EFFECTS OF PRESCRIBED PHYSICAL THERAPY EXERCISES ON BLOOD GLUCOSE, METABOLIC AND HbA1C PROFILES IN PREDIABETES AT MOI TEACHING AND REFERRAL HOSPITAL IN UASIN GISHU COUNTY IN KENYA

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ABSTRACT

Pre-diabetes is characterized by plasma glucose above the normal range (3-6mmol/L) but below that of clinical diabetes (>9.0mmol/L). In Kenya the estimated prevalence of diabetes was 7.2% in 2014 which comes as a result of prediabetes. This has become a threat to national development both economically and socially because very often they result in long standing complications that are very costly to treat. This burden gradually drains the strength and resources of an individual rendering them unproductive and poor. Almost 30% of the people with diabetes go undiagnosed and by the time diabetes is diagnosed nearly 25% of them have micro-vascular complications. Therefore, every effort must be done to diagnose prediabetes and reverse the condition before it develops to full blown diabetes. The purpose of this study was to investigate the metabolic parameters of prediabetes and to provide evidence of prescribed physical therapy exercises that can be quantified and reproduced. It was hypothesized that effective means for delaying or even preventing onset of diabetes can be realized with prescribed physical therapy exercises. The study aimed at determining the metabolic profile (fasting glucose, triglycerides, low density lipoprotein, high density lipoprotein and HbA1c) levels of prediabetes at MTRH; to establish the intensity, duration and frequency of exercise needed to achieve change in metabolic profiles of prediabetes at MTRH; to determine which gender responds first after the administration of equivalent prescribed physical therapy exercises among prediabetes at MTRH. The study was a randomized controlled trial and it adopted experimental study design to select the study participants. The formula used by Zhong (2009) was adopted for calculating sample size in a randomized controlled trial having two comparison groups Experimental Group (EG) and Control Group (CG) with both groups having the same size of subjects (17 each). Blood samples and BMI data was collected from the participants at three time-periods: pre-training, mid-training (at end of 6 weeks), and post-training (at end of 12 weeks). Blood glucose test was done in the morning after an overnight fast of at least 8 hours whereby the Blood specimen was drawn from a vein and tested before the commencement of exercises. Thereafter prescribed physical therapy exercises were expended for 210 minutes per week. All experimental results were evaluated and means of two groups pre and post prescribed exercises and the association between variables was determined and compared using independent samples t-tests (relationship between physical therapy exercises and metabolic components). The significance level was set at $p \leq .05$.Although the BMI in the EG decreased from $28.47 \pm 2.37$to $26.51 \pm 2.26$the difference was not statistically significant. During week six, FBG was significantly lower in the experimental group (mean difference: 0.46 mmol/L, p=0.01). FBG level further decreased during 12 weeks of training in the experimental group (mean difference: 0.68 mmol/L, $p<0.0001$) compared to the control. The results showed that training reduces FBG by 5% and 13%, in 6 and 12 weeks, respectively. The results showed HDL were significantly higher in the experimental than in the control group during post-training (z= -3.20.17, p=0.001). On the other hand the level of LDL decreased in the experimental group during both mid-training and post-training period relative to pre-training (z= -2.908.18, p=0.001). There was a significant reduction of HbA1c (of 3%) after six weeks and an even more marked drop (of 8%) after 12 weeks in EG compared to CG in which there was no drop in HbA1c levels. High correlation was found between FBG and HbA1c(r=0.95). All parameters at pre, mid and post training were not significantly different between males and females. It was concluded that PPTE exerted improvement on FBG, metabolic and HbA1c profiles in prediabetes. The knowledge of how much exercise is needed to impact change in disease progression would inform the prescription of exercise by physiotherapists to their clients.

CHAPTER ONE

INTRODUCTION

1.1 Study background

Pre-diabetes is characterized by plasma glucose above the normal range (3-6mmol/L) but below that of clinical diabetes (>9.0mmol/L) American Diabetes Association (ADA). In Kenya the estimated prevalence of diabetes is 7.2% (MoH, 2014). This has become a national threat to development both economically and socially because very often they result in long standing complications that are very costly to treat. Similarly this disease is long standing and if not managed well can be fatal. This gradually drains the strength and resources of an individual rendering them unproductive and poor. This burden in most cases is passed on to families and the community with untold retardation of economic progress and eventually aggravating poverty. The complications of undetected and untreated diabetes cause huge human suffering and disability. They as well lead to huge socio economic costs that result from premature morbidity and mortality. Apart from diabetes being the leading cause of blindness, renal failure and lower limb amputation, diabetes also triggers cardiovascular disease, which is the leading cause of deaths in diabetes patients. (The National Diabetes Strategy (NDS), 2015).

People with prediabetes have an increased risk of Type 2 diabetes (Tuso, 2014). Around 5% to 10% of people with prediabetes become diabetic every year (Cowie et. Al, 2006). An estimated 34% of adults have prediabetes and the lifestyle risk factors for this condition include overweight and physical inactivity (Aroda, 2008). The International Diabetes Federation (IDF) Diabetes Atlas has now recognized prediabetes as a reversible condition that increases an individual's risk for development of diabetes.

Diabetes is an important health problem in the world. The International Diabetes Federation (IDF) Diabetes Atlas has estimated that in 2010, 285 million people around the world have diabetes, representing nearly 7% of the adult world population (Shaw, Sicree & Zimme, 2010). Besides impairments in glucose metabolism, type 2 diabetes is associated with dyslipidemia increasing the risk of cardiovascular diseases in this population. Almost 30% of people with diabetes go undiagnosed (Cowie et. al, 2006), and nearly 25% of them have microvascular complications by the time their diabetes is diagnosed (Harris, 1993). Every effort must consequently be made to diagnose diabetes and the other forms of glucose intolerance (impaired glucose tolerance (IGT) and impaired fasting glucose (IFG)) as promptly as possible (ADA, 2010). Until now, diabetes has been diagnosed by measuring fasting Blood glucose (FBG) of more than 7mmol/L and/or with the oral glucose tolerance test (OGTT) more than 11 mmol/L. In agreement with an International Expert Committee suggestions, the latest ADA Standards of Medical Care in Diabetes 2010 state that "HbA1c is appropriate for diabetes screening, a confirmed HbA1c > 6.5% is diagnostic for diabetes," and that "mixing different methods to diagnose diabetes should be avoided"(ADA, 2010).

With reference to Africa, a disproportionate increase in pre-diabetes is anticipated in low- and middle-income countries, many of which are expected to experience several-fold increase in the number of diabetics (Woodward et al., 2003). Common features of these low-income countries, also called developing or resource-poor countries include, poverty, illiteracy and lack of adequate medical services. In South Africa for example, despite clinical recommendations, a large number of patients are not well controlled, and do not reach the target HbA1c value of < 7%. In striving to achieve glycemic control, it is important to minimize drug adverse events, such

as hypoglycemic episodes. Therefore, the best available treatment should be chosen to fit each individual patient's needs. The aim of therapy is to achieve a level of glycemic control that is associated with an acceptable level of side effects and patient convenience, providing control without compromise.

Like other developing countries, the epidemic of Diabetes is particularly serious in Kenya where living conditions are changing dramatically and urbanization and demographic changes are the greatest (King et al., 1998). Diabetics are at a higher risk of numerous medications and are more vulnerable to irrational prescription (Yuen et al., 1998, Chiang et al., 2006, Upadhyay et al., 2006). An essential component of evaluating and improving diabetic care is the assessment of drug prescribing standards and quality of care. According to the Kenya Ministry of health, division of Non-communicable diseases (DNCD) current prevalence is estimated to be 10% (DNCD, 2007) which the World Diabetes Foundation (WDF) claims to be an underestimate. Another research conducted in Kenya Mombasa region has shown that overweight/obesity, physical inactivity and high blood pressure are the most common registered risk factors for Common Non-communicable Diseases (CNCDs) among the Kenyan population (NassibTawa, 2011).

Physical activity in general and even exercises at moderate intensities such as walking significantly reduces the risk of the development of type 2 diabetes (Jeon et al., 2007). However it is still a matter of debate about the exercise prescription in terms of the exercises mode, intensity and frequency.

1.2 Statement of the problem

Thomas & Biuso address prediabetes as a central abnormality characterized by resistance to insulin in many tissues including liver, adipose tissue and muscle. The condition does not fall squarely into the primary or secondary health prevention domain but requires serious attention given the risks. There is substantial evidence to suggest that significant risk exists for both micro- and macrovascular complications even with prediabetes blood glucose levels. DM begins as prediabetes state characterized by multiorgan disease involving defects of glucose and fat metabolism in several organs, including not only the pancreatic beta cell, liver, and skeletal muscle, but also other organs such as the gut, kidney, brain, and nervous system.

Hypertensive patients who are prediabetes are at high-risk of developing full-blown DM sooner than non-prediabetic hypertensive patients. Available reports show that in Kenya there is approximately 80% of the disesase burden in DM, which is aftermath of prediabetes. Therefore emphasis should be put on early detection and possible intervention for controlling the already growing of DM cases in the low-and middle-income communities. Undiagnosed prediabetes and the diabetes are both prone to complications associated with diabetes. In our country (Kenya), the prevalence of DM rose from 4.3% in 2007 to 7.2% in 2013, with prevalence rates of up to 10% in some regions (Boule, 2013). Kenya does not have adequate funds for diabetes prevention or care and individuals who independently fund their care leaving their families at a risk of poverty or poorer health (Tiffany, 2013).

This study aimed at screening for prediabetes and provision of evidence based prescribed physical therapy exercises that can be quantified and reproduced. The author believes that these interventions present the most effective means for delaying or even preventing onset of diabetes in a prediabetes population.

1.4 General objective

To determine the effects of prescribed physical therapy exercise on the levels of fasting glucose, glucose tolerance and HBA1C levels.

1.4.1 Specific Objectives of the study

i) To determine the metabolic profiles (fasting glucose, oral glucose tolerance, triglycerides, low density lipoprotein, high density lipoprotein and HbA1c) levels of prediabetes at MTRH;

ii) To establish the intensity, duration and frequency of exercise needed to achieve change in metabolic profiles of prediabetes at MTRH;

iii) To determine gender differences in response to the administration of equivalent prescribed physical therapy exercises among prediabetes at MTRH

1.4.2 Research Questions

i. What are the metabolic profiles (fasting glucose, oral glucose tolerance, triglycerides, low density lipoprotein, high density lipoprotein and HbA1c) levels of prediabetes at MTRH;

ii. What is the intensity, duration and frequency of exercise needed to achieve change in metabolic profiles of prediabetes at MTRH;

iii. What is the gender differences in response to the administration of equivalent prescribed physical therapy exercises among prediabetes at MTRH

1.5 Significance of the study

Due to lifestyle changes the incidence of non-communicable diseases amongst the youthful and productive members of our society is on the rise. It is important therefore to determine the magnitude of this problem, as it is associated with onset of diabetes. Picked early enough during

prediabetes stage, a lot can be done to stem the progression to full blown diabetes and this can help improve the quality of our human resource in terms of reduced morbidity.

The knowledge of how much exercise is needed to impact change in disease progression would inform the prescription of exercise by physiotherapists to their clients.

Determination of the metabolic and clinical features of pre-diabetes in Kenya is also an essential component of the pathogenesis and management practices. The metabolic syndrome with or without hyperglycemia identifies people with high risk of developing cardiovascular disease. Thus investigating the metabolic syndrome in Kenyan pre-diabetes, including its relationship with HbA1C, especially on a sustainable basis would guide us to early detection and hence management and prevention of cardiovascular disease, the most common cause of deaths among diabetics worldwide. In other words, epidemiological data would be provided on pre-diabetes and cardiovascular disease that would support diagnosis, management, prevention and hence planning. All these strategies would reduce the magnitude and burden of diabetes and its associated cardiovascular disease in Kenya.

These strategies of exercises ultimately aim at achieving improved health care and hence sound health status for our diabetic patients. This in turn would bring obvious economic gains to the country. Prediabetes would also benefit from pre-test counseling on the nature of diabetes and the value of relevant laboratory tests. After this research, the prediabetes would be specifically advised on the nature of their subclass of diabetes, the value of continuous testing, including self-monitoring of blood glucose (SMBG), adherence to prescribed physical therapy exercises, as well as good life style practices, which would ensure that they live long if they pay heed to advice. This study is likely to shed light on the magnitude of prediabetes amongst our youthful and economically productive age group in the country and at the same time address the way

forward in preventing the disease from progressing to full blown costly diabetes with its attendant complications. The result is therefore informing intervention programs in preventive medical practice in this country.

1.6 Justification

Prediabetes is an abnormality characterized by resistance to insulin in many tissues including liver, adipose tissue and muscle. There is impressive evidence that when exercising insulin sensitivity increases by activating insulin regulated glucose transporter type 4 (GLUT 4) that is found in striated muscles reversing insulin resistance making the muscle to absorb more glucose thus maintaining glucose homeostasis (Boule, Kenny, Haddad , et al., 2003).

The prevalence of prediabetic conditions such as impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) are increasing rapidly. There is compelling evidence that individuals who are insufficiently active are more likely to develop T2DM. Most T2DM patients undergo a prediabetic stage for several years under which there is an opportunity to identify them and start early prevention. Prediabetes is a intermittent phase of overt diabetes (Nkatha, Meme, et al.,2015).

In combination with other lifestyle strategies, exercise training has beneficial effects on preventing the onset of T2DM and improving glycemic control in pre-diabetes (Boule, Kenny, Haddad et al., 2003). Exercise training additionally improves cardiovascular risk profile, body composition and cardiorespiratory fitness, and they are strongly related to better health outcomes. Diabetes is an expensive disease, and management remains suboptimal even in the best of countries. In developing countries where majority are poor and affording healthcare is beyond the reach of many the outcome and complications of diabetes paint a grim picture (Boule

et al, 2003). It is therefore logical that any attempt to prevent the subjects from developing full-blown disease is be a welcome move.

1.7 Scope of the study

The study was limited to the stated objectives. It was carried out in Moi Teaching and Referral Hospital and Physical Therapy gymnasium of Moi University orthopaedics and rehabilitation department. This being the second largest referral hospital in Kenya with catchment area of over 10 million people, it was to shed light on the burden of prediabetes in the country. The outcome of this study can then be extrapolated to low and middle-income countries across Africa. It primarily focused on all the overweight patients attending MTRH outpatient department. It adopted an experimental design in which subjects were tested before and after physical therapy exercises.

CHAPTER TWO

LITERATURE REVIEW

2.1 Theoretical Literature

This chapter elaborates the various aspects of pre-diabetes like the clinical definition, the symptomatology, pathophysiology and risk factors associated with this condition. A detailed description of the diagnostic tests, screening criteria, complications and advantages of early detection and prevention are also affirmed.

