Macronutrient intake and their association with risk factors of macro & micro-vascular diseases among Pakistani type 2 diabetic subjects



Meena Iqbal Farooqi Master of Philosophy(m.Phil) Community Nutrition (CN) Session: 2011-2012 Registeration No:

BHS

Department of Commun

Department of Community Nutrition
Bangladesh Institute of Health Sciences (BIHS)

Faculty of Biological Sciences
University of Dhaka

### **DECLARATION**

I hereby humbly declare that the thesis work entitled "Macronutrient intake and their association with risk factors of macro & micro- vascular diseases among Pakistani type 2 diabetic subjects", a requirement for the degree of Master of Philosophy (MPhil) in Community Nutrition (CN) from Bangladesh Institute of Health Sciences (BIHS), under the Faculty of Biological Sciences University of Dhaka, was carried out under the guidance of Prof Liaquat Ali, Professor, Department of Biochemistry and Cell Biology, Bangladesh Institute of Health Sciences (BIHS) and Prof Abdul Basit, Director, Baqai Institute of Diabetology and Endocrinology, Karachi, Pakistan.

No part of the work has been submitted for another degree or qualification in any other institute at home or abroad.

.....

Meena Iqbal (MPhil student) Community Nutrition (CN) (BIHS), Dhaka Registeration No:

#### CERTIFICATE

This is to certify that the thesis entitled "Macronutrient intake and their association with risk factors of macro & micro- vascular diseases among Pakistani type 2 diabetic subjects", is submitted by Meena Iqbal in partial fulfillment of the requirement for the degree of Master of Philosophy (MPhil) in Community Nutrition from Bangladesh Institute of Health Sciences (BIHS), under the Faculty of Biological Sciences University of Dhaka, was carried out under our guidance.

To the best of our knowledge no part of the work has been submitted for another degree or qualification in any other institute.

Supervisors
Prof Liaquat Ali
Bangladesh Institute of Health Sciences (BIHS),
University of Dhaka, Bangladesh
Prof Abdul Basit
Baqai Institute of Diabetology and Endocrinology (BIDE),
Baqai Medical University, Karachi, Pakistan

# University of Dhaka

# Faculty of Biological Sciences

The undersigned certify that they have carefully read and examined the student on this thesis and being satisfied, recommended to Bangladesh Institute of Health Sciences (BIHS), for acceptance of this thesis entitled "Macronutrient intake and their association with risk factors of macro & micro- vascular diseases among Pakistani type 2 diabetic subjects", by Meena Iqbal in partial fulfillment of the requirement for the degree of Master of Philosophy (MPhil) in Community Nutrition for the session 2011-2012.

Board of Examiners
Chairman:
Signature:
Name:
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Member:
Signature:
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Name:
Designation:
Member:
Signature:
Name:
Designation:
Date of approval:

# Dedicated to

My family specially my mother Mrs Feroza Iqbal for their immense support throughout the course

&

To my respected and eminent supervisors Prof Liaquat Ali and Prof Abdul Basit

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## LIST OF ABBREVIATIONS

ADA American Diabetic Association

BIDE Baqai Institute of Diabetology & Endocrinology

BIHS Bangladesh Institute of Health Sciences

BMI Body Mass Index

CHD Coronary Heart Disease

CVD Cardiovascular Diseases

FAO Food and Agricultural Organization

FPG Fasting Plasma Glucose

HDL-C High Density Lipoprotein Cholesterol

IDF International Diabetes Federation

LDL-C Low Density Lipoprotein Cholesterol

NCD Non-communicable Disease

RPG Random Plasma Glucose

SD Standard Deviation

SPSS Statistical Package for Social Sciences

T2DM Type 2 Diabetes Mellitus

WHO World Health Organization

### Abstract

Introduction: Intake of macronutrients by diabetic subjects has major implication on the development of diabetic complications as well as cardiovascular risk in general. The intake may vary substantially among populations depending on environmental, economic and socio-cultural factors. The degree of association of the intake with the above health outcomes may also vary among various population groups. The above issues, which are highly important in designing lifestyle modification programs (as a vital component of diabetes management and prevention) have not yet been adequately investigated among Pakistani population.

Objective: The objective of the present study was to assess the intake levels of carbohydrate, protein and fat among newly registered type 2 diabetic subjects at a tertiary level hospital in Karachi, Pakistan and also to explore the association between the intake and the risk factors of micro- and macrovascular complications among the study subjects.

Material and method: An observational analytical study was conducted on a retrospective cohort. First visit data of 9563 subjects were retrieved from the digital Hospital Management System of the Baqai Institute of Diabetology and Endocrinology (BIDE) in Karachi, Pakistan. In BIDE information related to macronutrient intake is collected following 24-hr recall method. Anthropometric (height and weight) and biochemical (FPG, RPG, HbA1c, lipid profile, and BP) measurements are done following standard protocol. For diagnosis of diabetes 2006 World Health Organization recommendations for the diagnostic criteria for diabetes and intermediate hyperglycaemia was used. Glycemic control using HbA1c was graded using diagnosed using the GRADE criteria. BMI was categorized following the criteria suggested for the Asian population. The criteria used for dyslipidemia was that was suggested by the American Association of Clinical Endocrinologists in 2012 and for blood pressure, guidelines by National

Heart, Lung and Blood Institute (under U.S. Dept. of Health and Human Services) recommendations were followed. Univariate, bivariate and multivariate analyses were done as appropriate.

