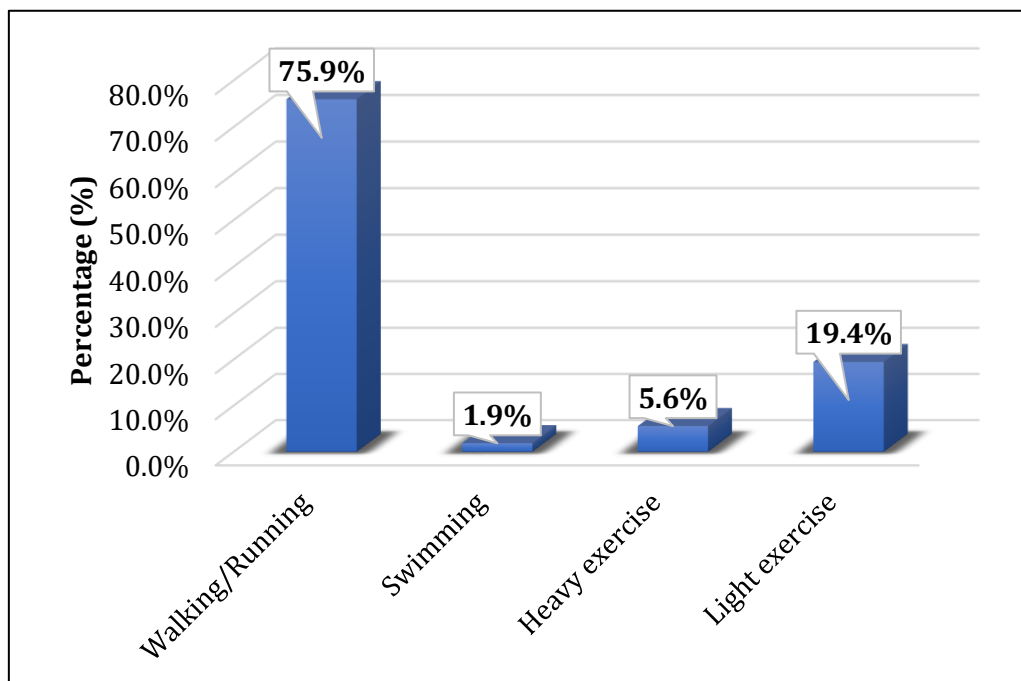


Figure 4.6: Percentage of Respondents Performing Different Types of Exercise

#### 4.7 Respondents Preferring to use Stairs or Elevators

In the graph, we can see the percentage of people performing elevators or stairs.

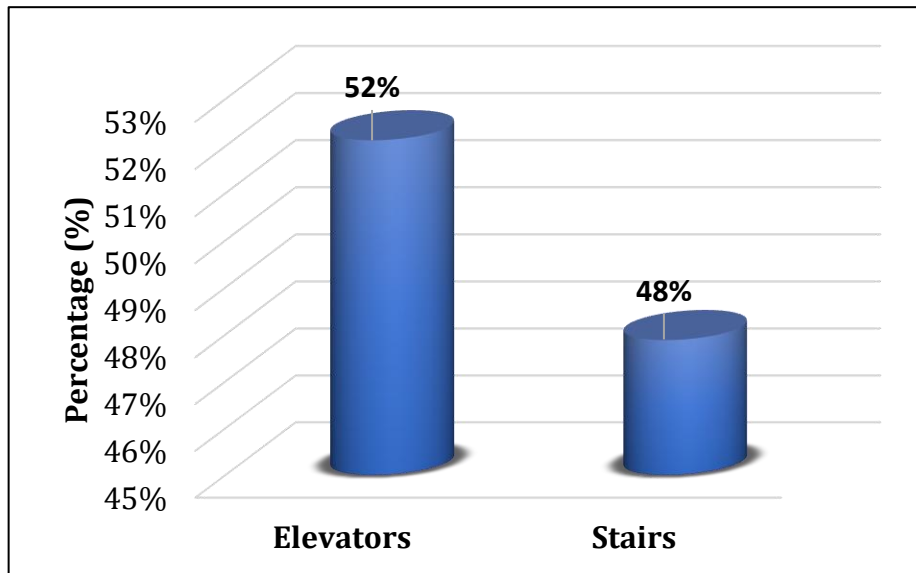


Figure 4.7: Percentage of Respondents Preferring to use Stairs or Elevators

#### 4.8 Respondents Food Habit (Breakfast)

85% of people have breakfast regularly while 15% don't.