2.2 Concept of pre-diabetes

The term pre-diabetes existed since the year 1960, however, at that time it only pertained to the high risk individuals like those with a strong family history of diabetes mellitus or those with adverse pregnancy outcomes like hydramnios or high birth weight babies. In the year 1980, World Health Organization (WHO) discontinued the use of this term as it had adverse emotional effects on people, it was not useful from a preventive aspect and the term also led to a few insurance coverage issues (Alberti, 2007). An expert committee of the diagnosis and classification of diabetes mellitus in the year 1997 and 2003 indentified that there was a set of population who had blood glucose levels higher than normal but not high enough to be diagnosed as diabetes. This population had fasting blood glucose (FBG) levels between100 mg/dl (5.6 mmol/L) and 125 mg/dl (6.9 mmol/L) called impaired fasting glucose (IFG) or they had an abnormal oral glucose tolerance test (OGTT) with the glucose values of 140mg/dl (7.8 mmol/L) to 200 mg/dl (11.0 mmol/l) known as impaired glucose tolerance (IGT) (ADA, 2010). The year 2002 witnessed the re-birth of the term pre-diabetes after the Department of Health and Human Services was alarmed by the growing prevalence of people with high glucose levels that were not high enough to be diagnosed as diabetes (Alberti, 2007). These individuals who had an

impaired fasting glucose and or impaired glucose tolerance were diagnosed as having pre-diabetes (ADA, 2010).

In the year 2003, the American Diabetes Association expert committee proposed to lower the cut off level of fasting plasma glucose from the original 110mg/dl (6.1mmol/L) to current 100mg/dl (5.6 mmol/L) (ADA,2010). This was done to ascertain that the prevalence of impaired fasting glucose was similar to impaired glucose tolerance. However, some other diabetes organizations and World Health Organization (WHO) (ADA, 2010) did not approve this change. In 2004, American Diabetes Association and American College of Endocrinology lowered the cut off levels for the diagnosis of IGT from the initial 160-200mg/dl after an OGTT to the current level of 140mg/dl to 200 mg/dl. This was primarily inspired by the results of several epidemiologic studies where the risk of cardiovascular complications were also seen at levels lower than the glucose levels for diagnosis of diabetes ("Pre-diabetes: Meeting an epidemic with new treatment goals," 2009).

2.3 Pathophysiology

The primary metabolic abnormality in the pre-diabetic state is the development of insulin resistance in various body tissues like skeletal muscle, liver and adipose tissue, which over time progresses to clinical diabetes. The pathology of pre-diabetes is associated with visceral fat deposition i.e. accumulation of free fatty acids in the different body tissues including the pancreas. This in turn induces the release of pro-inflammatory adipocytokines such as tumor necrosis factor-α, interleukin-6, leptin and macrophage migration inhibitor factor, which decrease insulin sensitivity (Fonseca, 2008). Insulin resistance and hyperinsulinemia in pre-diabetics are also associated with a cluster of other metabolic abnormalities like dyslipidemia characterized by high triglycerides and low high-density lipoprotein (HDL) levels, obesity and

hypertension which are collectively known as the insulin resistance (metabolic) syndrome (Biuso, Butterworth, & Linden, 2007) . The excessive accumulation of triglycerides in adipose and non-adipose tissues may also occur due to excessive intake of free fatty acids in diet which could initiate pre-diabetes in an individual. The fat deposition around the organs like liver determines insulin resistance not presence of subcutaneous fat. Hence, even a lean looking person with visceral fat deposition could have pre-diabetes (Biuso et al., 2007).

2.4 Diagnosis & Symptoms

Evaluating the glucose levels in the blood under various conditions makes the diagnosis of pre-diabetes. Tests are used to diagnose pre-diabetes, are the same tests used to diagnose diabetes, but the criteria are lower for a pre-diabetes diagnosis.

1. Oral Glucose Tolerance Test (OGTT) – This test is used to identify Impaired Glucose Tolerance (IGT). Blood glucose levels of 140-199 mg/dl (7.8 mmol/Lto11.0 mmol/l) 2 hours after oral administration of 75 grams of glucose is diagnostic of pre-diabetes. Certain precautions should be observed prior to the test being performed. The patient should have an adequate carbohydrate intake before the test, should not be physically active or smoking during the test (Sharma & Garber, 2009).
2. Fasting Plasma Glucose- This test is used to detect Impaired Fasting Glucose (IFG). Blood glucose levels of 100-125mg/dl (5.6 mmol/L-6.9 mmol/L)after an 8 hour fast denotes pre-diabetes. The patients should not have had caffeine or any other factors that affect the carbohydrate metabolism like physical activity before the test (Sharma & Garber, 2009).

3. HbA1c - People with an HbA1C level of 5.7 % to 6.4 % are as classified as having pre-diabetes. This test estimates the average blood glucose level in blood over the last 3-4 months (ADA, 2012).

Apart from these tests, the metabolic syndrome diagnosed by the NCEP (The National Cholesterol Education Program) an HbA1C is also considered diagnostic of pre-diabetes (Sharma & Garber, 2009) A person who has normal fasting plasma glucose could have an abnormal or raised postprandial glucose levels (Abdul-Ghani&DeFronzo, 2009; Biuso et al ., 2007). It has been seen that 30% of individuals having an impaired glucose tolerance can be missed if only the fast plasma glucose test is performed, thus indicating that the overlap between the 2 tests is incomplete as IGT and IFG are two heterogeneous conditions (Alberti, 2007). Thus these tests describe different metabolic abnormalities (Abdul-Ghani&DeFronzo, 2009; Biuso et al., 2007). The major cause for elevated glucose detected by the FBG test is an increased hepatic glucose output and a defective initial insulin secretion. The OGTT test detects elevated glucose levels due to peripheral insulin resistance (Unwin, Shaw, Zimmet, &Alberti, 2002). The analyses of the DECODE and DECODA study groups which consisted of data from 13 European and 10 Asian studies respectively found that there is a significant difference in the prevalence of IGT and IFG.

The prevalence of IGT in the population is greater and hence, the OGTT is more sensitive in detecting hyperglycemia as compared to FGT but is less specific. It has been seen that the prevalence of IGT is greater in women where as IFG is seen more commonly in men. Age is also a major factor influencing the number of people with IGT or IFG (Unwin et al., 2002).

In spite of denoting different pathophysiologic abnormalities of glucose or fat metabolism, both IGT and IFG confer an increased risk for Type 2 diabetes mellitus (Abdul-Ghani&DeFronzo,

2009; Biuso et al., 2007). Both isolated IGF and IGT are associated with a 5% conversion rate to type 2 diabetes mellitus as per many prospective studies (Abdul-Ghani &DeFronzo, 2009). Thus IGT and IGF are both equally associated with the risk of developing diabetes mellitus and if both co-exist, the risk increases further. Each test has its own advantages and disadvantages. A positive OGTT detects IGT and is more strongly associated with a CVD. It has been seen that as compared to IFG, IGT is an important risk factor for developing macrovascular disease (Alberti, 2007) whereas a FBG test is easier and more convenient to perform and can be easily repeated and is more economical (ADA, 2008).

Unlike the other two tests, HbA1C denotes long term glycemic levels and does not require overnight fasting and hence is convenient to the patient. HbA1C levels between 5.5 % and 6.5% are associated with an increased risk of diabetes. It was found that HbA1C levels lower than 5.5 % also had continuous association with development of diabetes. The 5 year risk of developing diabetes was about 25-50 % for HbA1C level of 6 % as compared to 9-25 % when the HbA1C level is 5% (Zhang et al., 2010).

Individuals diagnosed with pre-diabetes are most of the times free of symptoms or may have very few symptoms. Peculiar dark skin patches called as AcanthosisNigricans which may develop on the back of the neck or around the neck, elbows, knees, or knuckles or armpits can indicate insulin resistance (Eldin et al., 2008).

2.5 Progression to Diabetes

Pre-diabetes most certainly raises the risk of developing type 2 diabetes and its related complications like coronary heart disease, stroke, eye disease etc. Individuals with pre-diabetes are about 5-15 times more likely to develop type 2 diabetes than people with normal blood glucose value. Out of the total number of people diagnosed with pre-diabetes about 25% develop

diabetes within the next 3 to 5 years and majority of them develop diabetes within the next 10 years unless they adopt any of the preventive measures (CDC, 2012c, Deedwania & Fonseca, 2005). Over the period of lifetime, about 83% of those diagnosed with pre-diabetes and who did not undergo any type of intervention measures will go on to develop diabetes (Aroda & Ratner, 2008). Studies conducted in US and abroad show that the annual progression to diabetes differs among people diagnosed with IGT or IFG.

Approximately 2% to 34% out of those detected with IGT and 1.5% to 23% of those detected with IFG will develop diabetes annually (Santaguida et al., 2005). Some studies have shown that some long term damages to the organs especially heart and the circulatory system may begin to take place in the pre-diabetic state. Such individuals also are at an increased risk of dying from CHD as compared to people who are not pre-diabetics ("Prediabetes: Meeting an epidemic with new treatment goals," 2009). Many people with pre-diabetes already have macrovascular and microvascular damage like blindness, amputations, kidney failure even before they develop diabetes (Hanna-Moussa, Gardner, Kurukulasuriya, & Sowers, 2009).

People with pre-diabetes have a 2 to 3 time's greater risk of developing the insulin resistance metabolic syndrome as compared to people with normal glucose levels, which also increases their risk for cardiovascular diseases (Abdul-Ghani & DeFronzo, 2009). Various studies like the Whitehall study which was a longitudinal cohort study conducted in Britain, the Paris prospective study conducted in France, the Chicago Heart Association Detection Project and more recently the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study that analyzed data from 13 prospective studies found an increased risk of cardiovascular disease and mortality and increased all-cause mortality in patients with IGT as compared to those with normal glucose levels (Petersen & McGuire, 2005). The relative risk of

CHD is greater in people having IGT as compared to those having IFG. The risk of microvascular complications like neuropathy, and proteinuria is greater in people having IGT (Hanna-Moussa et al., 2009).

Many observational studies show that an acute phase reactive protein called C-reactive protein produced in the liver which is a marker of systemic inflammation is found to be elevated in atherosclerosis, impaired fasting glucose, impaired glucose tolerance, diabetes and metabolic syndrome. Elevated levels of this C-reactive protein are associated with increased risk of developing diabetes and coronary heart disease (Deedwania& Fonseca, 2005). The Whitehall II study also studied the progression of pre-diabetes to diabetes by assessing the β cell function and insulin sensitivity based on the plasma insulin level. They found that as compared to a person who did not develop diabetes, a person who did develop diabetes had 35% more insulin resistance 10 years before the onset of diabetes and then experienced a 4 year increase in insulin resistance until he finally develop diabetes. Also, in a person who finally developed diabetes, a compensatory increase in the β cell function was seen to make up for the insulin resistance until the function collapsed to 60% and he developed diabetes (Matthews & Levy, 2009).

However, progression to diabetes is not inevitable. It can be prevented or delayed by various interventions like lifestyle modification and pharmacological methods. Hence it is logical to target this population with abnormal glucose metabolism to prevent diabetes and associated morbidity and mortality.

2.6 Risk Factors

The factors that increase the risk of diabetes also increase the risk for pre-diabetes. These risk factors include:

1. Obesity: Obesity is a major risk factor for pre-diabetes. Insulin resistance is mainly determined by the visceral fat deposition. The epidemic of diabetes is mainly due to the concomitant increase in obesity.
2. Physical Inactivity: Diabetes Prevention Program has shown that modest physical activity like 30 minutes of walk per day for at least 5 days in a week can prevent or delay the onset of diabetes. Exercise increases the uptake of glucose by the muscle cells for energy by increasing their sensitivity to glucose in the blood.
3. Age: The risk of pre-diabetes increases as one gets older, especially after age 45.
4. Family history: The risk of pre-diabetes increases if a parent or sibling has type 2 diabetes.
5. Race: African-Americans, Hispanics, American Indians, Asian-Americans and Pacific Islanders are more likely to develop pre-diabetes.
6. Gestational diabetes: A woman diagnosed with gestational diabetes during pregnancy or who has given birth to a baby who weighed more than 9 pounds (4.1kg) is at a greater risk of developing diabetes later.
7. Polycystic ovary syndrome: It is characterized by an ovulation leading to infertility, menstrual irregularities and polycystic ovaries. Elevated androgen levels and upper body obesity which is commonly seen in these women puts increases their risk of glucose intolerance and diabetes (Ehrmann, Barnes, Rosenfield, Cavaghan, &Imperial, 1999).

8. Inadequate sleep: Several studies indicate that lack of sleep may lead to an increased insulin resistance. Research suggests that sleeping less than 5.5 hours per night regularly might increase the risk of pre-diabetes or type 2 diabetes (NDIC, 2011b).

Insulin resistance and hyperinsulinemia may also be associated with nonalcoholic fatty liver disease, prostate and pancreatic cancer, congestive heart failure, HIV lipodystrophy, antipsychotic medications and sleep disordered breathing. Insulin resistance is also common in systemic inflammatory diseases such as rheumatoid arthritis. Smoking, a diet high in sweet soft drinks, refined grains, and processed meats are associated with increased risk of diabetes (Biuso et al., 2007). Few other factors that have been identified as being associated with increased risk of pre-diabetes are having hypertension, increased levels of LDL cholesterol, triglycerides, low HDL levels, gestational diabetes, hyperuricemia, ischemic cardiomyopathy, cerebrovascular disease, peripheral vascular disease, women with polycystic ovarian syndrome who have a BMI $\geq$ 25 kg/m2, Glucose metabolism is also affected by antihypertensive drugs like thaizide diuretics and beta-blockers (Magalhães et al., 2010).

2.7 Screening

Diabetes has reached epidemic proportions all over the world and in US, the prevalence of pre-diabetes which is a predictor for the development of diabetes, is almost thrice that of diabetes. Hence, screening the at-risk population is a first step towards intervention for the reduction of this ever increasing disease burden. Three tests are used for the screening of pre-diabetes, a fasting blood sugar level after an overnight fast, 2 hour oral glucose tolerance level after an oral glucose tolerance test.

For screening purposes the population can be divided into 2 groups, high risk and low risk group. High risk group includes people who have one or more risk factors for diabetes. The screening tool that can be used for high risk group is the OGTT and the screening tools for the low risk group include an eligibility test questionnaire, FBG test or a tape measure. The questionnaire helps to further narrow down or limit the number of people who actually need glucose test. The tape measure is a method used in UK wherein women with a waist circumference of more than 80 cm (31.5 inches) and men with the waist circumference of more than 94 cm (37 inches) should get themselves screened for abnormal glucose or lipid profile (Alberti, 2007).

Both OGTT and IFG tests have their advantages and disadvantages. For example using the FBG test alone cannot detect IGT; however both tests detect an increased risk for diabetes mellitus (Alberti, 2007). American Diabetes Association has set up certain guidelines for screening people for pre-diabetes.