Result: The mean ( $\pm$ SD) intakes of carbohydrate, protein and fat among the study subjects were found to be 230.6  $\pm$  72.2, 68.1  $\pm$  23.6 and 27.5  $\pm$  26.3 respectively. In relative terms carbohydrate, protein and fat contributed to 65%, 19% and 16% of the calorie intake of these subjects. On group difference analysis daily carbohydrate intake varied significantly (p=0.011) between normal and over-weight groups. However it did not differ much among the various glycemic groups based on FPG, RPG or HbA1c criteria.

Daily mean protein intake was also significantly (p=0.001) higher among the obese and over-weight as compared to normal weight group. However, it did not differ among the various glycemic groups. Daily mean fat intake was not significantly different between any two of the BMI or glycemic groups but it showed significant (p=0.04) association with HbA1c. On correlation analysis BMI showed no significant association with any of the intake levels; however, FPG was found to be significantly (p=0.05) correlated with age, diabetes duration, physical activity and Hba1c was significantly correlated with, fat intake and carbohydrate intake respectively. Remaining parameter of hyperglycemia (RPG) did not show any significant correlation with the intakes.

On group difference analysis various groups of subjects with higher total cholesterol, higher LDL or lower HDL did not show any significant difference in the daily intake of any macronutrients. However, daily protein intake was found to be significantly higher (p<0.001) among hypertriglyceridemic and higher LDL-C group compared to normal group. Total cholesterol showed significant (p<0.001) positive correlation with age and duration of diabetes; triglyceride showed significant correlation (p<0.05) with age, duration of diabetes, carbohydrate intake and protein intake. Serum LDL-C showed similar positive

correlation with age, duration of diabetes and carbohydrate intake. Among total subjects HDL-C was not found to be correlated with any other parameters but among females' HDL-C group it showed significant (p<0.01) association with physical activity but HDL-C groups of men showed higher protein and fat intakes. Macronutrient intake did not differ between hypertensive and normotensive groups and blood pressure did not show any association with the intake levels of any macronutrient. On multivariate analysis (multiple regression) only BMI showed significant positive association with duration of diabetes, carbohydrate intake and protein intake.

Conclusion: The present data leads to the following conclusion:

- The prevalence of macro- and microvascular diseases risk factors are fairly high among the Pakistani diabetic patients who were outside any comprehensive care. Vast majority of them have uncontrolled diabetes, almost fifty percent have overweight, obesity and hypertension, and more than two-third had dyslipidemia.
- The proportion of macronutrient intake among general diabetic subjects in Pakistan substantially differs from the generally recommended proportions applicable for diabetic subjects. In particular, the proportion of carbohydrate as a source total daily calorie is around 20% higher than the usually recommended proportion for diabetic patients.

## 1. INTRODUCTION

# 1.1 Background

Diabetes is a global epidemic (WHO, 2016). According to IDF Diabetes Atlas 2015 the estimate of global prevalence of diabetes is about 339 to 536 million worldwide (; IDF, 2015). World Health Organization's (WHO) global status report on NCD mentioned diabetes caused additional 1.3 million death in 2008. It is projected that 439 million people will have diabetes by 2030 (WHO, 2016). Diabetes and its complications have become a major health problem in South East Asia. There are currently over 132 million people with diabetes in the region(IDF, 2015). World Health Organization 2014 ranks Pakistan at 7th position in diabetes prevalence list (Reporter, 2008). Furthermore, people with diabetes are at risk of developing a number of disabling and life-threatening health problems. Microvascular and macrovascular complications are the main causes for reducing quality of life and premature death (Mir, 2015).

Lifestyle and medical nutrition therapy are considered as the keystones of type 2 diabetes management. The American Diabetes Association has made several recommendations regarding the medical nutrition therapy of diabetes; these emphasize the importance of minimizing macrovascular and microvascular complications in people with diabetes. Many dietary regimens are available for

patients with type 2 diabetes to choose from, according to personal taste and cultural tradition. It is important to provide a tailor-made diet wherever possible in order to maximize the efficacy of the diet on reducing diabetes symptoms and to encourage patient adherence (Khazrai, Defeudis, & Pozzilli, 2014).

Control of blood glucose in an effort to achieve normal or near-normal levels is a primary goal of diabetes management. Dietary carbohydrate is the major determinant of postprandial glucose levels. Low-carbohydrate diets might seem to be a logical approach to lowering blood glucose. Both the quantity and the type or source of carbohydrates found in foods influence glucose levels (Bantle et al., 2008; Khazrai et al., 2014) and the RDA of carbohydrate (130 g/day) is an average minimum requirement for diabetes (IoM, 2005).

The primary goal with respect to dietary fat in individuals with diabetes is to limit saturated fatty acids, trans fatty acids, and cholesterol intakes so as to reduce risk for CVDs. Saturated and trans fatty acids are the principal dietary determinants of plasma LDL cholesterol. Reducing saturated fatty acids may also reduce HDL cholesterol. Importantly, the ratio of LDL cholesterol to HDL cholesterol is not adversely affected, because of a lack of information, it is recommended that the dietary goals for individuals with diabetes be the same as for individuals with preexisting CVDs, since the two groups appear to have

equivalent cardiovascular risk. Thus, saturated fatty acids with <7% of total energy, minimal intake of trans fatty acids, and cholesterol intake <200 mg daily are recommended (Khazrai et al., 2014).