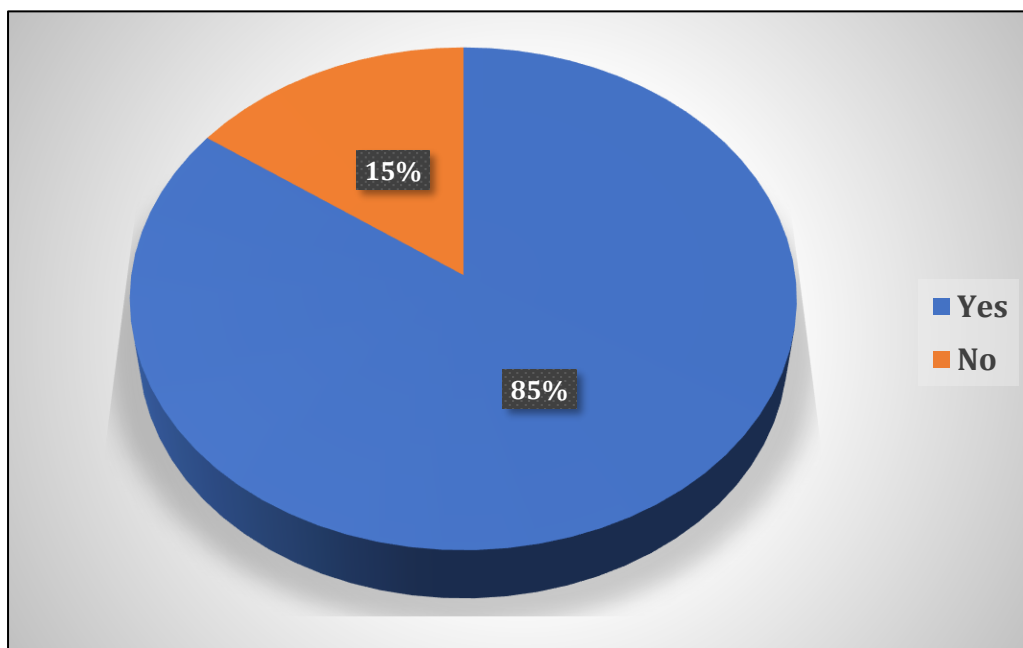


Figure 4.8: Percentage of Respondents Food Habit (Breakfast)

### 4.9 Respondents Food Habit (Dinner Time)

There were different results about the participants time for having dinner.

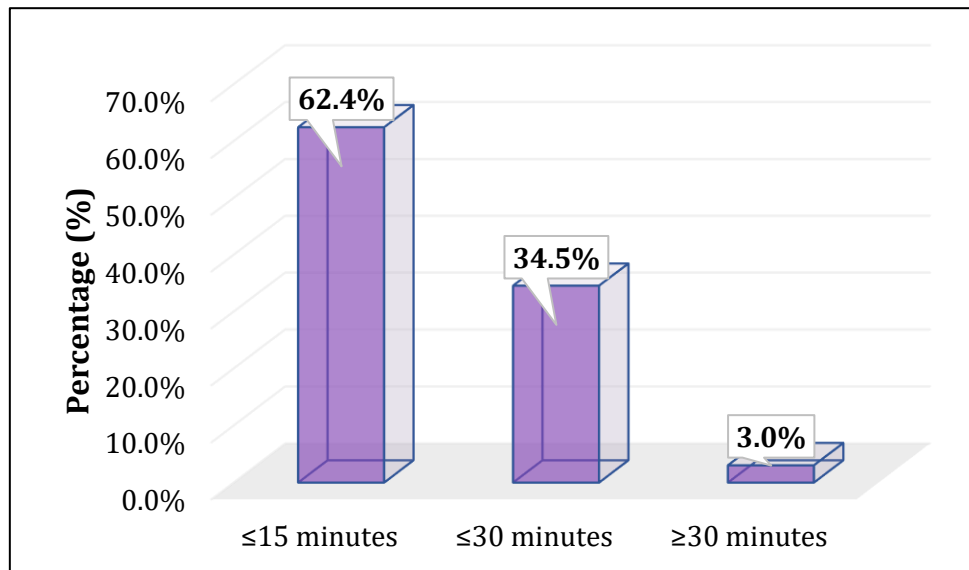


Figure 4.9: Percentage of Respondents Food Habit (Dinner Time)

### 4.10 Respondents Food Habit (Amount of Rice or Roti in Dinner)

There were different results about the participants food habit like amount of rice or roti they have.