1. As per ADA guidelines, all people ≥45 years of age should be screened for pre-diabetes at their routine health checkup visits especially those who are overweight (BMI > 25kg/m2)
2. People < 45 years of age who are overweight (BMI>25kg/m2) and have any of the following risk factors.

   a) Habitually physically inactive.

   b) Have first-degree relatives with diabetes.

   c) Members of high-risk ethnic population like African American, Latino, Native American, Asian, American and Pacific Islander.

d) Woman who has delivered a baby weighing > 9 lbs or has been diagnosed with gestational diabetes

e) Person who is hypertensive (blood pressure ≥140/90mmHG)

f) High-density lipoprotein (HDL) cholesterol < 35mg/dl and or triglyceride level > 250mg/dl

g) Person who has impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) on previous testing

h) Anyone who has other clinical conditions associated with insulin resistance like severe obesity and acanthosisnigricans

i) Person with history of cardiovascular disease

j) Women with polycystic ovarian syndrome. If the results are normal, tests should be repeated at least at 3 year intervals. If pre-diabetes is detected then the tests should be conducted every 1-2 years (ADA, 2008).

2.8 Early Detection & Prevention

Research states that the damage to certain organs may begin in the pre-diabetic state itself. Lowering the blood glucose level cutoffs for diagnosis of pre-diabetes has helped in the earlier detection of people with pre-diabetes and thus delay the progression to diabetes and its complications by certain simple interventions. Studies indicate that simple intervention measures like regular exercise, life style modifications and modest weight loss could prevent or delay progression to type 2 diabetes by about 58% (ADA, 2012). Thus progression of pre-diabetes to diabetes is not inevitable.

Insulin resistance which is a major pathology in pre-diabetes is mainly determined by the visceral fat deposition. A lean person could have visceral fat deposition and could suffer from

insulin resistance. On the other hand, an obese individual could have lower levels of visceral fat and normal insulin sensitivity. For intervention purposes, patients can be grouped into 3 categories depending on the obesity and insulin resistance. These are obese insulin resistant, metabolically obese normal weight (MONW) and metabolically healthy but obese (MHO) individuals. The MONW individuals have higher visceral fat and are more insulin resistant (Biuso et al., 2007).

The intervention or preventive measures to prevent or delay the progression to diabetes mellitus should be directed to achieve two main goals (Sharma & Garber, 2009).

1. Lower the blood glucose levels so as to prevent diabetes and all the related complications
2. Control the cardiovascular risk factors like hypertension and hyperlipidemia in order to prevent cardio-vascular diseases

These goals can be achieved if the intervention measures target the main pathophysiology in diabetes mellitus, i.e. insulin resistance and β cell dysfunction which leads to defective insulin secretion. These measures mainly include lifestyle management like weight loss, exercise or use of pharmacological methods. Based on several randomized control trials, lifestyle modification is considered a preferred intervention measure to delay the development of diabetes and its progression (Sharma & Garber, 2009).

As a part of the Diabetes Prevention Program people with pre-diabetes were divided into 2 groups, one of which was the lifestyle intervention group and was subjected to intensive training in diet, physical activity and behavior modification (Sharma & Garber, 2009). The main aim of this group was to eat fewer calories and fat, exercise for about 150 min per week and to lose 7% of the body weight in 24 weeks. The second group was given metformin 850mg twice daily. Another group received placebo. The metformin and placebo group were also given some advice

on diet and exercise. At the end of the study, it was observed that the people in the lifestyle modification group reduced their risk of developing diabetes by 58%. This was irrespective of their ethnic backgrounds or gender. However, it was observed that for people 60 years and older, the risk reduced by 71%. The metformin group reduced their risk by 31%. This intervention was mainly effective in the people of age group 25- 44 years and in those with BMI $\geq$ 35 kg/m2. Further analysis found 83% of the people treated with standard intervention measures developed diabetes in a lifetime, whereas only 63% of people who underwent lifestyle modification and 71% who were treated with metformin developed diabetes in a lifetime. Thus weight loss was found to be a major predictor in the prevention of progression of pre-diabetes to diabetes. Lifestyle modification was also found to have other benefits. The incidence of blindness was decreased by 39% and that of end stage renal disease was reduced by 38%, amputation by 35%, stroke by 9% and coronary heart disease by 8%. Hence, the authors concluded that diabetes prevention efforts should be focused on the lifestyle intervention measures like diet control and exercise (Aroda& Ratner, 2008).

In March 2007 American Diabetes Association suggested that life style changes should be offered to all the people diagnosed with pre-diabetes. However 850 mg of the drug metformin should also be added if the person had other risk factors like IFG and IGT together, age less than 60, BMI $\geq$ 35 kg/m2, HbA1C > 6%, high triglycerides and low HDL, positive family history of diabetes in first degree relatives (Nathan et al., 2007).

2.9 Diabetes Rates by Gender

Men and women have physiological differences that may put one group over the other for risk of certain health outcomes. It is noted that as of 2010, 13.0 million men have T2DM (11.8%), 12.6

million women (10.8%) do as well. The adiposity or fat distribution is different for men than for women (Dagogo-Jack, 2003).

Women that are overweight or obese tend to gain weight centrally, compared to men that gain the weight peripherally (Teixeira,-Lemos, 2011).

Interestingly, excess adiposity affects men differently than for women. Increasing weight is a risk factor for T2DM, yet is more adverse in women (Paek, 2010). This is due to adiposity around the waist, and circumference of the waist and BMI is a stronger predictor of risk for T2DM in women than in men (Paek, 2010).

Women also have different health-seeking behaviors. Women are more likely to seek the advice of a physician, yet it is less likely they will implement recommended lifestyle improvements (Gavin, 2011). In addition, women who have had children may be more at risk for T2DM if during pregnancy, they had gestational diabetes mellitus (GDM) (American Diabetes Association, 2010).

Lipoproteins

Lipoproteins are biochemical assemblies of phospholipid monolayers which are embedded with apolipoproteins along with free cholesterol that enclose cholesterylesters, triacylglycerols, vitamins such as A and E and also lipid. The number of vital functions that they perform within the body, include transport of fatty acids (in the form of triglycerides) and cholesterol from the intestine and liver (Antalis, 2012). They can be differentiated based on their density and apolipoprotein content i.e. the more protein it contains, the lower the density. The proportion of lipids and proteins in a lipoprotein determines its density – the more protein the lipid contains, the higher its density (Hegele, 2009).

Lipoproteins are 5 major groups namely: 1] chylomicrons- which transport dietary lipids from enterocytes to other tissues like the adipocytes, cardiac and skeletal muscle. The triglyceride components of chylomicrons are hydrolyzed at these sites by lipoprotein lipase (LPL), which releases free fatty acids and monoglycerides for uptake by the target cells (Hegele, 2009). Once the triglycerides have been hydrolyzed, the residue of chylomicrons is taken up by the liver via endocytosis(Hegele, 2009). 2] Very-low density lipoproteins (VLDL) whose particles are triglyceride-rich lipoproteins synthesized in the liver following cytoplasmic accumulation of triglycerides by hepatocytes (Adiels, 2008). The VLDLs function is to deliver triglycerides and fatty acids to various tissues. They primarily contain apoE and apoB, which are also found on LDL particles and aid in their binding to the LDLR (Chappell, 1993; Mamotte, 1999). 3] Intermediate-density lipoproteins (IDLs) 4] High-density lipoproteins (HDLs) are the smallest lipoproteins in this group and their high density is because of high proportion of proteins in them. HDL also known as good cholesterol, transport cholesterol from peripheral tissues back to the liver for excretion into bile. This process, called the reverse cholesterol transport pathway (Schmitz, 2009), accounts for HDL being commonly known as "good cholesterol", as high levels of HDL can reduce the risk of heart disease (Mahdy, 2012; Schmitz, 2009). HDL also transports cholesterol to adrenals, ovaries and testes for the synthesis of steroid hormones (Havel, 1980). Apolipoproteins act as cofactors for enzymes and ligands for cell surface receptors to enable them transport lipids into and out of cells (Saito, 2004). Apo-A is located on HDL particles and promotes efflux of cholesterol from tissues by binding to the transporter protein ABCA1 (Schmitz, 2009). ApoA is also a cofactor for lecithin cholesterolacyltransferase (LCAT), that converts free cholesterol into cholesteryl esters. ApoE is found on VLDL particles and acts as a

ligand for the VLDLR. ApoB is located on the surface of LDL particles and is a ligand of the LDLR (Saito, 2004).

5] Low-density lipoproteins (LDL): LDL molecules are denser than VLDL particles as they contain a higher amount of cholesteryl esters (Havel, 1984). They are formed from VLDL particles following exposure to LPL. As triglycerides are removed from a VLDL particle, it becomes first an intermediate-density lipoprotein (IDL) and then a low-density lipoprotein (LDL) (Shelness, 2001).

LDLs undergo endocytosis after binding to LDLRs on target cells, including the liver. Following fusion with lysosomes, endocytic vesicles containing recently engulfed LDL components, cholesteryl esters and triglycerides are broken down into free cholesterol and free fatty acids via the action of lysosomal acid lipase, which is released into the vesicles from lysosomes (Papackova, 2015). An inhibitor of lysosomal acid lipase is the small molecule Lalistat (Robinet, 2013; Civallero, 2014), was used for some of the experiments in that particular study. The free fatty acids and cholesterol that result from the action of lysosomal acid lipase were processed for use elsewhere in the endoplasmic reticulum. For example, free cholesterol is incorporated particularly into plasma membranes. Excess free cholesterol can be toxic to cells and is repackaged by acyl-CoA cholesterol acyltransferase (ACAT) into cholesterol esters and stored in lipid droplets. High density lipoprotein also transports cholesterol to adrenals, testes and ovaries for the synthesis of steroid hormones (Havel, 1980).

2.10 Empirical Review

Manders et al. (2010) assessed the impact of a single bout of low- or high-intensity aerobic exercise on the prevalence of hyperglycemia throughout the 24-h post-exercise period, in 9 sedentary males with type 2 diabetes in Italy. Interestingly, they found that the low-intensity

aerobic exercise, but not the high-intensity exercise, was able to reduce the average glucose levels over the following 24 hours versus the control non-exercise day. More recently, the same group reported a similar reduction of blood glucose levels after 24-h and 48-h of either daily or alternate day moderate aerobic exercise, in both insulin and non- insulin treated type 2 diabetic patients (Vanjiik et al, 2012).

Again, the same authors, in another study (2013), assessed the effect of a single bout of moderate- intensity exercise on the subsequent 24-h glycemic profile in 60 insulin or non-insulin treated subjects with type 2 diabetes in USA. In this study they examined whether the individual responses to exercise were related to subjects' baseline characteristics. These authors found that average 24-h blood glucose concentrations were lower than in a control non- exercise day. Moreover, the reduction after exercise in average glucose concentrations correlated significantly with patients' HbA1c level, but not with age, body mass index, diabetes duration or maximal watt. More recently, this group also compared the effect of 45 min of moderate intensity aerobic exercise with an equivalent time spent in three short bouts of low-intensity daily life activities (VanDijk et al, 2013).

Mikus et al. (2012), in a group of sedentary prediabetic patients, assessed by Continuous Glucose Measuring (CGM) the glucose profiles over three days of habitual life activities and in the last three days of a seven-day period in which 60 min of daily vigorous aerobic training was introduced in Thailand. They reported that average glucose levels in the 24-h period following these exercise sessions were not different from values measured during habitual sedentary

conditions. However, post-prandial glucose and duration of hyperglycemia were significantly lowered after exercise.

Karstoft et al. (2013), in 27 prediabetic subjects randomized to a continuous walking training group, an interval walking training group - matched in terms of mean intensity of exercise and overall energy expenditure - or a non-exercise control group for 4 months, reported that interval training was superior to moderate intensity exercise in lowering average daily glucose levels in South Africa.

Consistently, Little et al. (2011) reported lowered average 24-h glucose and cumulative postprandial glucose levels, as compared to pre-training values, after a total of six supervised sessions of high intensity interval training over two weeks in a study done in Nigeria. However, in both these studies post-intervention CGMs performed 48-72 hours after completion of the training program. Therefore these data cannot be used to analyze the acute effect of exercise, although they may reflect the long-term metabolic changes induced by regular physical activity. Interestingly, in a small study carried out on seven of the subjects investigated by Little et al. (2011), postprandial glucose and time spent in hyperglycemia in the 24-hr period following the first bout of high intensity interval training were both significantly reduced, although average 24-h glucose levels were not significantly reduced (Gillen et al, 2012).

Praet et al. (2006) did not show any significant reduction in mean blood glucose concentrations during the 24-h period following exercise, in comparison with a non-exercise day in a study done in the UK. Similarly, in a study by Bacchi et al (2012) they did not detect a significant change in

blood glucose Area Under the Curve (AUC) over a 48-h period following a session of moderate resistance exercise, in a group of trained diabetic patients performing regular physical activity. Similar findings were reported by Figueira et al. (2013) after a session of more vigorous exercise, either combined or aerobic alone.

Cauza et al. (2005), in a 4-month intervention study in which participants were randomized to strength or endurance training, reported that strength training led to a significant decrease in average glucose concentrations, as measured by CGMS, while aerobic training did not. However, post-intervention measurements were performed several days after patients had completed the training programme and therefore these data only explored the long-term effect of exercise.

Nonetheless, these preliminary findings indicate the urgent need for larger studies, now made possible by the CGMS technology, designed to clarify this very important clinical issue. Future research should take into account a number of factors potentially affecting glucose response to exercise in diabetic patients, such as the characteristics of exercise (frequency, intensity, duration and type), training status of the patients, metabolic control, antidiabetic therapy, diet composition, and distance of exercise sessions from the meals and timing of exercise bouts.
Available reports show significant relationships with regards to increased LDL, total cholesterol and decrease in HDL. Dunn et al. (2007) investigated the effects of a 6-month aerobic exercise training programme in Canada, which advanced from 50 to 85 % of maximum aerobic power for 20–60 min three times weekly, and resulted to significant decreases in total cholesterol (-0.3 mmol/L, p\0.001) and in the total: HDL cholesterol ratio (-0.3, p\0.001). In this case, the intervention period and intensity were relatively long and high respectively. In a 16-week study,

reported significant reductions in plasma triglycerides (from 1.4 to 1.2 mmol/L, p\0.05) and increases in HDL cholesterol (from 1.4 to 1.8 mmol/L, p\0.05) after training three times weekly at 70–75 % HRmax for 30 min for the first 8 weeks, progressing to four times weekly at 85 % HRmax for 45 min thereafter. LeMura et al. (2000).

Further, there is 13 % reduction in the body fat percentage (from 26.4 to 22.9 %, p\0.05), LeMura et al. (2000), thus suggesting that the additional volume of training generated an additional metabolic response a parameter not reported by Kraus et al. (2002) that investigated the impact of increasing the volume and intensity of aerobic exercise upon the lipid profiles of 111 sedentary overweight participants, all with mild to moderate dyslipidaemia.