Small, short-term studies in diabetes suggest that diets with protein content with >20% of total energy reduce glucose and insulin concentrations, reduce appetite, and increase satiety (Gannon & Nuttall, 2006; Gannon, Nuttall, Saeed, Jordan, & Hoover, 2003) Glucose produced from ingested protein does not increase plasma glucose concentration but increases serum insulin responses (Franz et al., 2003) (Gannon, Nuttall, Damberg, Gupta, & Nuttall, 2001). Abnormalities in protein metabolism may be caused by insulin deficiency and insulin resistance; however, these are usually corrected with good blood glucose control (Gannon et al., 2003). Although numerous studies have attempted to identify the optimal mix of macronutrients for the diabetic diet, it is unlikely that one such combination of macronutrients exists. The best mix of carbohydrate, protein, and fat appears to vary depending on individual circumstances. For those individuals seeking guidance as to macronutrient distribution in healthy adults, the Dietary Reference Intakes (DRIs) may be helpful (IoM, 2005). It must be clearly recognized that regardless of the macronutrient mix, total caloric appropriate to weight management goals. intake must be Further,

individualization of the macronutrient composition will depend on the metabolic status of the patient (e.g., lipid profile) (Khazrai et al., 2014).

The main aim of diet therapy is to help persons with diabetes in making appropriate changes in their lifestyle both in their diet and exercise habits, which would lead to improved metabolic control. The diet should help reduce symptoms of diabetes by keeping blood sugar, lipids, blood pressure and body weight under control (Cornerstones4Care, 2015) and delay the development of complications.

Inappropriate macronutrient intake can adversely affect the blood glucose level, lipid profile, blood pressure, body fat percentage and composition, and also reduce the level of physical activity which, in turn, leads to or worsen obesity. All these factors are major determinants of increased risk of developing micro- and macrovascular complications. Prevention and control of macrovascular complications (coronary artery disease, peripheral arterial disease and stroke) and microvascular complications (nephropathy, neuropathy and retinopathy) are at the tertiary level in diabetes treatment in order to improve the quality of life of a diabetic patient, which is achieved by improvement of lifestyle and diet.

Pakistanis have always been a food loving nation who have enjoyed rich foods from different cultures of the world for decades; the reason behind such high

prevalence of diabetes and CVDs can be the exposure and food culture. According to FAO, in Pakistan, carbohydrates cover 63% of total dietary intake of an individual on daily basis whereas protein covers only 10% and fats 27% (FAO, 2011). American Diabetes Association, International Diabetes Federation and more such entities have developed dietary guidelines for diabetic patients which need to be followed by diabetic subjects for the prevention of diabetic complications (Amos, McCarty, & Zimmet, 1997).

It is generally accepted that diet modification provides beneficial effects on metabolic parameter, including blood glucose, blood lipids, blood pressure, and body weight (Evert et al., 2013; Thomas & Elliott, 2010) A meta-analysis of prospective studies has demonstrated a 20% reduced risk of future type 2 diabetes through the healthy diets (Esposito et al., 2015). In addition, clinical trials have reported that diet modification including high consumption of fruit and vegetables, caloric restriction, and consumption of lower glycemic index/glycemic load decreases the levels of hemoglobinA1c (HbA1c) of type 1 and 2 diabetes (Franz et al., 1995; Kulkarni et al., 1998). Also, several observational studies have shown that diet modification improves glycemic control (Barclay et al., 2008; Livesey, Taylor, Hulshof, & Howlett, 2008), insulin resistance (Kahleova et al., 2011) and reduces risk of cardiovascular diseases and overall mortality in diabetic patients (He, van Dam, Rimm, Hu, & Qi, 2010).

The Baqai Institute of Diabetology & Endocrinology (BIDE) has been designated as an International Diabetes Federation (IDF) Centre of Diabetes Education for the period 2009-2012. Founded in 1996, the institute has grown from a single room diabetes clinic to a tertiary care centre, providing comprehensive services to diabetic patients. They have developed a software based hospital management system in which they store patient details with their medical record number. Information about 8000 type 2 diabetic patients is available in the BIDE hospital management software. With the help of this system one may get the information on patients' dietary pattern, nutritional status and the history of complications. The data may not be representative of all Pakistani population but those may be considered to be fairly close to it as a big number of diabetic patients from Karachi that represent the masses visiting BIDE.

## 1.2 Justification

Intake of macronutrients (i.e., carbohydrate, protein, and fat) has major implication on the development of diabetic complications. It determines glycemic status and also affects blood pressure, changes lipid status and increases weight and body mass index (BMI). However, to the best of our knowledge, no studies have so far been undertaken to assess the association between the macronutrient intake and the risk factors of developing micro- and macrovascular complications in Pakistani diabetic subjects. The present study was an initiative

to help in understanding the healthy limits of macronutrients according to which diabetic patients should manage their diet so that they can better manage diabetes and avoid the diabetic complications. Dietary habits of a large number of Pakistani diabetic subjects were also known with the status of diabetic complications among them. The data will be helpful for behavior change communication programs and policy making issues. It will, in turn, help in preventing, controlling and reducing the increasing burden of NCDs, which eventually will help in better productivity and improving the economic condition of the nation.