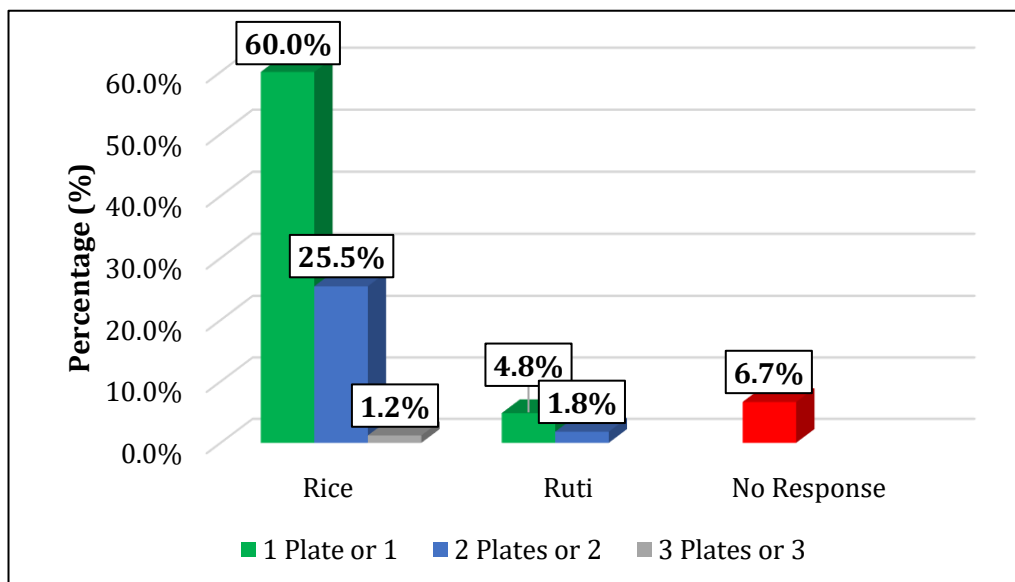


Figure 4.10: Percentage of Respondents Food Habit (Amount of Rice or Roti in Dinner)

### 4.11 Respondents Food Habit

Percentage of people who eat out, have meat dishes, fast food, fried items and sweets are shown in the graph.

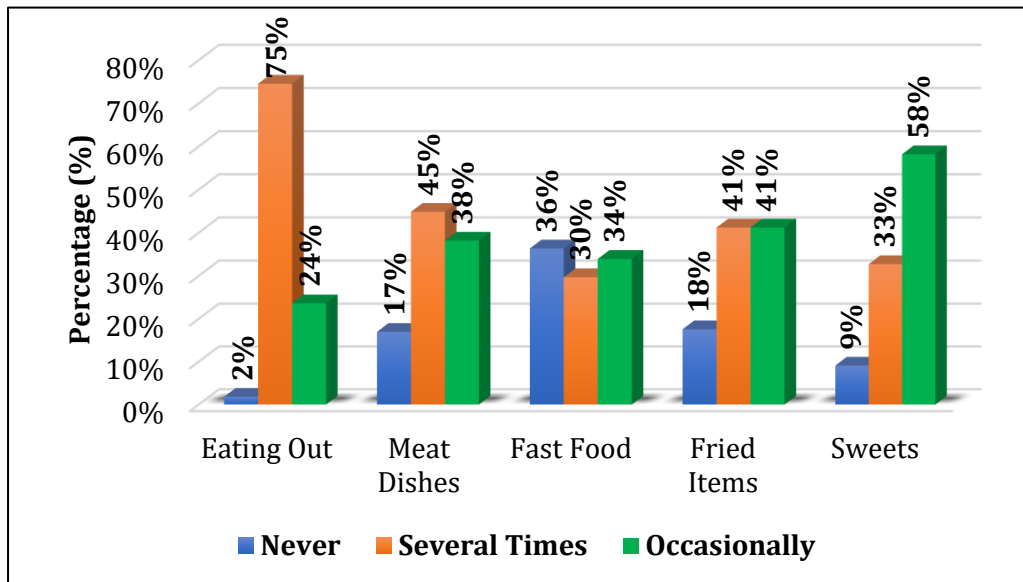


Figure 4.11: Respondents Food Habit

### 4.12 Knowledge About Lifestyle or Food Habit Related Diseases

Participants knowledge about different life style and food habit related diseases are shown in the graph.