A study done by Cadeddu (2004) in Belgium on the effects of metformin and exercise training, alone or in association, on cardio-pulmonary performance and quality of life in insulin resistance patients, the findings showed in all the enrolled patients a reduced average peak VO2 (61.8% ± 12%) compared with the theoretical values of a normal population paired for age and anthropometric characteristic, s this study did not touch on the metabolic parameters that are highlighted to be investigated in this study.

Another study was done by Arnarson (2012) in Australia on the effect of 12-Week Resistance Exercise Program on Body Composition, Muscle Strength, Physical Function, and Glucose Metabolism in Healthy, Insulin-Resistant, and Diabetic Elderly Icelanders, the results indicated that participants completing the study (n = 213) experienced significant changes in muscle strength or muscle function, which did not differ significantly between healthy (n = 198),

prediabetic (n = 20), and T2DM participants (n = 17). Changes in serum glucose during the intervention differed by group: only glucose improved significantly in the prediabetic group, glucose and triacylglycerol improved significantly in the healthy group, whereas no serum parameter improved significantly in the T2DM group, this again however was far from the study's objective. This has created a study gap for this study to be done. There is no specific study that has investigated the effects of prescribed physical therapy exercises on metabolic components in prediabetes. Specifically there are no reports on the levels of fasting glucose, glucose tolerance and HbA1C in prediabetes subjected to prescribed physical therapy exercises. Therefore the present study was carried out to investigate/determine the effect of physical exercises on the variables.

The condition has not been adequately addressed by interventions in either health promotion or disease management. As pointed out in the 2008 Canadian Diabetes Association (CDA) Clinical Practice Guidelines, lifestyle therapy that includes regular physical activity and dietary advice should be the first line of defense against diabetes development from a state of prediabetes, although it is somewhat unclear who should be giving the prescription and what exactly the prescription should be (CDA, 2008). Another major barrier is that many individuals and some health-care practitioners may be naïve in exercises such that they do not put emphasis on the importance of exercises and patients may not get the knowledge of exercise benefits in prevention of diabetes development from prediabetes state.

CHAPTER THREE

RESEARCH METHODOLOGY

3.1 Study Area

The present study was carried out at the Moi Teaching and Referral Hospital in Uasin Gishu County, Western Kenya The county is comprised of 3 districts (Eldoret East, Eldoret West and Wareng). MTRH was be purposively selected because they have a large number of patients and its proximity to the experimental lab and physical therapy department thus forming the target population of the study. All testing sessions were conducted in the physiotherapy department of Moi University School of Medicine.

3.2 Study design

The study adopted a Randomized Controlled Trial design (RCT). This is a study design that randomly assigns the participants into an experimental group and a control group. As the study is conducted, the only expected difference is in the outcome variable being studied between the control and experimental groups (Saunders, Lewis &Thornhill, 2012).

3.3 Target population

The target population included all the overweight patients attending MTRH Outpatient Department.

3.4 Sample Size and Sampling Technique

3.4.1 Sample size

Mugenda and Mugenda (2003) points out that, when the population is large and time together with resources allow, a big sample should be taken. This enable findings to be a true representative of the whole population in the study. When samples are small the findings do not reproduce salient characteristics of the accessible population to an acceptable degree. Zhong (2009) provides a formula for calculating sample size in a randomized controlled trial having two comparison groups with both groups having the same size of subjects as:

$$N = 2 \times \left[\frac{z_{1-\alpha} + z_{1-\beta}}{\delta - \delta_0}\right]^2 \times s^2$$

Where

N is the size per group

z_x is the standard normal deviate for a one sided

δ is the hypothesized mean difference between the two groups

δ_0 is the clinically admissible margin of superiority

s^2 is the pooled variance of both comparison groups

Power standard to set this at 80% requiring a greater sample size

For this study HbA1c was used to compute the sample size. We have

: 0.05 , : 0.20 , : 0.3 , = 0.1 , = 0.2 . Hence

$$N = 2 \times \left[\frac{1.645 + 0.845}{\delta - \delta_0}\right]^2 \times 0.2 = 17$$

Each arm was having 17 participants

3.4.2 Recruitment of the participants

Participants were recruited at MTRH after awareness was made about the diabetes screening in Eldoret and its environs.

Interested participants underwent an eligibility assessment before recruitment.

3.4.3 Randomization procedure & Assessment schedule

The sample of 34 participants formed the population for both the control and the experimental group. The division of control and experimental group was achieved through simple randomization. The researcher first, came up with 34 opaque envelopes containing an identifier for the treatment group 1 (prescribed exercises n_1) and an identifier for the control group n_2. (n_1 + n_2 = N). The envelopes were then shuffled. The order of the shuffled envelopes was used to determine the allocation of the participants to the treatment group and the control group after they meet the eligibility criteria. This process is relatively simple to organise, preserves the predetermined design parameters, and can be readily extended to situations where multiple treatments are to be compared (Saunders, Lewis & Thornhill, 2012). In this particular study the relevant characteristics were subjects with HbA1c of between 5.7%-6.7%, Fasting Plasma Glucose of between 5.6mmol/L-6.9mmol/L, oral glucose tolerance tests of between 7.8mmol/L-11.0mmol/L, triglycerides level of more than 150mg/dL, LDL levels of more than 100mg/dL and HDL levels of lower than 40mg/dL. The control group refrained from the prescribed physical therapy exercises after being educated according to American College of Sports Medicine Chapter 8 Adherence to exercise: helping the client stay alive, they continued with the normal physicians advises and interventions. There was blinding whereby the control group did not meet with the experimental group. The controls were attending health education in a different room from the one the experimental group were receiving prescribed exercises. All variables were

tested for both the control and the experimental group and they were tested at the same intervals. All the participants were instructed on the importance of sticking to the agreed regime.

3.5 Inclusion and Exclusion Criteria

3.5.1 Inclusion criteria

Only persons aged 18 to 60 years

Participants with HbA1c of between 5.7% to 6.7%, Fasting Plasma Glucose of between 5.6mmol/L to 6.9mmol/L.

3.5.2 Exclusion criteria

Patient already on treatment for dyslipidemia

Diabetic patients

Persons with disabilities

3.5.3 Study Procedures

Participants participating in this study were invited to attend a familiarization and initial glucose screening session. Participants were instructed to refrain from exercise for 48 hours and fast for 8 - 12 hours prior to pretesting and for all scheduled assessments. On reporting to the lab, participants were asked their medical history and provide personal information regarding exercise habits and health status. They then underwent a general physical examination to determine whether they met eligibility criteria. Participants were required to obtain medical clearance from a physician prior to participating in baseline assessments. Once medical clearance is obtained, participants were familiarized to the study protocol via a verbal and written explanation outlining the study design. (See appendix 3).

Adherence was determined by time-line flow back approach at the 4th and 8th week of the experiment time points, using a patient-reported outcomes survey questionnaire Patient Functional Scale (PFS) Short Form 36 (SF-36) (See Appendix 4).

Body mass was measured to ensure participants met the entry criteria for BMI (≥25 kg/m2). The tests were done with the participants wearing simple clothing without metals, such as earrings rings or necklaces. Tests commenced after they have rested for 30 minutes after arriving at the laboratory.

3.5.4 Blood Sample Collection Procedure

Experimental blood samples collection is a crucial pre-analytical activity and accurate identification of both blood samples and the patient is a key priority as for other healthcare activities. Errors occurring during this pre-analytical step may impair sample quality and characteristics, or else modify the final results of testing. The standardization of blood sampling, patient position and psychological state of the patient are therefore crucial for mitigating the impact of pre-analytical variability (Giavarina & Lippi, 2017).

The tests for fasting glucose, triglycerides, low-density lipoprotein, high-density lipoprotein and HbA1c, the participant were comfortably positioned in a chair sitting upright. The procedure was clearly explained to the participant giving time to ask any question. The lab scientist ensured all the equipment was ready next to the participant. Identification of the median cubittal vein was done and blood was withdrawn through venipuncture at the vein. The tourniquet was placed 3 inches above the selected site in the upper arm ensure engorgement of the vein with blood. Next the participant was asked to make a fist. Swiftly, the needle was inserted through the skin into the lumen of the vein and blood was withdrawn. Once the tube is filled the tourniquet was

removed and gauze pad placed over the needle site with some pressure to facilitate clotting of blood.

3.6 Data collection

The prescribed physical therapy exercises were done in the Moi University Orthopedics and Rehabilitation's Physical Therapy Department Gymnasium and thereafter, the data was collected using a laboratory-based experiment where by blood samples were taken by a medical lab scientist at the end of every 6 weeks after administration of prescribed physical therapy exercise regimen as indicated in the table (Table 3.3). During the day of the laboratory tests, the identified participants (experimental group and the control group) were instructed to fast for 8 – 12 hours prior to the tests.

Fasting blood glucose and glucose tolerance test

The research instrument was soft style Omron blood glucose monitoring system (0364). Omron is the prominent blood glucose monitoring market since 1960 built on innovative designs through research and most importantly the accuracy and precision of the equipment. The machine is easy to use and gives results that are correlated well (r = -0.96) with standard laboratory methods (Gebrekidan & Gill 2016).

The FBG was executed by putting blood on a glucose meter strip that has been inserted into the machine and the results were shown on the screen in 10 -20 seconds.

Triglycerides, Low - Density Lipoproteins and High - Density Lipoproteins

The research device was Accurate Cholesterol test by Roche diagnostics ASIN B00EU9014M. This next generation meter uses the strip technology that healthcare professionals have trusted in the ACCU-CHEK instant plus since 1997.

The blood droplet was placed on the test strip; the test strip has special chemicals that change colours after few minutes. The researcher matched the final colour against the colour guide that is included in the kit. Validity and reliability of this equipment has been suggested in a study done by (Partiente & Sungwoo, 2017)

HbA1C

Glycosylated hemoglobin was measured using Quo-Lab A1c automated analyzer. This machine uses bonate affinity methodology which is widely recognized by scientists as interference free.

The blood sample of 4ul was placed in a strip that is inserted into the Quo-Lab A1c automated analyzer and the test results were out within four minutes. Validity and reliability of this equipment has been suggested in a study done by (Partiente & Sungwoo, 2017).

Body weight and BMI

These parameters were measured using body composition analyzer (Inbody 370,Biospace, Soeul, korea). Validity and reliability of this equipment has been suggested in a study done by Sungwoo, (2017) necessity of a valid and reliable assessment tool. Weight, height, and body composition were measured with the participants wearing simple clothing, without shoes in the

morning. BMI was calculated as weight in kilograms (Kg) divided by height in meters squared (M^2) (Wen, Cheng, & Chan 2016).

Exercise prescription

Exercise prescription was guided by the FITT (Frequency, Intensity, Time and Type) principle.

Stretchings

The participants started the prescribed exercises with a 5-minute stretching of major muscle groups (legs, hips, chest, back, abdomen, shoulders, and arms).

Warm up

This was a 5 minute drill of several multiplanar movements such as forward an backward leg swings that incorporate some rotation, as well as donkey kicks, squat jumping, prone alternate arm and leg extension.

Intensity

Intensity of training is defined by either the physiologic response of the individual, or the intensity of the exercise performed. For example, in this program of prescribed exercises intensity were aimed at a Heart Rate Reserve (HRR) and Borg's Scales for Ratings of Perceived Exertion (RPE).

Aerobics were performed in form of cycling at a moderate intensity of 12-13 (Fairly Light To Somewhat Hard) on (RPE) and HRR of 70%. These were used to measure the level of effort the participant was applying.

Vigorous exercises was a prescription of 25-minutes of treadmill Walking on aerobic Zone of 70%--80% HRR at 14-16 RPE and resistance exercises of 70 – 80% HRR using thera Band on major muscle groups of the legs, hips, chest, back, abdomen, shoulders, and arms for a duration of 10 minutes.

There was a cool down of 5-minutes whereby the participants were instructed to gradually reduce the exercise intensity whilst gently stretching the major muscle groups.

Table 3.1 Borg's Scales for Ratings of Perceived Exertion

RPE	Description	Intensity Level
7	Easy	
8		
9	Very Light	
10		50% MHR
11	Fairly Light	
12		60% MHR
13	Somewhat Hard	
14		70% MHR
15		
16	Hard	80% MHR
17		
18	Very Hard	90% MHR
19	Very, Very Hard	
20		

Frequency

Frequency of training is defined as how often exercise is performed over a fixed time period, and is usually expressed in sessions per week. It is a fine balance between providing enough stress for the body to adapt and allowing time for healing and adaptations to occur. At a minimum, training programs should be done three times per week. The prescribed physical therapy exercises were spread out to 3 days a week with no more than two consecutive days between the bouts of exercises.

Duration

This is the time the each participant spent exercising. The prescribed physical therapy exercises were expended for 210 minutes per week. These were distributed as a combination of 5-min stretch, 5-min warm-up, 30-min aerobics, 25 min vigorous and resistance exercises with 5-min cool down (70-minute set).

Table 3.2 Exercise recommendations for prediabetes

Type of exercise	Intensity	Duration (210 min total)	Frequency
Stretching	Moderate RPE 8-9	5 minutes	3 X/week
Warm-up	Moderate RPE 10-11	5 minutes	3 X/week
Aerobic (large muscle activities) cycling	Moderate: RPE 12–13 or 70%HRR 55–69% HRmax	30 minutes	No more than two consecutive days without exercising
Treadmill Walking aerobic Zone 70%--80%	Vigorous: 80 %HRR 70–89% HRmax RPE 14–16	15 min total	3 X/week
Resistance (multi joint exercises, progressive, large muscle groups)	Moderate to vigorous 70 – 80% of 1RM 2–4 sets 8–10 repetitions 1–2 min rest interval	10 min	2 or more times/week
Cool down	Low RPE 7-8	5 minutes	3 X/week

HRR = heart rate reserve ≈ (HRmax− HRrest)
HRmax = (220-Age)

A Resistance training repetitions should be performed at a weight that cannot be lifted more than 8–10 times (70–84% of 1 RM). New 1RM was be determined every week.

3.8 Ethical considerations

Approval was sought from Institutional Research and Ethics Committee (IREC) at Moi Teaching and Referral hospital, there after permission was sought from the Moi University administration. The objectives of the study were explained and made available to all the participants in the form of an informed consent form (Appendix 7). Participation was voluntary and participants were given the opportunity to withdraw from the study at any time with no consequences. Informed written consent was obtained from all participants and assured of respect, confidentiality and anonymity before participating in the study. To ensure safety or harm of blood draws, hand hygiene was maintained by using soap and water or alcohol swabs, well-fitting gloves, single use disposable needles and syringes. This was practiced before and after each participant contact. The investigator ensured that there was availability of sufficient laboratory sample tubes for blood storage. Incase of accidental exposure the incidence was to be reported and recorded in a register and thereafter, the support services were to be promoted e.g post exposure prophylaxis (PEP) to avert HIV. Blood sampling was done in a private and clear manner. After the draw the used needles and syringes were discarded into the robust sharps container. Incase of bleeding or bruising excessively during blood drawing, the physician was to be contacted as quickly as possible meanwhile the blood drawer continues to apply pressure as recommended by medical practice as the PI tries to stem the blood flow. And incase of exercise accident e.g exertional or exercise induced rhabdomyolysis (ER) the participant was to be stopped for doing the exercises, and the physician be contacted immediately. All the data was kept secure and confidential, password protected in a locked lab.