#### 1.3 Research Questions

- 1) What are the intake levels of carbohydrates, proteins and fats among the study subjects?
- 2) What are the proportions and levels of obesity, hyperglycemia, high blood pressure and dyslipidemia among the study subjects?
- 3) Is there any association between the intakes of macronutrients and various risk factors of micro- and macrovascular complications of diabetes?

## 2. OBJECTIVES

# 2.1 General Objective

The general objective of the present study was to explore the association between the macronutrient intake and the risk factors of micro- and macrovascular complications among type 2 diabetic subjects registered at a tertiary level hospital in Karachi, Pakistan

# 2.2 Specific Objectives

The specific objectives of the present study were

- To assess the intake levels of carbohydrates, proteins and fats among the study subjects;
- To investigate the proportions and levels of obesity, hyperglycemia, hypertension and dyslipidemia among the study subjects; and
- To assess the association between the intake of individual macronutrients and various risk factors of micro- and macrovascular complications of diabetes.

#### 3. LITERATURE REVIEW

Following reviews focus its attention on macronutrient intake and their association with risk factors of microvascular and macrovascular complications among type II diabetes subjects.

#### 3.1 An Overview of Diabetes

Diabetes mellitus in bio-medical science is generally regarded as an endocrine disease resulting from a deficiency or absence of insulin, or insulin resistance, characterized by hyperglycemia and possible long-term complications (H. Canada, 2013). Type 2 diabetes mellitus (T2DM) is characterized by hyperglycemia resulting from a deficiency of insulin. As a result of this, the level of glucose in the blood becomes elevated and results in a condition commonly known as high blood sugar where the body makes insulin but cannot use it effectively (nine out of ten people with diabetes have type 2 diabetes) (P. H. A. Canada, 2011).

It has been recognized that Type 2 diabetes is caused by a combination of multiple, interlinked and complex risk factors. In bio-medical science, risk factors for this health complication have been largely classified into modifiable and non-modifiable risk factors. Modifiable risk factors are those that can be controlled to reduce risk of developing Type 2 diabetes. These include lack of physical activity,

unhealthy weight, unhealthy diet and smoking. Non-modifiable risk factors are those that cannot be reduced or acted upon, such as age, genetic predisposition, ethnicity, family history, etc (Millar & Dean, 2012). A review based study by Ghosh and Gomes (Hanley, Harris, et al., 2005) classified socio-economic and political marginalization, legacy of colonization, access to health care, etc. as intermediate risk factors of Type 2 diabetes, particularly for Aboriginal Peoples; these factors are modifiable to some extent. They also developed an etiologybased classification of 'direct' and 'indirect' risk factors of Type 2 diabetes, which focuses on psychosocial imbalances, hereditary predisposition, physiological disturbances, etc. The common comorbidities and complications of Type 2 diabetes include macrovascular diseases like CVDs and stroke, and microvascular diseases like nephropathy, neuropathy and retinopathy resulting in end-organ damage to the kidneys, eyes, peripheral nerves, and heart. It is well elaborated in the literature that Type 2 diabetes is a multifactorial disease. Thus, adopting a holistic approach is needed to address the multiple and complex risk factors to prevent and alleviate Type 2 diabetes and its complications.

Diabetes is emerging as a particular concern in Asia, where more than 110 million individuals were living with diabetes in 2007, a large proportion of whom were young and middle aged. Asians tend to develop diabetes at a relatively young age and low BMI, and by 2025 the number of individuals with diabetes in

the region is expected to rise to almost 180 million, of which approximately 70 million will be in India and almost 60 million in China. The reasons for this increased risk are still being fully elucidated; however, "normal weight" Asians often exhibit features of abdominal or central obesity, which is particularly detrimental to insulin resistance and glucose metabolism. Moreover, the increased risk of gestational diabetes combined with exposure to poor nutrition in utero and overnutrition in later life may contribute to increased diabetes, resulting in a situation of "diabetes begetting diabetes" (J. C. Chan et al., 2009).

There is an increased prevalence of Type 2 diabetes in Pakistan and main risk factors identified were obesity, overweight, family history of diabetes mellitus, and hypertension.87 A community based study showed that The proportion of diabetes was more among those who had family history of diabetes (8.6%), BMI more than 25 (24.1%) and those with sedentary lifestyle (10.4%) (Burke, Williams, Haffner, Villalpando, & Stern, 2001).

#### 3.2 Prevalence of Diabetes Mellitus Worldwide

According to IDF in 2015 there were 415 million people with diabetes worldwide and by 2045 this number will increase to 642 million if it keeps increasing at the assumed pace. In 2015 five million adult died with diabetes (IDF, 2015). Looking at the regional data it can be seen that the number of diabetic people have

raised and it will be more than double by 2040 if present day lifestyle is not improved. In 2015 44.3 million people had diabetes in North America and it will rise to 60.5 million by 2040, in South and Central America from 29.6 to 48.8 million, in Europe from 59.8 to 71.1 million, in Africa 14.2 in 2015 to 34.2 million in 2040, in Middle East and North Africa from 35.4 to 72.1 million, in South East Asia from 78.5 to 140.2 million and in western Pacific from 153.2 million to 214.8 million respectively(IDF, 2015). The increase in diabetes mellitus in the developing world has been attributable to urbanization, urban residence, acculturation, abdominal obesity, globalization, westernization, sedentary lifestyle, behavioural habits, systemic arterial hypertension, physical inactivity, low intake of fruits and vegetables, high intake of animal fat and protein, industrialization, health transition, lifestyle changes, and the adoption of western lifestyle (Azevedo & Alla, 2008).