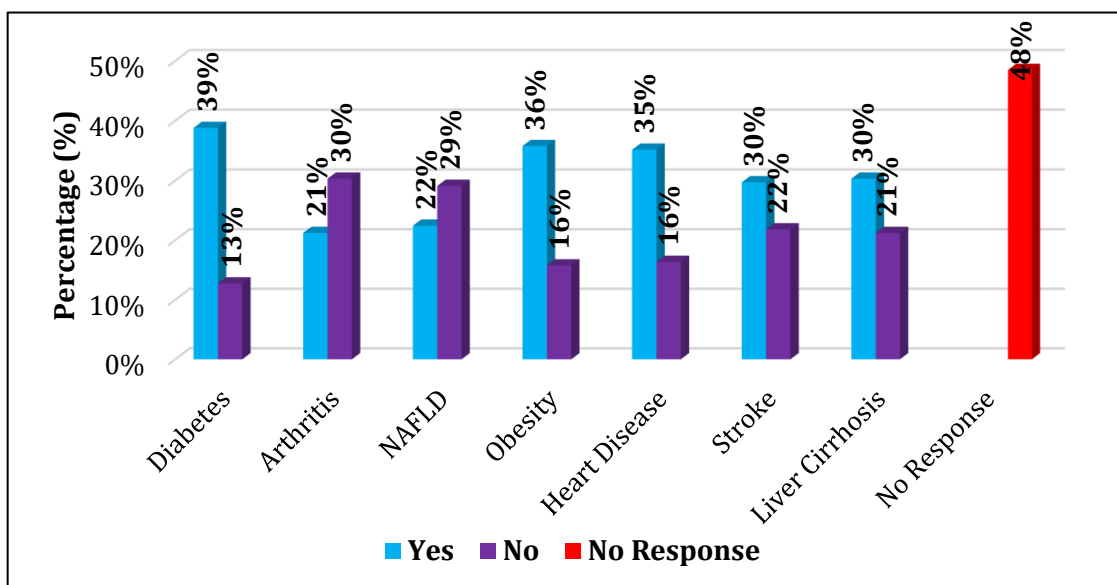
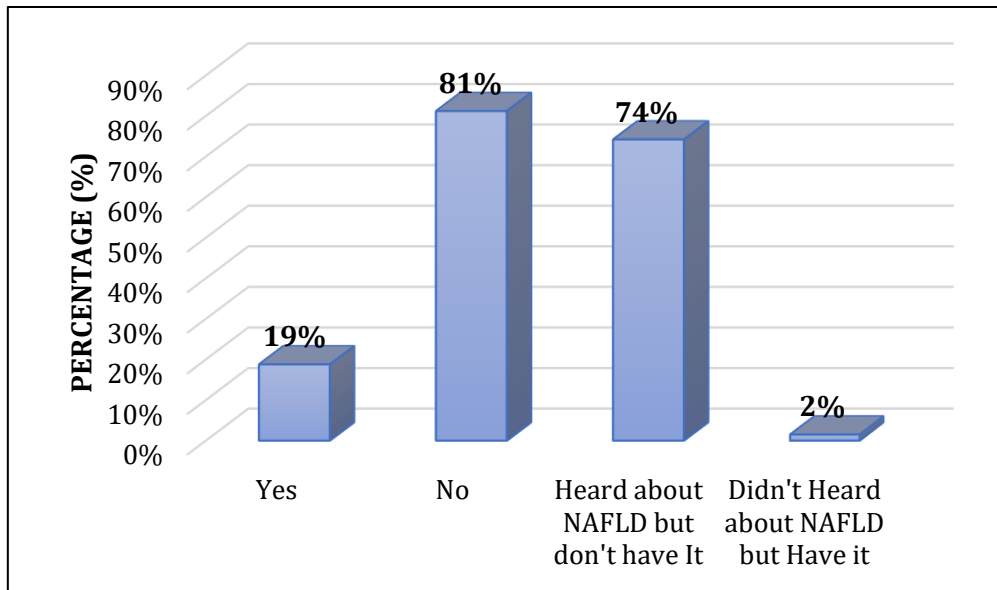