3.9 Data Analysis

All experimental results were evaluated and analysis of variance (ANOVA) was used to investigate associations between variables (relationship between physical therapy exercises and metabolic components). Presentation was done by use of charts, tables and graphs. The significance level was set at $p \leq .05$ for both the control and experimental groups for all the parameters to be tested. Differences in fasting glucose, glucose tolerance and lipoprotein levels in both pre- and post-tests were measured by comparing the maximum glucose excursion recorded after an exercise. Data was averaged and presented as means ± SD. In order to make sure subjects in before and after were similar, descriptive measurements from the pretest, including age, weight, height, and BMI were analyzed for differences between groups using an independent samples t-test. Differences in maximum fasting glucose, glucose tolerance and lipo-protein levels pre- and post-test were analyzed within each group using paired samples t-test: repeated measures design.

3.10 Limitations

Confounders could not be totally eliminated i.e extra exercise on individual patients. During study period any extra exercise done beyond daily/routine activities of the participants could result to an outlier in results.

Dietary advice could not strictly be followed during study duration. Diet diary or diet plan is recommended

3.11 Summary of the chapter

In this chapter the researcher described the research methods to be used. The choice of research setting was based on the number of respondents. The study design, methodology and data

analysis was motivated and supported with the references. Procedures to ensure that the study was conducted in an ethical manner have been explained. The results of the study are presented in the next chapter.

CHAPTER FOUR

RESULTS

4.1 Introduction

This chapter presents the results of data collected on the effects of prescribed physical therapy exercise on the levels of fasting glucose, glucose tolerance and HBA1C levels of prediabetes at MTRH. The study collected data from 34 respondents (17 each for the experimental and control groups). Data were collected from the participants at three time-periods: pre-training, mid-training (at end of 6 weeks), and post-training (at end of 12 weeks).

4.2 Demographic Profile of Respondents

The data from this section gives biographical information of the participants in the study in order to understand their profile. The information sought included the respondents' gender, age, and highest educational level.

Table 4.1 Biographic information of respondents

Bio-graphic information	Overall (n=34)	Experimental group (n=17)	Control group (n=17)
Respondents' gender			
1. Male (%)	19 (55.9)	9 (52.9)	10 (58.8)
2. Female (%)	15 (44.1)	8 (47.1)	7 (41.2)
3. Total (%)	34 (100.0)	17 (100.0)	17 (100.0)
Highest education level			
1. Primary (%)	6 (17.6)	3 (17.6)	3 (17.6)
2. Secondary (%)	18 (52.9)	8 (47.1)	10 (58.8)
3. Tertiary (%)	10 (29.4)	6 (35.3)	4 (23.5)
4. Total (%)	34 (100.0)	17 (100.0)	17 (100.0)
Respondents' age			
Mean years + SD	35.94±9.35	34.59±9.53	37.29±9.25

Key: SD = standard deviation; n = number of respondents

Descriptive results (Table 4.1) showed that the study sampled slightly more males (56%) compared with female (44%) participants. Gender distribution among the experimental and control groups generally reflected the overall proportion, with 53% male and 47% female in the experimental group. On the other hand, there were 59% and 41% male and female participants, respectively, in the control group. The fact that the study sampled both male and females suggested that results from this study were largely reflective of the results from both gender.

Majority of respondents (n=18, 53%) in the study had secondary schooling as their highest educational level, followed by 29% (n=10) who had tertiary education. Only 18% of the participants had primary education. This pattern was maintained, when the data were decomposed into experimental and control groups, with most participants having secondary education, followed by those with tertiary and lastly, primary schooling. The results suggested that participants in the study area were fairly educated.

The mean age of the respondents was 36 years. Since the standard deviation for age was roughly nine, and assuming a Gaussian distribution (skewness=0.41 and kurtosis= -0.58) it implied that most of the participants were aged between 27 and 45 years. This suggested that participants in the study area were relatively youthful. Participants in the control group were slightly older (mean 37 years) compared to those in the experimental group (mean 35 years).

4.3 Metabolic profiles of prediabetes

Table 4.2 presents the metabolic profiles of the prediabetes enrolled in the study at the baseline (pre-training period).

Table 4.2 **Baseline values of metabolic profiles of prediabetes**

Variable	Overall Mean ± SD	Experimental Mean ± SD	Control Mean ± SD	t-value	p
BMI (Kg/m^2)	28.62±2.49	28.47±2.37	28.77±2.66	-0.34	0.74
FBG (mmol/L)	6.15±0.51	6.11±0.47	6.19±0.55	-0.42	0.68
TC (mg/dL)	211.35±24.33	206.29±27.56	216.41±20.17	-1.22	0.23
HDL (mg/dL)	45.53±8.99	48.00±9.68	43.06±7.73	1.64	0.11
TRI (mg/dL)	141.32±32.64	138.47±34.72	144.18±31.21	-0.50	0.62
LDL (mg/dL)	138.06±25.91	131.12±29.30	145.00±20.59	-1.59	0.12
HbA1c (%)	5.96±0.25	5.93±0.23	5.97±0.28	-0.42	0.68

Key.BMI: body mass index, FBG: fasting blood glucose, TC: total cholesterol, HDL: high-density lipoprotein, TRI: triglycerides, LDL: low-density lipoprotein, HbA1c: glycosylated haemoglobin,
SD: standard deviation

The overall baseline values were characteristic of prediabetes, according to guidelines given by ADA (2012) and Sharma & Garber (2009). Independent samples t-tests were conducted to determine if parameter levels were significantly different between experimental and control groups at the start of the study and all were found to be non-significant (all had $p>0.05$). Thus, all the seven variable levels were similar in both experimental and control groups at the onset of the study. This showed that random allocation of subjects into the two groups was largely successful.

4.4 Exercise Regimen required to change Prediabetes Metabolic Profiles

Table 4.3 shows the metabolic profiles of prediabetes recorded at pretraining, mid-training and post-training.

Table 4.3 Metabolic profiles of prediabetes at pre-, mid-, and post-training

Variable	Treat.	Pre-training	Mid-training	Post-training	Main effects (F values)		Interaction (F value)
		Mean±SD	Mean±SD	Mean±SD	Group	Time	Group*Time
BMI (Kg/m^2)	Exp.	$28.47\pm2.37^{a,k}$	$27.85\pm2.17^{a,k}$	$26.51\pm2.26^{b,k}$	1.28^{ns}	18.27^{**}	3.49^{*}
	Cont.	$28.77\pm2.66^{a,k}$	$28.80\pm2.77^{a,k}$	$28.04\pm2.74^{b,l}$			
FBG (mmol/L)	Exp.	$6.11\pm0.47^{a,k}$	$5.81\pm0.53^{b,k}$	$5.30\pm0.46^{c,k}$	7.22^{*}	15.20^{**}	5.05^{*}
	Cont.	$6.19\pm0.55^{a,k}$	$6.28\pm0.48^{a,l}$	$5.99\pm0.76^{a,l}$			
TC (mg/dL)	Exp.	$206.29\pm27.56^{a,k}$	$203.41\pm26.06^{a,k}$	$194.35\pm32.77^{b,k}$	0.22^{ns}	7.27^{**}	2.24^{ns}
	Cont.	$216.41\pm20.17^{a,k}$	$208.65\pm21.80^{b,k}$	$209.88\pm20.32^{a,k}$			
HDL (mg/dL)	Exp.	$48.00\pm9.68^{a,k}$	$49.53\pm7.69^{a,k}$	$51.47\pm6.77^{b,k}$	8.17^{**}	2.32^{**}	1.33^{ns}
	Cont.	$43.06\pm7.73^{a,k}$	$43.18\pm7.73^{a,k}$	$43.53\pm4.06^{a,l}$			
TRI (mg/dL)	Exp.	$138.47\pm34.72^{a,k}$	$134.29\pm34.61^{a,k}$	$123.24\pm25.03^{b,k}$	1.38^{ns}	5.41^{*}	1.30^{ns}
	Cont.	$144.18\pm31.21^{a,k}$	$146.47\pm30.59^{a,k}$	$139.59\pm25.03^{a,k}$			
LDL (mg/dL)	Exp.	$131.12\pm29.30^{a,k}$	$128.26\pm25.59^{a,k}$	$118.15\pm33.91^{b,k}$	2.71^{ns}	6.91^{**}	2.79^{*}
	Cont.	$145.00\pm20.59^{a,k}$	$136.04\pm24.20^{a,k}$	$138.44\pm22.10^{a,l}$			
HbA1c (%)	Exp.	$5.93\pm0.23^{a,k}$	$5.78\pm0.30^{b,k}$	$5.46\pm0.25^{c,k}$	6.18^{**}	21.00^{**}	4.02^{*}
	Cont.	$5.97\pm0.28^{a,k}$	$6.00\pm0.28^{a,k}$	$5.80\pm0.41^{b,l}$			

Key.BMI: body mass index, FBG: fasting blood glucose, TC: total cholesterol, HDL: high-density lipoprotein, TRI: triglycerides, LDL: low-density lipoprotein, HbA1c: glycosylated haemoglobin,
SD: standard deviation, Treat.: Treatment, Exp.: experimental, Cont.: Control. For every group, means with similar letters in a row (a, b, and c) and for every variable, means with similar letters in a column (k and l) are not significantly different by Tukey HSD test. **, * : significant at 99% and 95% significance levels, respectively.

The levels of BMI decreased in the experimental group during both the mid-training and post-training period. A mixed-design (repeated-measures) ANOVA with a within-subjects factor of time of training (pre-, mid-, and post-training) and a between-subject factor of treatment type (experimental and control groups) was run to determine the effects of these factors. There were no outliers in the data, as assessed by inspection of a boxplot. BMI scores for each level of treatment were normally distributed, as assessed by Shapiro-Wilks test ($p > 0.05$) whereas the Levene's Test indicated error variance to be equal across the groups (all $p > 0.05$). However, the assumption of compound symmetry or sphericity (the presence of a single variance for all the three time points) was violated, [$\chi^2(2) = 12.55$; $p=0.002$]. Consequently, Geisser-Greehouse ($\varepsilon = 0.75$) method was used to adjust the degrees of freedom for the averaged tests of significance. A significant main effect of time, $F\ (1.5, 48.01) = 18.27$, $p < 0.0001$ and the interaction between

time and group, F (1.5, 48.01) = 3.49, p = 0.04were found on BMI recorded. However, grouphad no significant influence on BMI levels, F (1, 32) = 1.28, p=0.26. The results showed that over time, BMI levels, significantly reduced in both groups. However, the most substantial decrease was recorded in the experimental group relative to the control group (Figure 4.1).

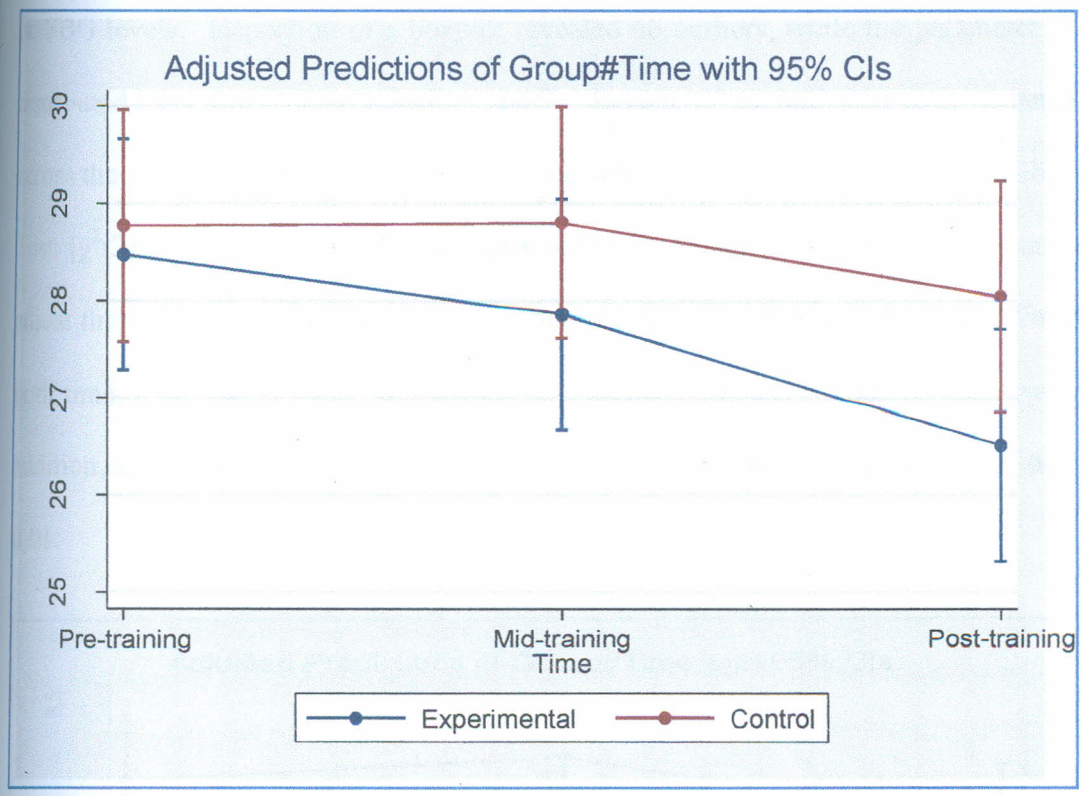

Figure 4.1 Predicted BMI interactions between group and time

Post-hoc pair wise comparisons of adjusted predictions revealed that BMI levels did no significantly differ between mid-training and pre-training in both the experimental and control groups (Table 4.3). However, post-training levels of BMI were significantly lower compared to both mid- and pre-training. In addition, there were no significant differences in BMI between experimental and control groups during pre-training: z=0.34, p=0.73 and mid-training: z=1.10, p=0.27 and as seen by overlapping confidence intervals for the two groups in Figure 4.1. However, during post-training (z=1.78, p=0.07), BMI was significantly lower in the

experimental group compared to the control. The results indicated the exercise regime required to reduce BMI levels is after 12 weeks.

The levels of FBG generally decreased in the experimental group during both mid-training and post-training period. A mixed ANOVA was conducted to determine the effect of time and group on FBG levels. Inspection of a boxplot revealed no outliers, while the parameter was normally distributed (Shapiro-Wilks test had $p > 0.05$). Levene's Test indicated error variance to be equal across the groups (all $p > 0.05$). Although the sphericity assumption was not tenable (Mauchly's Test: [$\chi^2(2) = 8.35$, $p=0.02$]), the Geisser-Greehouse epsilon was high ($\varepsilon = 0.81$) and was used to adjust the degrees of freedom for the averaged tests of significance. Significant main effects of both time, $F(2, 64) = 15.20$, $p < 0.0001$ and group, $F(1, 64) = 7.22$, $p = 0.01$ were found. In addition, a significant interaction between group and time was also found, $F(2, 64) = 5.05$, $p = 0.01$.