# 3.3 Burden of Diabetes Mellitus in Developing Countries

There is increased number of people suffering from non communicable diseases and this have been linked to unhealthy ways of living and lifestyle such as consumption of excess calories and reduction in the level of physical activities with the consequent development of obesity and insulin resistance (Ogbera & Ekpebegh, 2014). Obesity, type 2 diabetes mellitus, and their associated long-term complications are emerging as critical, worldwide public health problems.

Although few groups have been spared increased in the burden of these conditions, those undergoing rapid westernization, with the transition in diet and activity profiles have been especially affected. Among the most affected groups are those in Africa and the African Diaspora including the Caribbean, Europe, and North America (Gucciardi, Wang, DeMelo, Amaral, & Stewart, 2008). The probable cause of obesity in developing countries has been attributed to the current lifestyle, where urbanization, better economic development and an increase in income have resulted in diet changes and less physical activity. The care for diabetic patients includes a change in their life style, where the diet plan represents an important pillar of care so they can meet their goals. Obesity increases the risk of developing not only type 2 diabetes, cardiovascular disease, stroke, osteoarthritis and some forms of cancer (Evaristo-Neto, Foss-Freitas, & Foss, 2010). Obesity has been clearly linked with diabetic patients from all the major ethnic regions (Ogbera & Ekpebegh, 2014). Over the past century, diabetes was considered a rare medical condition. However epidemiological studies carried out in the 90's have provided evidence of a different picture (Gavin, Stolar, Freeman, & Spellman, 2010). The number of people with diabetes is increasing due to population growth, aging, diet, lifestyle, urbanization, and increased prevalence of obesity and physical activity (Zafar et al., 2011). Diet and lifestyle are the biggest culprits at least in the case of type 2 diabetes but

genetics also have a role to play. Although obesity is an important factor in the diabetes epidemic, it does not alone explain the vast increase in prevalence especially in the developing world (WHO, 1997).

### 3.4 Risk Factors of Diabetes Mellitus

The study was carried out to identify the contribution of risk factors to the susceptibility to T2DM among the people of Jammu region of Jammu and Kashmir state in North India. For this, a total of 250 diabetic patients (140 male, 110 female) and 150 non- diabetic controls (90 male, 60 female) were recruited from Jammu. A general health questionnaire was used to collect information about age, sex, onset of diabetes, smoking, alcohol intake, diet pattern, physical activity, household information and family history of diabetes. The mean BMI value did not vary among diabetic and non-diabetic subjects (25.91±3.82 vs.24.91± 3.65; P=.011) but male diabetics have higher BMI as compared to females. Diabetic complications are higher in T2DM subjects than in Control population (28 percent CHD, 32 percent Hypertension, 40 percent Ocular Problem). It is concluded that the Jammu population in North India is at a higher risk of developing diabetes and its related complications (Metcalf, Scragg, Tukuitonga, & Dryson, 1998).

Another cross-sectional study was carried out to estimate the prevalence of type 2 diabetes mellitus and its' risk factors in an urbanizing rural community of Bangladesh. The study population was lean with mean body mass index (BMI) of 20.48. The total prevalence of type 2 diabetes was 8.5%, men showed higher prevalence (9.4%) compare to women (8.0%). Increasing age and higher BMI

were found to be significant risk factors following both FBG and OGTT. The study has shown that prevalence of diabetes has increased in the populations who are in transitional stage of urbanization, and may indicate an epidemiological transition due to fast expanding urbanization (Bell et al., 2001).

The report of World Health Organization (WHO) shows that India tops the world with largest number of diabetic subjects. This increase is attributed to the rapid epidemiological transition accompanied by urbanization and changes in the life style, which is occurring in India. A cross-sectional descriptive study was conducted in the Department of Biochemistry of Calcutta National Medical College among the patients who were doing first time blood examination for diagnosis of diabetes. Prevalence of diabetes was more (63.6%) among those who had BMI (Body Mass Index) 25 or more, where as the proportion of diabetes was less among the persons having BMI less than 18.5. This association was found to be statistically significant. Prevalence of diabetes was also high among persons consuming tobacco (34.5%) and animal protein (51.5%). Lifestyle modifications, reduction of body weight, increasing physical activity are some of the important primary preventive measures to halt the upward trend of diabetes epidemic in India (Linhart et al., 2016).