Figure 4.12: Respondents Knowledge About Lifestyle/Food Habit Related Diseases

### 4.13 Knowledge About NAFLD

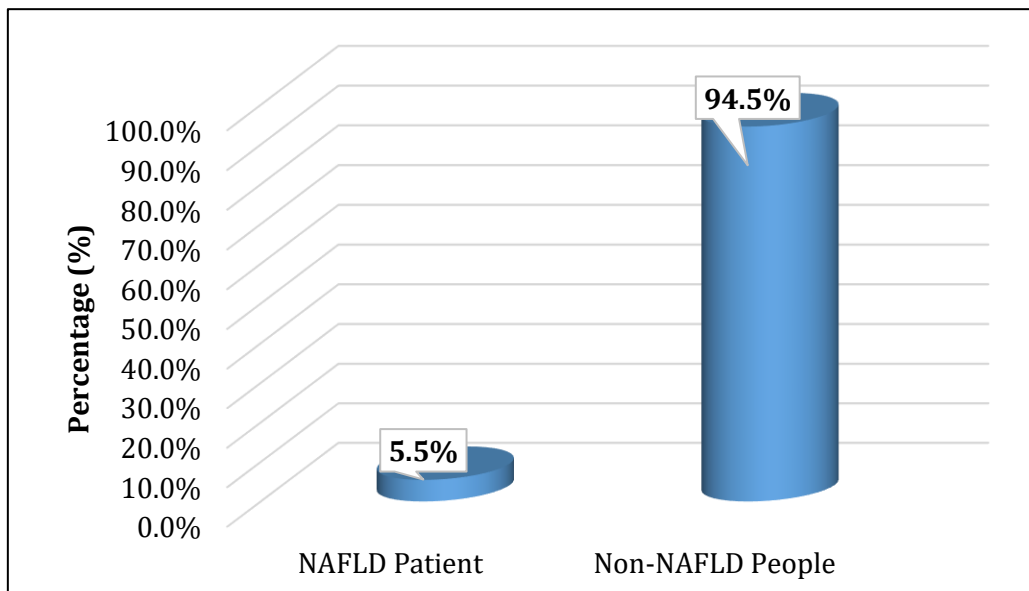
Participants knowledge about NAFLD are shown in the graph.



**Figure 4.13: Percentage of Respondents Know About NAFLD**

### 4.14 NAFLD Patient

5.5% of people have NAFLD while 94.5% don't have NAFLD.



**Figure 4.14: Percentage of NAFLD Patient**



### 4.15 People with Different Diseases

Percentage of people who have diabetes, high cholesterol and high blood pressure among the total people and in NAFLD patient are shown in the graph.

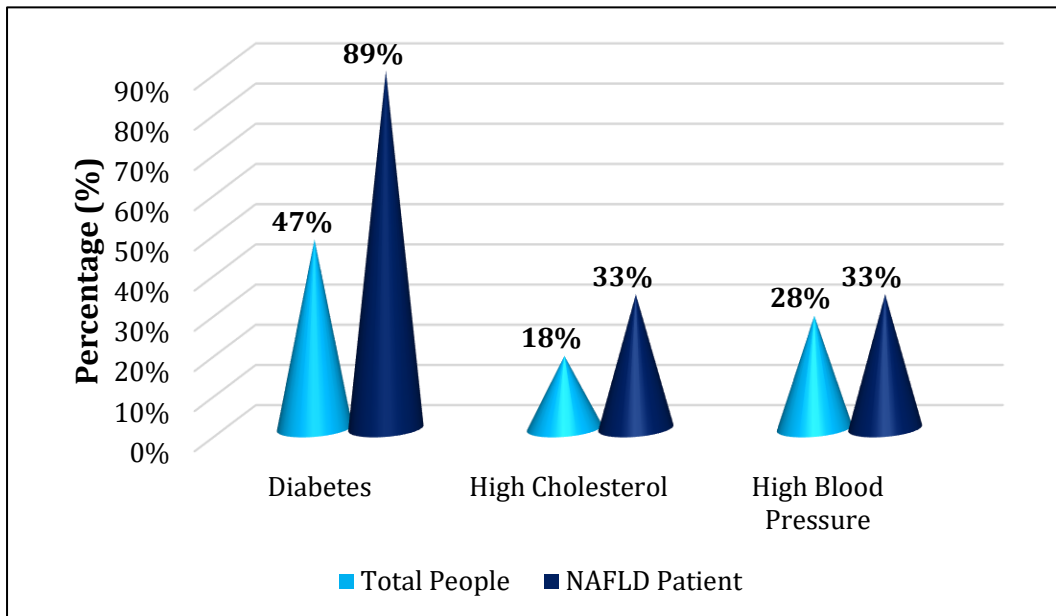


Figure 4.15: Percentage of People with Different Diseases

### 4.16 Family History of Diabetes

Participants family history of diabetes are shown in the pie chart.