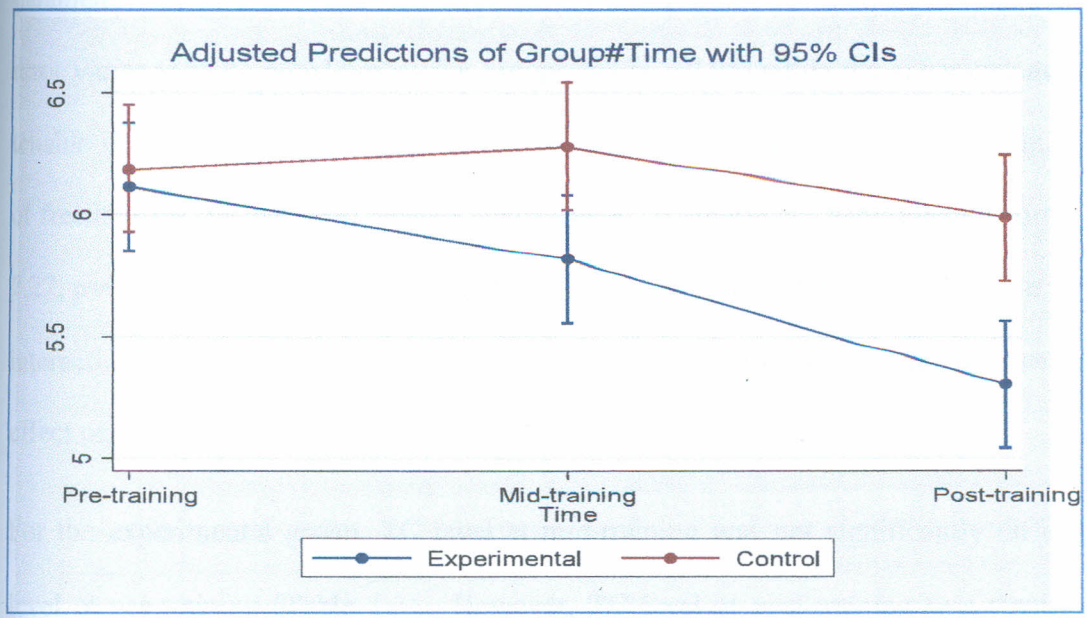

Figure 4.2 Predicted FBG interactions between group and time

Pairwise comparisons showed that in the experimental group, training significantly lowered the level of FBG in six weeks compared to pre-training period. In addition, training significantly lowered the FBG value in 12 weeks compared to week six (Table 4.3 and Figure 4.2). There was no significant difference in the level of FBG in both experimental and control groups at pre-training, as seen from the overlapping confidence intervals in Figure 4.2. However, during week six, FBG was significantly lower in the experimental group (mean difference: 0.46 mmol/L, $z=2.46$, $p=0.01$). FBG level further decreased in 12 weeks of training in the experimental group (mean difference: 0.68 mmol/L, $z=3.63$, $p<0.0001$) compared to the control. The results showed that training reduces FBG by 5% and 13%, in six and 12 weeks, respectively.

The levels of TC generally decreased in the experimental group during both mid-training and post-training period relative to pre-training. A mixed ANOVA was conducted to determine the effect of time and group on TC levels. Inspection of a boxplot revealed no outliers, while the parameter was normally distributed (Shapiro-Wilks test had $p > 0.05$). Levene's Test indicated error variance to be equal across the groups (all $p > 0.05$) while the sphericity assumption was tenable (Mauchly's Test: [$\chi^2(2) = 4.35$, $p=0.11$]). Thus, there was no need to adjust the degrees of freedom for the averaged tests of significance. A significant main effect of time, $F(2, 64) = 7.27$, $p=0.001$ was found on the level of TC. However, group, $F(1, 64) = 71.27$, $p = 0.22$ and the interaction between group and time, $F(2, 64) = 2.24$, $p = 0.11$, were found to have no significant effect on the level of TC.

For the experimental group, TC level at mid-training was not significantly different from the level at pre-training (Table 4.3). However, TC level at post-training was significantly lower compared to both mid- and pre-training, suggesting that a longer exercise regime (12 weeks) is required to reduce the level of TC in the body. However, there were no significant differences in

BMI between experimental and control groups at all time periods (pre-training: $z=1.17$, $p=0.24$; mid-training: $z=0.61$, $p=0.55$; and post-training: $z=1.80$, $p=0.07$) and overlapping confidence intervals on Figure 4.3.

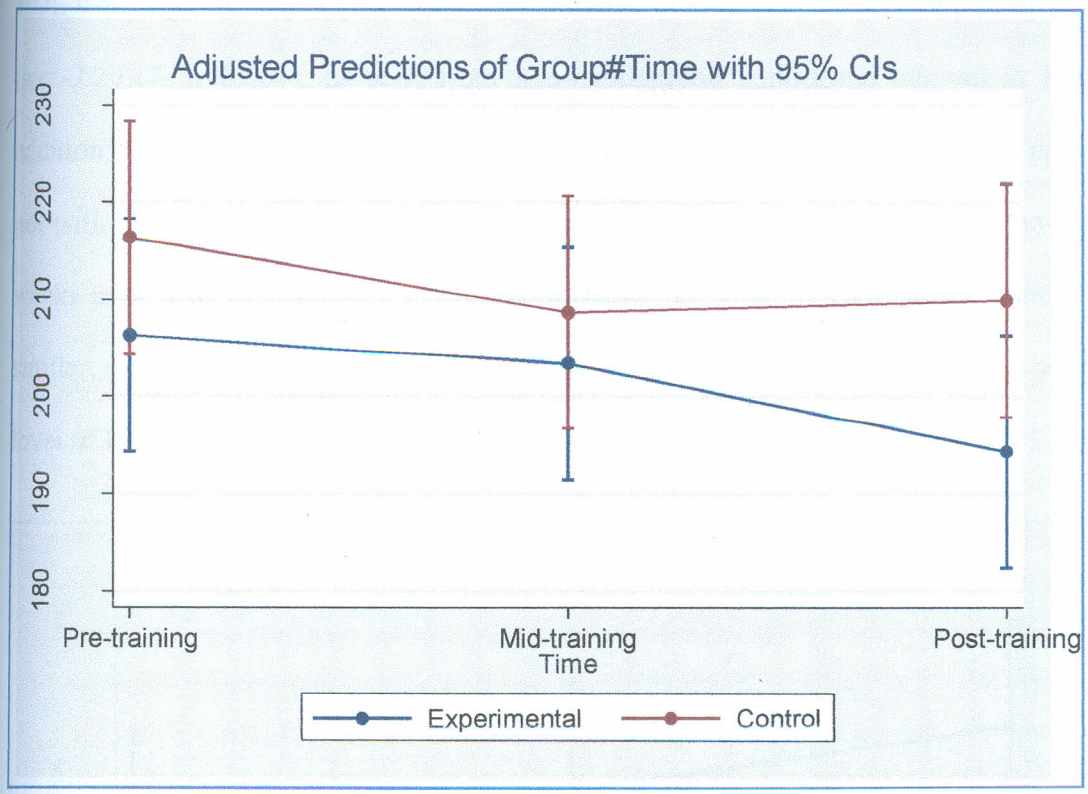

Figure 4.3 Predicted TC interactions between group and time

The level of HDL generally increased in the experimental group during both mid-training and post-training period compared to pre-training. A mixed ANOVA was conducted to determine the effect of time and group on HDL levels. There were no outliers in the data as shown by a boxplot examination while the parameter was normally distributed (Shapiro-Wilks test had $p > 0.05$). Levene's Test indicated error variance to be equal across the groups (all $p > 0.05$) while the sphericity assumption was not attained (Mauchly's Test: $[\chi^2(2) = 16.09, p<0.0001]$). Thus, degrees of freedom for the averaged tests of significance were adjusted by Geisser-Greehouse method.

A significant main effect of group, F (1, 64) = 8.17, p=0.007and time, F (2, 64) = 2.32, p = 0.01 were found on the level of HDL. However, the interaction between group and time, F (2, 64) = 1.33, p = 0.27, was found to have no significant effect on the level of HDL. The results showed HDL were significantly higher in the experimental than in the control group during post-training (z= -3.20.17, p=0.001), as seen from non-overlapping confidence interval in Figure 4.4. In addition, the level of HDL was significantly higher in post-training relative to pre-training but not with mid-training (Table 4.3). This suggested that training only increases the HDL level 12 weeks after start of exercise. On the other hand, the level of HDL in the control group was similar, regardless of the period (Table), suggesting that absence of training does not increase the level of HDL.

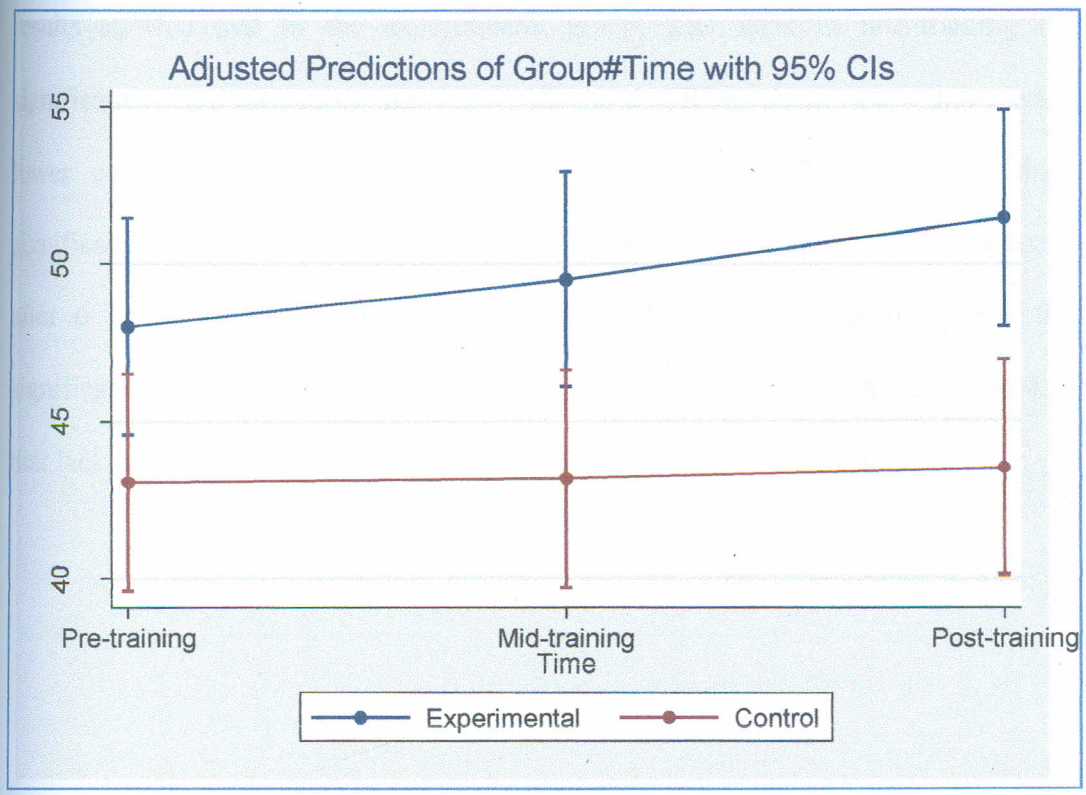

Figure 4.4 Predicted HDL interactions between group and time

The level of TRI generally decreased in the experimental group, from pre-training to post-training period (Table 4.3). A mixed ANOVA was conducted to determine the effect of time and group on FBG levels. Inspection of a boxplot revealed no outliers, while the parameter was normally distributed (Shapiro-Wilks test had $p > 0.05$). Levene's Test indicated error variance to be equal across the groups (all $p > 0.05$). Although the sphericity assumption was not tenable (Mauchly's Test: $[\chi^2(2) = 13.55, p=0.001]$), the Geisser-Greehouse epsilon ($\acute{\varepsilon} = 0.74$) was used to adjust the degrees of freedom for the averaged tests of significance.

The main effect of time was the only factor found to significantly influence TRI levels, $F(2, 64) = 5.41$, $p = 0.01$. The main effect of group, $F(1, 64) = 1.38$, $p = 0.25$ and the interaction between group and time, $F(2, 64) = 1.30$, $p = 0.27$, had no significant influence on TRI levels. The results showed that in the experimental group, TRI level in mid-training did not differ significantly from the pre-training level. However, TRI levels in post-training was significantly lower compared to both mid- and pre-training levels. This suggested that TRI levels significantly reduce after a 12-week exercise regime. In addition, TRI decrease more rapidly after 6 weeks of training than before (Figure 4.5). For the control group, there were no significant differences in TRI levels during, pre-, mid-, and post-training (Table 4.3), suggesting that lack of exercise does not lead to a decrease in the level of this parameter.

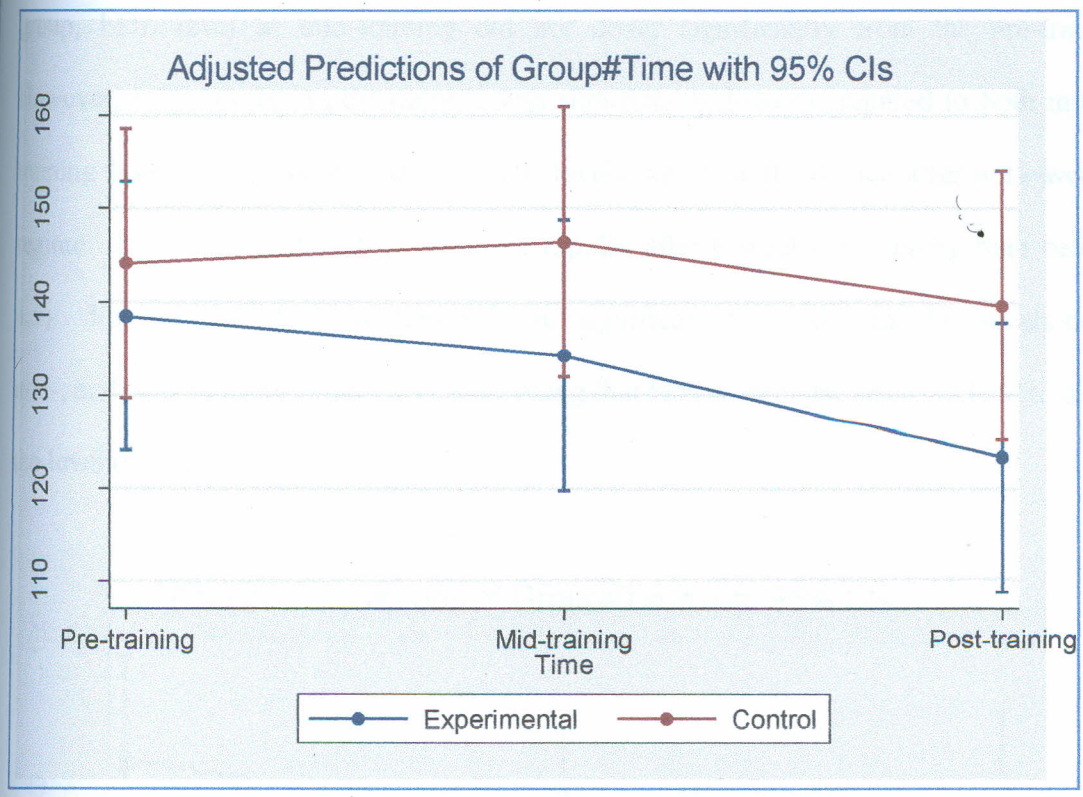

Figure 4.5 Predicted TRI interactions between group and time

The level of LDL decreased in the experimental group during both mid-training and post-training period relative to pre-training. The effect of time and group on LDL level was tested using a mixed ANOVA. Inspection of a boxplot revealed no outliers, while the parameter was normally distributed (Shapiro-Wilks test had $p > 0.05$). Levene's Test indicated error variance to be equal across the groups (all $p > 0.05$) while the assumption of sphericity was tenable (Mauchly's Test: $[\chi^2(2) = 5.08, p=0.08]$). Hence, the degrees of freedom for the averaged tests of significance were not adjusted.