Results from large, prospective studies suggest that the metabolic syndrome is an important risk factor for CHD and type 2 DM, and it increases cardiovascular

and total mortality (Grundy, 2006). A 12-year follow-up data of 2682 middleaged Finish men showed that death from cardiovascular disease was 2.9-4.2 times more likely among men with metabolic syndrome than those without metabolic syndrome at start of study (Lakka et al., 2002). Since detecting subjects at risk of future disease and implementing programs to reduce the risk of progression to disease is a fundamental objective of preventive medicine, the metabolic syndrome can be used as a predictor to identify subjects at high risk of developing CVD and diabetes. The dysglycemia of type 2 diabetes coexists with other metabolic abnormalities such as obesity, dyslipidemia, and hypertension, leading one to postulate that the increased CVD risk in subjects with prediabetes may be largely due to the coexistence of other metabolic syndrome components (Eckel, Grundy, & Zimmet, 2005). Several studies have shown that the metabolic syndrome predicted T2DM independent of other factors (Hanley, Karter, et al., 2005). Lorenzo et al. showed that the odds ratio (OR) using different definitions of the metabolic syndrome (ATP III [OR 2.00], IDF [OR1.69]), and the World Health Organization (WHO) [OR 1.73]) were almost similar in predicting incident CHD independent of age, sex, ethnic origin, history of CHD and T2DM, non-HDL-C, smoking status, and family history of myocardial infarction (Lorenzo, Williams, Hunt, & Haffner, 2007). Subjects free from CHD and/or CHD risk equivalents, when evaluated with ATP III, IDF, and WHO definitions, were also shown to

have similar ORs for predicting CHD. Although some studies have shown that conventional risk factors may also predict T2DM or CHD, it appears that the metabolic syndrome adds to the prediction provided by individual components (Forouhi, Sattar, Tillin, McKeigue, & Chaturvedi, 2006). A study showed strong association of the metabolic syndrome with diabetes (RR, 7.47) in South Asians, however, with CHD it was less strong (RR, 1.27) (Sattar et al., 2008). Forouhi et al. showed higher cardiovascular risk in South Asians compared to white Caucasians (Forouhi et al., 2006). The awareness of ethnicity as a potential independent risk factor for chronic disease has clinical importance because lower thresholds would have to be considered when planning primary prevention strategies in certain populations.

# 3.5 Micro- and Macrovascular Complications of Diabetes

Diabetes mellitus is a chronic disease with a long-term macrovascular and microvascular complications including diabetic nephropathy, neuropathy and retinopathy (Kyari et al., 2014). Macrovascular complications such as stroke, heart disease, peripheral vascular disease and foot problems.

# 3.5.1 Neuropathy, Nephropathy and Retinopathy

Miocrovascular complications are diabetic eye diseases (retinopathy and cataracts), renal disease, erectile dysfunction, and peripheral neuropathy (Olatunbosun, Ojo, Fineberg, & Bella, 1998). From various African studies,

clinical diabetic nephropathy in Sudan 11.6% (Buowari, 2013), 19% in 1971 in Nigeria (Burgess et al., 2013), 46% in Kenya (Harper, 2004) and 6% in Ethiopia (Diabetescouk, 2016). The exact cause of diabetic induced complications are not fully understood, the underlying factor that appears to make those with diabetes more prone to many health problems is prolonged and frequently elevation of blood sugar (Nwafor & Owhoji, 2001). Diabetes mellitus is a complex metabolic disease that can have devastating effects on multiple organs in the body. It is the leading cause of end stage renal disease in the United States of America and is a common cause of vision loss, neuropathy, and cardiovascular diseases (McKinleyHealthCenter, 2014). One of the most potentially serious complications regards neuropathy is when it is most severe can lead to amputation (Diabetescouk, 2016). The effects of diabetes mellitus include long-term damage, dysfunction, and failure of various organs including the kidneys. The prevalence of clinical nephropathy has been reported to be between 15 % and 40% generally in the developed countries (Nwafor & Owhoji, 2001).

# 3.5.2 Peripheral Vascular Disease

Peripheral vascular disease lead to a condition called diabetic foot, a macrovascular complication, in which due to numbness the diabetic patients cannot feel a wound in their foot getting severe. In some cases amputation is left to be the last possible treatment. This condition results in a large increase in

the use of general practice care and in the use of medical specialist care and hospital care (WoundsInternational, 2016) This is the case in developing countries where most of the populace are poor and do not have access to quality medical care. Amputation is the removal of a body extremity by trauma or surgery. As a surgical measure, it is used to control pain or a disease process in the affected limb such as malignancy or gangrene. Some diabetic foot ulcer patients shy away from attending the hospital for fear of amputation and eventually some of them die due to infections (Olatunbosun et al., 1998).

#### 3.5.3 Cardiovascular Diseases

Around the world, diabetes is growing increasingly common and is a significant contributor to CVD risk. People with diabetes have a more than two-fold greater risk of fatal and nonfatal CVD compared to non-diabetics, with some indication that diabetes mellitus may confer an equivalent risk of having had a cardiovascular event (Holman, Paul, Bethel, Matthews, & Neil, 2008). In fact, CVD is the leading cause of morbidity and mortality in people with diabetes (Kelly et al., 2009).

The magnitude of the risk of CVD associated with diabetes is even greater in women and younger individuals. Indeed, there is substantial evidence that diabetes mellitus may erase, or substantially attenuate, the "female advantage"

in the risk of CVD observed in non-diabetics, and that having diabetes may be equivalent to aging by at least 15 years with regard to the clinical manifestations of CVD.