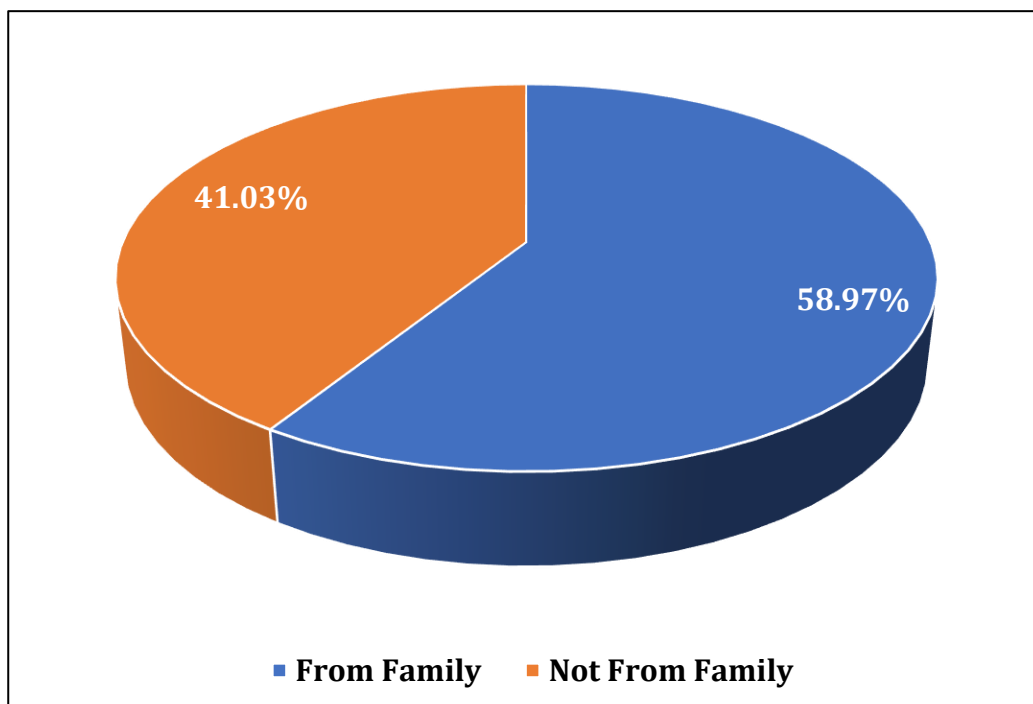
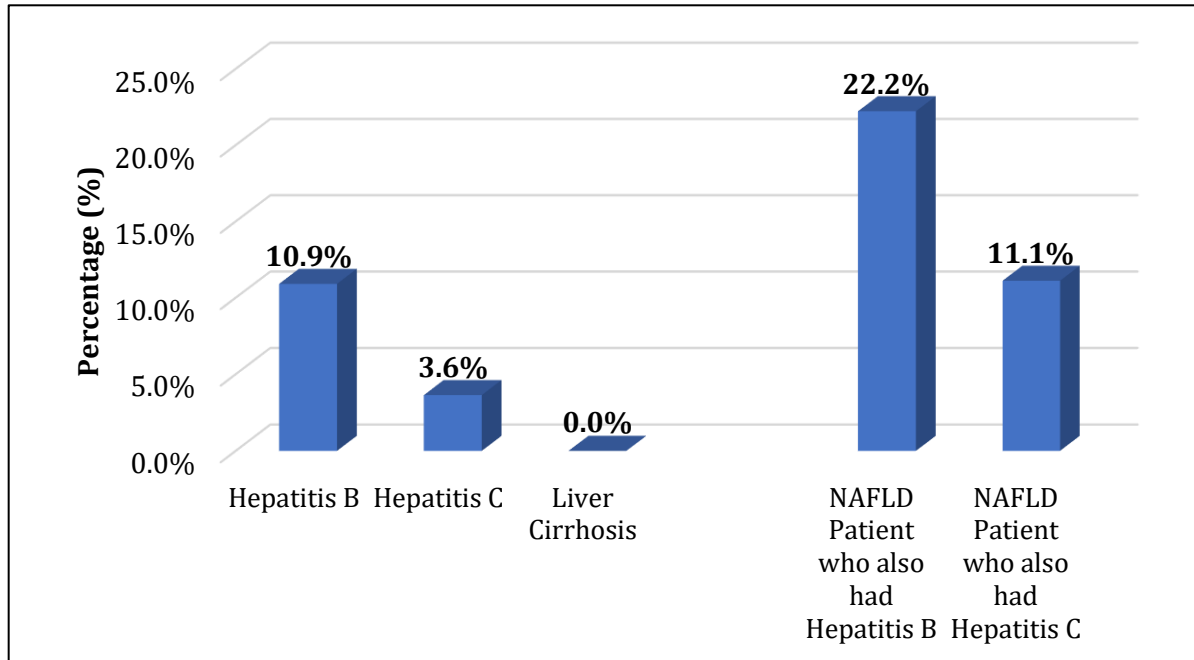