A significant main effect of time, $F(2, 64) = 6.91$, $p=0.001$ was found on the level of LDL. However, group, $F(1, 64) = 2.71$, $p = 0.11$ did not significantly influence LDL levels (Table 4.3). The interaction between group and time, $F(2, 64) = 2.79$, $p = 0.049$, was also found to have a significant effect on the level of LDL. Pairwise comparisons showed that for the experimental

group, LDL level in mid-training did not differ significantly from the pre-training level. However, LDL levels in post-training was significantly lower compared to both mid- and pre-training levels. This suggested that LDL levels significantly reduce after a 12-week exercise regime. In addition, LDL decrease more rapidly after 6 weeks of training than before (Figure 4.5). For the control group, there were no significant differences in LDL levels during, pre-, mid-, and post-training (Table 4.3), suggesting that lack of exercise does not lead to a decrease in the level of this factor.

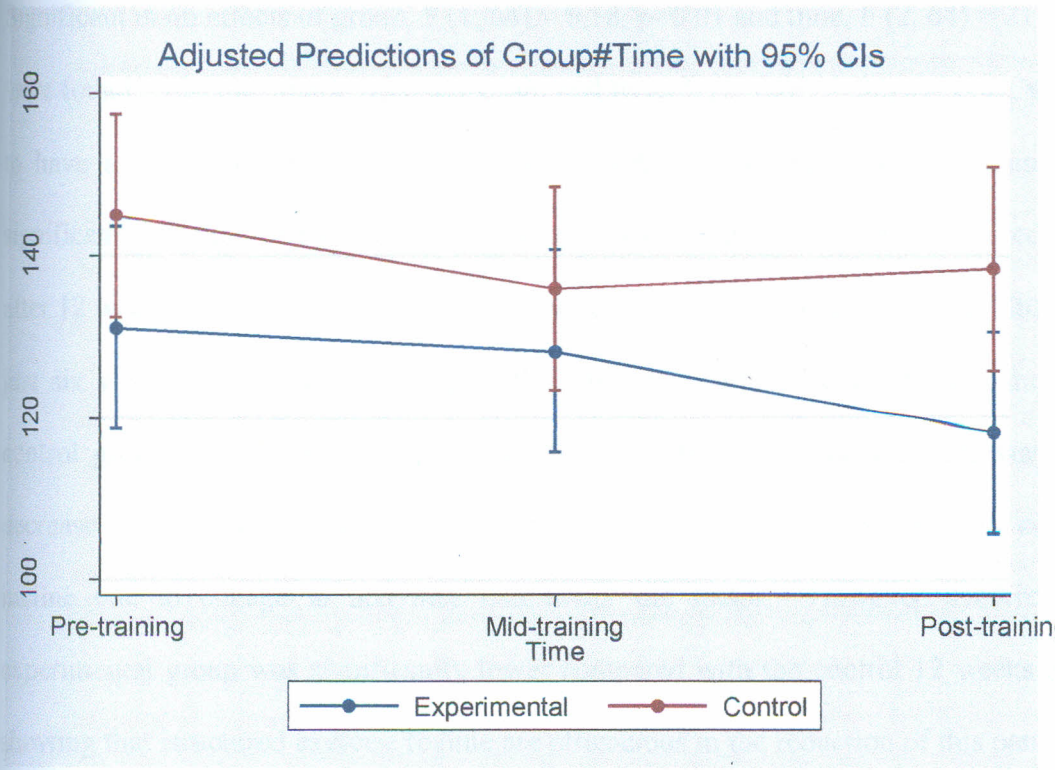

Figure 4.6 Predicted LDL interactions between group and time

The experimental and control groups differed significantly in LDL during post-training (mean difference: 20.28, z=2.25, p=0.02) but not during mid-training (mean difference: 7.79, z=0.86, p=0.39) or pre-training (mean difference: 13.88, z=1.54, p=0.12).

HbA1c decreased in the experimental group during both mid-training and post-training period compared to pre-training. The effect of time and group on the level of HbA1c was analysed using a mixed ANOVA. There were no outliers in the data as shown by a boxplot examination while the parameter was normally distributed (Shapiro-Wilks test had $p > 0.05$). Levene's Test indicated error variance to be equal across the groups (all $p > 0.05$) while the sphericity assumption was tenable (Mauchly's Test: $[\chi^2(2) = 2.32, p=0.31]$). Hence, degrees of freedom for the averaged tests were left as they were.

Significant main effects of group, $F(1, 64) = 6.18$, $p=0.01$ and time, $F(2, 64) = 21.00$, $p < 0.0001$ were found. The interaction between group and time, $F(2, 64) = 4.02$, $p = 0.02$, was also found to have a significant effect on the level of HbA1c.In the experimental group, there was a significant reduction of HbA1c (of 3%) after six weeks and an even more marked drop (of 8%) after 12 weeks. This showed that the exercise regimen will significantly lower HbA1c level after just six weeks. Continued exercises will further decrease the level of this parameter. In the control group, there was no drop of HbA1c level after week six but there was a significant decrease after 12 weeks, suggesting that knowledge about the seriousness of the condition might incline one to engage in activities that lower the factor. However, HbA1c level in the experimental group was significantly lower compared with the control 12 weeks after training, showing that structured exercise regime are efficacious in the reduction of this parameter (Figure 4.7).

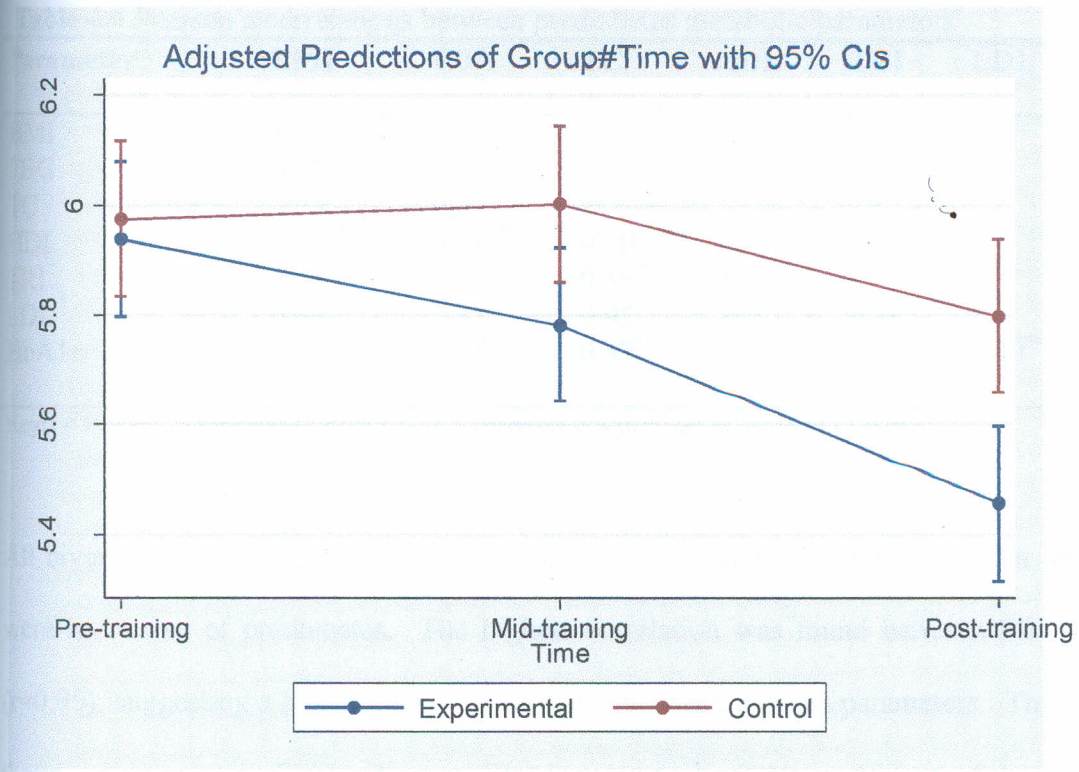

Figure 4.7 Predicted HbA1c interactions between group and time

4. 5 Concordance between Prediabetes Metabolic Parameters

Table 4.4 presents the Pearson's correlation amongst the prediabetes metabolic parameters measured among the participants of the study.The correlation coefficient could take any value between -1.00 and +1.00. A value of +1.00 represents perfect positive correlation while a value of -1.00 is a perfect negative correlation. Correlationcoefficients (in absolute value) which are ≤ 0.35 are generally considered to represent low or weak correlations, 0.36 to 0.67 moderate correlations, and 0.68 to 1.0 strong or high correlations with r coefficients > 0.90 very high correlations (Field, 2005).

Table 4.4 Pearson's correlations between prediabetes metabolic parameters

Parameter		BMI	FBG	TC	HDL	TRI	LDL	HbA1c
BMI	r	1						
FBG	r	0.47**	1					
TC	r	0.43**	0.40**	1				
HDL	r	-0.39**	-0.52**	-0.49**	1			
TRI	r	0.35**	0.29**	0.56**	-0.34**	1		
LDL	r	0.44**	0.45**	0.95**	-0.67**	0.38**	1	
HbA1c	r	0.49**	0.95**	0.37**	-0.46**	0.32**	0.40**	1

Key:r = Pearson correlation coefficient; ** = correlation significant at .01 level (2-tailed)

All bivariate relationships were found to be significant ($p<0.05$), suggesting that all parameters were indicative of prediabetes. The highest correlation was found between FBG and HbA1c ($r=0.95$), suggesting a high level of concordance between the two parameters. The results show that a unit increase in FBG will cause HbA1c to go up by 90% (coefficient of determination = $r^2 = 0.95^2 = 0.90$) and vice versa. A very high correlation was also found between TC and LDL ($r=0.95$), because the latter is used in the computation of the former. BMI was positively and moderately related with all metabolic parameters showing that increase in BMI leads to increase in FBG, TC, TRI, LDL and HbA1c and vice versa. However, a decrease in BMI is associated with a higher HDL.

4.6 Gender differences in Metabolic Profiles after administration of Exercises

The study recorded gender differences in metabolic profiles after the administration of training. Table 4.5 shows the parameters recorded during baseline. Independent samples t-tests were conducted to determine gender differences in metabolic profiles of prediabetes.

Table 4.5 Baseline values of metabolic profiles grouped according to respondents' gender

Variable	Male Mean ± SD	Female Mean ± SD	t-value	p
BMI (Kg/m^2)	28.73±2.69	28.48±2.27	0.29	0.77
FBG (mmol/L)	6.16±0.48	6.14±0.55	0.06	0.95
TC (mg/dL)	209.58±24.53	213.60±24.74	-0.47	0.64
HDL (mg/dL)	44.16±6.91	47.27±11.10	-1.00	0.32
TRI (mg/dL)	137.47±35.95	146.20±28.35	-0.77	0.45
LDL (mg/dL)	138.42±23.99	137.60±29.01	0.09	0.93
HbA1c (%)	5.95±0.25	5.96±0.26	-0.07	0.95

All parameters at baseline were found not to be significantly different between males and females (all had $p > 0.05$). The results showed that the distribution of the factors at the start of the experiment was independent of the gender, suggesting that the randomization process conducted was successful.

Table 4.6 presents the metabolic profiles recorded in male and female participants during the mid-training period. TC and LDL were higher in males than in females whereas HDL and TRI reversely distributed.

Table 4.6 Metabolic profiles segregated according to respondents' gender at mid-training

Variable	Male Mean ± SD	Female Mean ± SD	t-value	p
BMI (Kg/m^2)	28.35±2.79	28.30±2.17	0.04	0.97
FBG (mmol/L)	6.05±0.52	6.05±0.60	0.02	0.98
TC (mg/dL)	207.53±24.83	204.13±23.15	0.41	0.68
HDL (mg/dL)	45.53±6.64	47.40±8.82	-0.71	0.48
TRI (mg/dL)	134.95±33.47	147.27±31.58	-1.09	0.28
LDL (mg/dL)	136.13±23.38	127.12±26.53	1.05	0.30
HbA1c (%)	5.89±0.30	5.89±0.32	0.03	0.97

Independent samples t-tests were run to determine the effect of gender of the levels of the parameters and all were found (Table 4.6) to be non-significant (all had $P>0.05$). The results showed that the response of participants to training was not affected by their gender.

The metabolic profiles recorded in male and female participants during the end of the experiment are presented in Table 4.7. TC and LDL were higher in males than in females whereas FBG, HbA1c, HDL and TRI were slightly higher in females than in males.

Table 4.7 Metabolic profiles segregated according to respondents' gender at post-training

Variable	Male Mean ± SD	Female Mean ± SD	t-value	P
BMI (Kg/m^2)	27.04±2.73	27.57±2.47	-0.59	0.56
FBG (mmol/L)	5.57±0.64	5.73±0.79	-0.66	0.51
TC (mg/dL)	204.11±33.07	199.60±20.66	0.46	0.65
HDL (mg/dL)	47.53±6.09	47.47±7.86	0.02	0.98
TRI (mg/dL)	125.47±22.31	138.93±29.09	-1.53	0.14
LDL (mg/dL)	131.48±34.29	124.25±24.05	0.69	0.49
HbA1c (%)	5.61±0.33	5.65±0.44	-0.27	0.78

Independent samples t-tests were conducted to determine the effect of gender of the levels of the parameters and all tests were found not to be significant (Table 4.7). The results showed that the response of participants to training was not affected by their gender. Overall, gender was found to have no significant influence on the respondent's ability to respond to training regime with respect to metabolic parameters (Figure 4.8).