Proximal risks for CVD include those associated with consumption patterns (mainly linked to diets, tobacco and alcohol use), activity patterns, and health service use as well as biological risk factors such as increased cholesterol, blood pressure, blood glucose, and clinical disease. The Framingham Study first centered attention on the concept of "risk factors" associated with CVD, and most recently reported substantial 30-year risk data showing the accumulation of risk over time (Lee et al., 2013). Importantly, risk factors for the incidence of CVD and those associated with CVD severity or mortality are not synonymous. Risk factors for incidence become important starting very early in life and accumulate with behavioral, social, and economic factors over the life course to culminate in biological risks for CVD such as increased cholesterol, blood pressure, blood glucose, and clinical disease. Over the past few decades, the effectiveness of early screening and long-term treatment for biological risks or early disease has contributed to the sharp declines in CVD mortality seen in many countries (Danaei, Lawes, Vander Hoorn, Murray, & Ezzati, 2006). It is for this reason that it is essential to control the risk factors including high plasma glucose.

Relatively few major behavioral and biological risk factors account for CVD incidence around the world. Tobacco use, diet (including alcohol, total calorie intake, and specific nutrients) and physical inactivity serve as the three major behavioral risks. Between them, they account for a significant proportion of cancer, diabetes, and chronic respiratory disease incidence in addition to CVD (Karppanen & Mervaala, 2006). Concerted action focused on these behavioral risks, along with biological risks such as high blood pressure, high blood lipids, and high blood glucose, would have a wide impact on the global incidence and burden of disease. High blood pressure, tobacco use, elevated blood glucose, physical inactivity, and overweight and obesity are the five leading factors globally. In middle income countries, alcohol replaces high blood glucose in the top five; in low income countries, a lack of safe water, unsafe sex, and undernutrition are important. These latter points are discussed further in this report in relation to both the role of early childhood nutrition in the later onset of CVD as well as the need to integrate the management of HIV/AIDS more closely with CVD in low income countries (Iqbal et al., 2008).

- 3.6 Risk Factors of Diabetic Complications
- 3.6.1 Overweight and Obesity

Obesity has been identified as the single most important risk factor for Type 2 diabetes complications. The WHO estimated that there were 1.9 billion people who were overweight and over 600 million obese in 2014 (WHO, 2015). Longitudinal studies have shown obesity to be a powerful predictor for type 2 diabetes and its complications (J. M. Chan, Rimm, Colditz, Stampfer, & Willett, 1994). This is further strengthen by the fact that interventions aimed at reducing obesity also reduce the incidence of Type 2 diabetic complications. The average BMI value in South Asians is lower than seen in white Caucasians, Mexican-Americans, and blacks, but unfortunately South Asians have a higher percentage of body fat compared to white Caucasians and blacks at this lower BMI values (Cleland & Sattar, 2005). Because of this increased cardiovascular risk among Asian people occurring at lower waist circumference compared to European populations, both the WHO and the IDF have adopted the definition of overweight and obesity in Asians at a BMI of 23 kg/m2 or above and 25 kg/m2 or above, respectively, while central obesity is defined as a waist circumference of 90 cm or above in men and 80 cm or above in women (Misra & Khurana, 2008).

### 3.6.2 Blood Lipids

Researchers have studied the role of blood lipids in the development of atherosclerosis and the increase of CVD risk for decades. The Framingham Study

first demonstrated the link between hypercholesterolemia and increased risk of CVD in the 1960s with the finding that lower levels of high-density lipoprotein (HDL) cholesterol as well as elevated levels of low-density lipoprotein (LDL) cholesterol were associated with increased CVD risk (Misra & Khurana, 2008). Subsequent studies confirmed these results and further established that elevated triglycerides also increase CVD risk (Kengne et al., 2009). Furthermore, randomized controlled trials have shown that reduction of LDL cholesterol, both in primary and secondary prevention, is associated with reduced coronary event rates (Huxley, Barzi, & Woodward, 2006). Reductions in LDL cholesterol have also been associated with a lowered incidence of stroke, although the data are not as strong as for CHD (J. C. Chan et al., 2009). The INTERHEART study recently confirmed that there was a graded relationship between abnormal lipid levels and risk for CHD in all regions of the world. In fact, the INTERHEART study found that abnormal blood lipids were the most important risk factor for myocardial infarction by odds ratio in all global regions (Nathan et al., 2005).

#### 3.6.3 Blood Glucose

The balance of risks and benefits associated with intensive glucose control has been assessed in recent clinical trials, which have convincingly demonstrated beneficial microvascular outcomes of diabetes. By contrast, these trials have individually failed to show such an effect on cardiovascular outcomes. However, the extension of the follow-up of the Diabetes Control and Complications Trial in type 1 diabetes (Nathan et al., 2005) and the United Kingdom Prospective Diabetes Study in type 2 diabetes (Holman et al., 2008) have shown that intensive glucose control substantially lowered the risk of cardiovascular outcomes, suggesting a legacy effect with still unexplained underlying mechanisms. Recently conducted meta-analyses of relevant trials in people with type 2 diabetes have also consistently shown that intensive glucose control reduces the risk of major cardiovascular events by approximately 10 percent, primarily driven by a 10 to 15 percent reduction in the risk of CHD, compared with standard treatment in people with diabetes (Kelly et al., 2009).