Figure 4.16: Family History of Diabetes

### 4.17 Different Liver Diseases

Percentage of people who have different liver diseases among total population and in NAFLD patient are shown in the graph.



**Figure 4.17: Percentage of Respondents having Different Liver Diseases**



*CHAPTER 5*  
*DISCUSSION*

## 5. Discussion

This study was based on a face-to-face survey for exploring the knowledge and awareness of the people on NAFLD in Dhaka of Bangladesh. In this study, people were asked about their lifestyle, food habit, knowledge on different lifestyle and food habit related diseases like diabetes, arthritis, NAFLD etc. However, there were certain limitations. The main drawback of the survey was the population number, which was very poor due to lack of time. In most of the cases, clinical data of the patients could not be gathered.

Among the total participants male and female participants were 41.8% and 58.2% respectively. Many recent studies have reported that males are at a higher risk for fatty liver disease (Vernon et al. 2011). For example, in a study of 26527 subjects undergoing medical checkups, the prevalence of NAFLD was 31% in men and 16% in women (Adams et al. 2005). Percentage of participant's age between 15-30years, 31-45 years, 46-60 years and 60+ years are respectively 38%, 25%, 28% and 8%. However, age do not influence the development of NASH.

In the study, participants level of education was found that 16% have education level below S.S.C, 8% have passed S.S.C, 19% have passed H.S.C, and 57% are graduated and post graduated.

Currently, lifestyle intervention including strategies to reduce body weight and to increase regular physical activity represents the mainstay of NAFLD management (Della Pepa et al. 2017). From the response, it was observed that 65.5% of people perform exercise while others don't. 75.9% of the participants performs walking/running/jogging, 1.9% performs swimming, 5.6% performs heavy exercises and, 19.4% performs light exercises. 52.1% of the participants prefer to use elevators while 47.9% of them prefer stairs. Almost half of the population are less likely to perform exercise which can be a serious issue. Again 52% of the people preferred using elevators over stairs which is an indication of adoption of a luxurious lifestyle. These results obviously indicate that people are relying on a sedentary lifestyle day by day.

The liver plays an essential role in the intermediary metabolism, transforming dietary nutrients into the major chemical elements crucial for life and human health. An excessive intake of refined carbohydrate and saturated fats, the increased consumption of fructose and other simple sugars, and the progressive diffusion of high-calorie Western diets, have

been associated with a dramatic increase in overweight/obesity and insulin resistance and, more recently, also with NAFLD (Della Pepa et al. 2017). In my survey, there were different response about food habits from the participants. 84.8% of the participants have breakfast everyday while 15.2% don't have breakfast regularly. 26.7% have more than 1 plate of rice in everyday dinner. Percentage of people eat outside of home several times in a week and occasionally is 75% and 24% consecutively. 45% and 38% people respectively have meat dishes several times in a week and occasionally. 30% and 34% of people have fast food several times in a week and occasionally. Percentage of people have fried items several times in a week and occasionally are both 41%. Percentage of people have sweets several times in a week and occasionally were respectively 33% and 58%. These food habits of people indicate high risk for developing NAFLD. As total caloric intake plays a very important role in both the development and the treatment of NAFLD the food habit should be maintained very strictly.