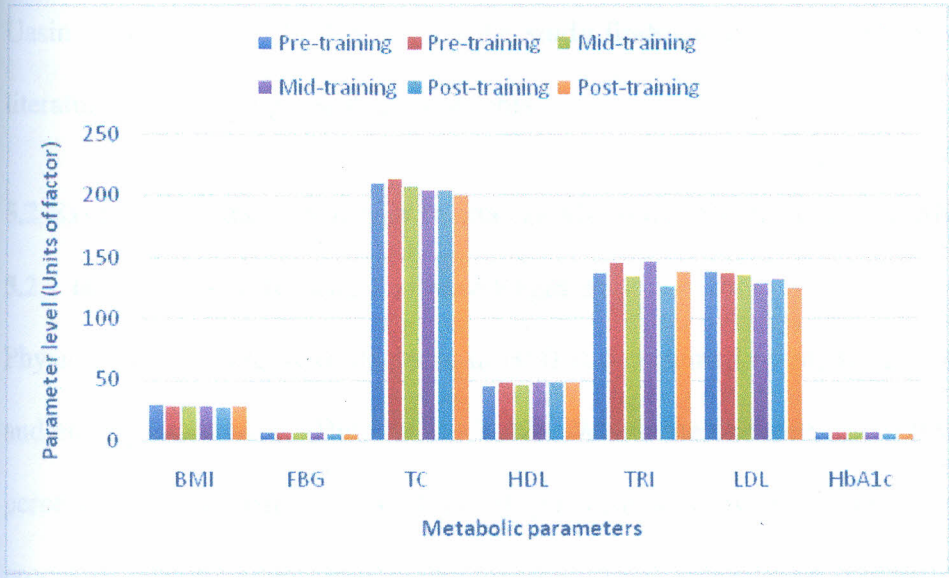

Figure 4.8 Levels of metabolic parameters:
Units of factors: BMI: body mass index (kg/m^2), FBG: fasting blood glucose (mmol/L), TC: total cholesterol, HDL: high-density lipoprotein, TRI: triglycerides, LDL: and low-density lipoprotein (all in mg/dL), HbA1c: glycosylated haemoglobin (%).

CHAPTER FIVE

DISCUSSION OF FINDINGS, CONCLUSION AND RECOMMENDATIONS

5.1 Introduction

The aim of this study was to determine the effects of prescribed physical therapy exercises on FBG, metabolic and HBA1c profiles in prediabetes at Moi Teaching and Referral Hospital in Uasin Gishu County. In this section the study findings are discussed in relation to the relevant literature and known physiologic concepts.

5.2 Exercise Regimen required to change Metabolic Profiles in prediabetes

5.2.1 Body Mass Index and Exercise Regimen

Physiologically increase or decrease in BMI is determined by the balance between energy intake and energy expenditure (Butte et al., 2012). Where there is increase in BMI physiologically it is perceived as an adaptation to lack of physical activity and down regulation of metabolic processes geared towards energy and macronutrients expenditure. On the other hand, a reduction in BMI results from induction of an overall body energy deficit or prevention of a positive energy balance (Westerterp, 2015). Data from the present study revealed that over time BMI levels, substantially decreased in the experimental group compared to the control group. These findings show that prescribed physical therapy exercises have the potential to positively influence body metabolism in obesed prediabetes. It is postulated that the prescribed physical therapy exercise probably induced an energy deficit which most likely arose from the body's ability to increase lipid oxidation above lipid and other nutrients' intake. Studies have reported that regular physical activity induces multiple adaptations within the skeletal muscles and the cardiovascular system all of which provide positive outcomes for the prevention and treatment of

metabolic disorders (Leibel, 2005). In the light of the data presented in this report the prescribed physical therapy exercises in enhancing burning of calories in the study participants probably also induced a more pronounced enhancing effects on the oxidation potential of skeletal muscles. Skeletal muscles are usually more active in metabolism in any exercise since they are involved in moving the body parts. Since this was done regularly over a period of time the exercises produced metabolic adaptations that usually occur in association with fat loss and hence reduced BMI. As a whole these findings confirm that exercise regimen can be used to reduce the body mass index and therefore, prescribed physical therapy exercises can be used as a remedy for obesity and hence prediabetes.

These findings were similar to other findings in a study done by Mora, Lee and Buring, (2008) in the US where lower levels of physical activity and higher levels of BMI were independently associated (P for trend <.001). High BMI showed stronger associations with physical inactivity. Cameroon as well as Aspray et al. (2000) in Tanzania concluded that physical inactivity was associated with obesity, diabetes, and hypertension in the people they studied in urban and rural settings in both Cameroon and Tanzania. A qualitative study in Cameroon also found that the reduced physical activity accompanying sedentary occupations in the cities explained the higher rate of obesity observed in people with these sedentary occupations (Treloar et al., 1999). Steyn et al. (1999) showed an independent association between low levels of physical activity and having diabetes in a poor, peri-urban community near Cape Town.

The study by Boule et al. (2001) in Canada showed that there was no association between physical activity and anthropometry profiles and body fat percent. Besides, a study by Mishra et al. (2006) in Australia also did not find any association between physical activity level and the risk of obesity in terms of body mass index. This might be due to obese individuals being

motivated to increase their physical activity to reduce body weight (Mishra et al., 2006). In the present study, a sedentary lifestyle was associated with low physical activity level ($p<0.05$). Another study on adult Malaysian Nor Shazwani MN, Suzana S, HanisMastura Y, Lim CJ, Teh SC et al. 110 diabetic patients also reported that 52.0% of the patients were not active in their non-leisure time (occupation and housework) (Tan & Magarey, 2008).

In contrast with the above studies, there was no difference in the outcome of body mass index and exercise regimen.

5.2.2 Fasting Blood Glucose and Exercise Regimen

Physiologically with exercise training, a significant recovery is being observed in glucose metabolism in the present study. The results in this study lead to a similar conclusion in a study done by Peyoosha & Rajan (2017) that demonstrated passive static stretching and Resistance exercises being effective treatment in reducing blood sugar levels. High-intensity aerobic exercises have led to the recovery of insulin sensitivity. Because of the benefits on weight management, blood glucose control, and insulin sensitivity on tissues exercise are generally recommended for the treatment of pre- diabetes (Diabetes Prevention Program Research Group, 2002). The prevalence of obesity can be reduced by active lifestylewhich also prevent hyperglycemia and impaired fasting glucose, all of which are significant risk factors in the development of cardiovascular disorders (Boule et al., 2001). Physiological studies have shown that lowering blood glucose through exercise delays the onset and progression of long-term complications of symptomatic cardiovascular disease in diabetes (Erikson et al., 2001). Lifestyle modification through regular physical activity also has a protective effect against the development of diabetes independent of obesity, age, history of hypertension, and parental history of diabetes (Erikson et al., 2001). The study indicated the levels of FBG generally

decreased in the experimental group during both mid-training and post-training period. Therefore this meant that exercise has been proved to be the most effective method of reducing the fasting blood glucose for prediabetes. In this study it was found that fasting blood glucose is significantly decreasing after exercise.

Similar results were found in a study done in Ghana by Nayak, Maiya and Hande (2005), the findings found a mean fall in FBG was 39.4 mg % for the study group and 27.4mg% for the control group and the intergroup fall in FBG was significant (p value <0.05). The fall in FBG was 44.4mg% for the study group and 32.2 mg% for the controls; the inter-group fall in FBG. Another similar study done in Irag by Saihood, Samir and Majeed (2010) revealed that all prediabetic patients had decrease level of fasting blood sugar significantly ($P < 0.001$) in comparison to control after 15 minutes of moderate exercise, with non-significant increase of HR ($P > 0.05$). The controls group showed non-significant ($P > 0.05$) decrease in level of sugar, but they showed significant increase in vital capacity of lungs ($P < 0.001$).

This result is also in agreement with another previous study done in Canada by Minuk et al (2001) who noted that a greater decline of glucose in non-insulin dependent diabetes mellitus (NIDDM) than in non-diabetic subjects during moderate intensity exercise. Exercise increasing glucose uptake by the muscles and enhancing the ability to store glucose. During exercise the level of FBG diminished because muscle contraction stimulate glucose uptake into the muscle even when insulin is absent.

5.2.3 Total Cholesterol, HDL, LDL and exercise regime

Physiologically regular participation in physical activity as well as a single exercise session can positively alter cholesterol metabolism (Durstine& Haskell, 1994). Exercise is involved in increasing the production and action of several enzymes that function to enhance the reverse cholesterol transport system (Durstine& Haskell 1994). The findings is concurred by Huffman, Hawk, Henes, Ocampo, Orenduff, Slentz, Johnson, Houmard, Samsa, Kraus, and Bales (2013) who revealed that exercise had significant effects on LDL-cholesterol particle number, LDL-cholesterol size, HDL-cholesterol, HDL-cholesterol size, and triglycerides. The current study revealed that the levels of Total Cholesterol generally decreased in the experimental group during both mid-training and post-training period relative to pre-training. The results also showed HDL were significantly higher in the experimental than in the control group during post-training (z= -3.20.17, p=0.001). These findings meant that regular exercise is particularly helpful in improving HDL along with the total cholesterol and LDL decrease.

These findings were in agreement to other previous studies also done in Canada, for example Dunn et al. (2007) investigated the effects of a 6-month aerobic exercise training programme, which progressed from 50 to 85 % of maximum aerobic power for 20–60 min three times weekly, and reported significant decreases in total cholesterol (-0.3 mmol/L, p\0.001) and in the total: HDL cholesterol ratio (-0.3, p\0.001). In this case, the intervention period was relatively long and the intensity was relatively high. Mozaffarian, Appel, and Van Horn (2011) supported the findings where they found out that excessive exercising helps in reducing LDL-cholesterol particle number, LDL-cholesterol size, HDL-cholesterol and HDL-cholesterol size.

Participants were allocated to either 6 months in a control group or 8 months in one of three aerobic exercise groups. The three aerobic exercise groups were high-intensity/high-volume

aerobic exercise (jogging for the calorific equivalent of 20 miles/week at an intensity of 65–80 % of the peak aerobic capacity (VO2peak), high-intensity/low-volume aerobic exercise (jogging for the calorific equivalent of 12 miles/week at an intensity of 65–80 % VO2peak) and moderate-intensity/low-volume exercise (walking for the calorific equivalent of 12 miles/week at an intensity of 40–55 %VO2peak). It was reported that the high-intensity/high-volume training combination resulted in the greatest improvements in 10 of 11 lipid variables (LDL cholesterol decreased from 130.1 to 128.2 mg/dL, p\0.05; HDL cholesterol increased from 44.3 to 48.6 mg/dL, p\0.05; triglycerides decreased from 166.9 to 138.5 mg/dL,p\0.05). These data suggest that in relation to aerobic exercise, both total energy expenditure and intensity are factors in lipid reduction.

5.2.4 HbA1c and exercise regime

Physiologically exercise can help lower HbA1C levels over time. Exercise increases the effectiveness of insulin, which results in more glucose entering cells and lower levels in the blood. A study reported in the Sept. 18, 2007, issue of "Annals of Internal Medicine" conducted by lead author Ronald Sigal, M.D., of Canada found that either aerobic exercise or weightlifting or a combination of the two over a 26-week period reduced HbA1c levels on average by 0.6 percent. Since a 1 percent drop in HbA1c levels can reduce heart disease by 15 to 20 percent and vascular complications by 37 percent, according to Dr. Sigal, a 0.6 percent drop can significantly reduce complications of diabetes. The study findings indicated that HbA1c decreased in the experimental group during both mid-training and post-training period compared to pre-training. The decrease in HbA1c in this study is of clinical importance in positively affecting the management of pre-diabetes as well as in reducing the potential for development of

complications from the disease. It is therefore important to interpret the findings that exercise regimen is effective in reducing hemoglobin HbA1c.

Similar findings were seen in Cauza et al, (2012) in China showing a greater improvement in FBG control following 4 months of strength training as opposed to endurance exercise. In the current study the highest correlation was found between FBG and HbA1c (r=0.95) suggesting a high level of concordance between the two parameters. This study results are in consistent with the observations of Solomon et al. (2013) who found that improvements of glycemic control were positively influenced by high pre- training hyperglycemia after a 12 to 16-week aerobic exercise training period in type 2 diabetes patients. A recent meta-analysis done in Spain by Ishiguro et al. (2016) showed that resistance training using high set numbers was the most effective strength training strategy to reduce glycosylated hemoglobin (HbA1c) in prediabetes.

5.2.5 Gender and Exercise Regime

All parameters at baseline were found not to be significantly different between males and females (all had $p > 0.05$). The results showed that the distribution of the factors at the start of the experiment was independent of the gender, suggesting that the randomization process conducted was successful. The results showed that the response of participants to training was not affected by their gender. Overall, gender was found to have no significant influence on the respondent's ability to respond to training regime with respect to metabolic parameters

White, Daneshvari, Lilyquist, Luo, Steffen, Bivin, Gurule, Ducasa, Torres, Lindeman, Sankarappan and Berwick (2015) supported the findings where they found out that offering exercise training it decreases both HbA1cl and FPG levels. It also shows there is no significant effect on gender and ethnicity.

5.3 Conclusion

In conclusion the present study found that:

1. The data provides evidence that there is a significant relationship between physical exercise and metabolic profiles of pre-diabetes.
2. It was concluded that Body Mass Index Fasting Blood Glucose Total Cholesterol, HDL, LDL and HbA1c requires physical exercises and training to have a range of health benefits.
3. Prescribed exercises reduce FBG.
4. Training increases HDL
5. Exercise regime reduces BMI, TC, TRI, LDL levels but after a long time of training.
6. Increase in BMI leads to increase in FBG, TC, TRI, LDL, and HbA1c and the vice versa.
7. These findings are clinically important with regard to diabetes management and delaying the premature onset of complications.

5.3 Recommendations

The study recommends that:

1. Regular screening of metabolic profile should be incorporated in the daily clinical profiles in our health institutions to help pick the abnormalities early for effective prevention measures.

2. Kenyan health sector to develop clinical guidelines for Health practitioners on how to identify and manage patients with prediabetes. These guidelines will help us determine a standardized approach to treating prediabetes and allow us to develop measurable

outcomes to determine if all patients with prediabetes are completing a lifestyle modification program and achieving weight loss, hba1c, and physical activity goals.

3. Develop a registry similar to registries that have been developed for hypertension, diabetes, and asthma for the prediabetes.

4. Develop a low-cost, easily accessible lifestyle management program that would potentially be available for the prediabetes.

5. Exercise should be made part of treatment for the prediabetes.

6. The time is right to develop a proactive approach to prediabetes and for future studies, the author suggests using higher exercise intensities and a longer duration of the study, with nutritional control.

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