People were asked about their knowledge on different lifestyle and food habit related diseases where 48% people had no response. Among the others, 13%, 30%, 29%, 16%, 16%, 22%, and 21% didn't know that diabetes, arthritis, NAFLD, obesity, heart disease, stroke, and liver cirrhosis are lifestyle related disease which shows a very less knowledge of people about these diseases.

From the survey, it was found that only 19% of people have heard about NAFLD and among them 74% of people were not diagnosed with NAFLD while 81% of people have not heard about NAFLD but among them 2% of people were diagnosed with NAFLD.

Among the total population 5.45% have been diagnosed with NAFLD. Among the NAFLD patients 33.3% are pre-obese and 66.7% are overweight according to their BMI. It confirms that excess body weight is a risk factor for developing NAFLD. It is also to include that BMI percentage of normal, overweight, pre-obese and, obese people among the total are respectively 14%, 26%, 42% and, 17.0%.

The presence of both NAFLD and diabetes increases the likelihood of the development of complications of diabetes (including both macro- and micro- vascular complications) as well as augmenting the risk of more severe NAFLD, including cirrhosis, hepatocellular carcinoma and death (Hazlehurst et al. 2016). From the study, it was found that 88% of the NAFLD patients also have diabetes which means diabetic people are in high risk for

developing NAFLD. It is also to include that 47% of the total population have diabetes which is a concerning matter. It is also to mention that 18% and 28% of people have high cholesterol level and high blood pressure respectively among the general people while in NAFLD patients the percentages were both 33%.

Among the people, 10.9% were diagnosed with Hepatitis B, 3.6% were diagnosed with Hepatitis C, and none were diagnosed with liver cirrhosis. Among the NAFLD patients only 22.2% were diagnosed with Hepatitis B while 11.1% were diagnosed with Hepatitis C.

The result of this survey, highlights that people have lack of knowledge and awareness despite of having some serious health related conditions.



*CHAPTER 6*

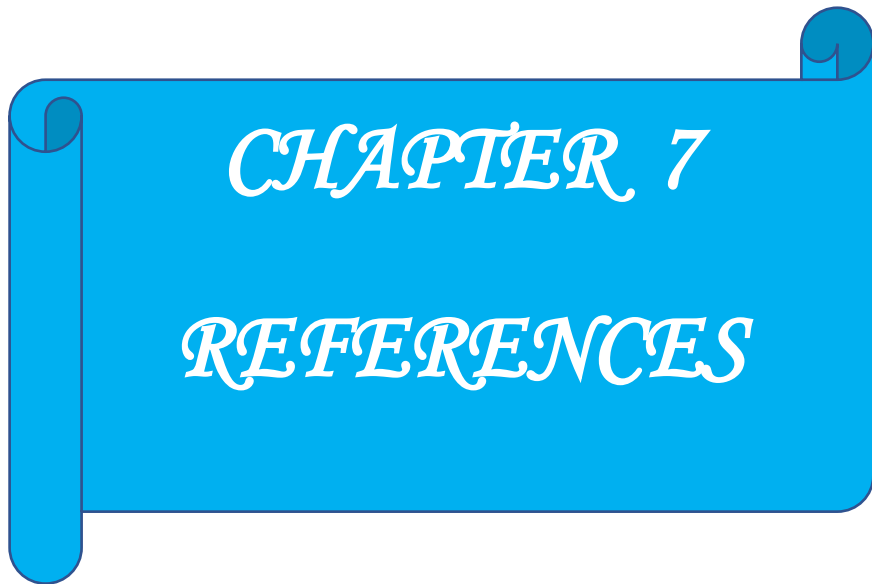
*CONCLUSION*

## **6. Conclusion**

The result of this survey revealed that there is a need to increase the public awareness of NAFLD in Dhaka. The drastic increase in the number of diabetic patients as well as overweight and obese people because of modernization and an increased tendency to adopt a luxurious lifestyle has become a concerning matter. Majority of the people have lower awareness levels despite of their higher living standards or higher educational level.

As NAFLD can't be fully cured dietary control and regular exercise could improve some of the metabolic factors and potentially offset the development of NAFLD. Reducing disease burden by prevention is always better than providing treatment. Counseling of the patients by primary care practitioner can be a useful method in controlling NAFLD. Increase of awareness about the risk factors of NAFLD and maintaining healthy diets, performing exercises and keeping an ideal body weight can reduce the chance of progression of NAFLD and it will be very crucial in controlling this serious health issue.





*CHAPTER 7*

*REFERENCES*

## 7. References

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