### 3.6.4 Blood Pressure

A recent review of the global burden of high blood pressure found that approximately 54 percent of stroke, 47 percent of IHD, 75 percent of hypertensive disease, and 25 percent of other CVDs were attributable to hypertension. This equates to an annual burden of approximately 7.6 million deaths, or 13.5 percent of the total number of annual global deaths, attributable to high blood pressure. Furthermore, Lawes et al. (2008) found that more than 80 percent of the attributable burden of hypertension in 2001 occurred in low and middle income countries, and both another recent review and an analysis commissioned for this report found the prevalence of hypertension to be equally high in developed and developing countries (Gaziano, Reddy, Paccaud, Horton, & Chaturvedi, 2006). In Sub-Saharan Africa, hypertension is a predominant driver of CVD. Hypertensive heart disease and stroke, rather than ischemic heart disease, account for the majority of the CVD burden in the region, especially among black Africans (Mayosi et al., 2009).

## 3.7 Behavioral Habit Affecting Diabetic Complications

Lifestyle has major effect on the management of diabetes and aggravation of its complications. Lifestyle encompasses mainly two areas that are dietary habits and physical activity. Improper dietary habits and lack of physical activity or excess of sedentary lifestyle can elevate the risk factors and eventually initiate the complications.

## 3.7.1 Dietary Patterns and Risk Factors of Diabetes Complications

The main aim of diet therapy is to help persons with diabetes in making appropriate changes in their lifestyle both in their diet and exercise habits, which would lead to improved metabolic control. The diet should help reduce symptoms of diabetes by keeping blood sugar, lipids, blood pressure and body weight under control (Cornerstones4Care, 2015) and delay the development of complications. On looking at a detailed example from Fijian population we see the dietary patterns of indigenous Fijians are changing rapidly. Dietary relationships in regard to the prevalence of diabetes are poorly studied but a survey was conducted to show the relationship of dietary patterns and other lifestyle factors for the development of diabetes among urban indigenous women in Fiji. The results showed high rates of obesity manifested in high percentage body fat, high body mass index (BMI) and high waist and hip ratio (WHR). The mean 24 h dietary intake exhibited a moderate intake of protein, high intake of

fat and a low intake of carbohydrate. The carbohydrate reduction was a result from the decline in consumption of traditional staples. Consumption of cereals and related products favored the high intake of butter and margarine and also encouraged the use of cooking oil in frying varieties of flour products. The daily intake of anti-oxidant vitamins of -carotene and vitamin E were low, however there was a high intake of vitamin C. The food frequency study revealed cassava, bread and sugar were consumed daily as the main carbohydrate foods. Fish and meat were the most frequently consumed protein foods. The main beverage was sweet tea with whole-cream milk. Butter, margarine, coconut cream, cheap lamb flaps and cooking oil provided the main sources of fat. Levels of physical activity included high sedentary lifestyles with a high rate of subjects being overweight and obese. Ceremonial dietary customs showed a high consumption of meat and fish. Fruits were rarely consumed. Glycosuria existed among the age group under study. The impact of dietary transition, coupled with dietary excesses and physical inactivity, seem to be potential risk factors of diabetes among the indigenous women in the urban area (Lako & Nguyen, 2001).

Excess energy intake is one of the key contributors to obesity. Lack of data in developing countries limits policy makers' abilities to focus attention on which dietary components lend themselves to effective interventions that would reduce total calorie intake. In those countries that do have data, the collection methods

vary so direct comparisons are not possible; however, a review of the data does indicate that the dietary contributors to total energy intake vary by country. National surveys of calorie intake from India indicate that in urban areas, cereals account for 56 percent of intake, compared to about 9 percent each for edible oils and dairy, 1 percent for meat and fish, and 0.4 percent for all beverages. In China, cereals also dominate and account for 58 percent of total calorie intake compared to meat (13 percent) and cooking oils (17 percent) (Chatterjee, Rae, & Ray, 2007).

In some developing countries, consumption of sugar-sweetened beverages has increased dramatically in recent decades. In Mexico, for example, it is estimated that adolescents consume more than 20 percent of their total energy intake from caloric beverages (Barquera et al., 2008). Because of its excess caloric and sugar content, increasing consumption of sugar-sweetened beverages may have important implications for obesity and cardiometabolic risk. Maintaining the relatively low per capita consumption of sugar-sweetened beverages in countries like India and China is a potential target of prevention programs. In India, all beverages account for less than 0.5 percent of total calories. The equivalent figure in the United Kingdom is about 16 percent for all beverages for young adult men between 19 and 24 years of age with sweetened soft drinks accounting for about a third and alcohol the remainder (Pot et al., 2012).

Diabetes and its complications have become a major cause of morbidity and mortality in Korea (Lim, Ha, & Song, 2014) of which the prevalence has increased from 8.6% in 2001 to 10.5% in 2012 (Kweon et al., 2014). The increased prevalence is likely attributable to economic development, and a westernized lifestyle (Kim, 2011). The goals of management of diabetes are to restore glucose metabolism and to minimize chronic diabetic complications. Among the management of diabetes in order to achieve the goals, dietary therapy has been high-lightened ranging from nutritional balancing to ambulatory diet care (Burger et al., 2012; Hu, Block, Sternfeld, & Sowers, 2009; Khazrai et al., 2014). Despite the beneficial effects of diet modification in diabetes, it has been challenged because of lack of dietary compliance in general practice (Vijan et al., 2005; Williamson, Hunt, Pope, & Tolman, 2000). Indeed, lack of dietary compliance was considered as a major limiting factor in achieving glycemic control in type 2 diabetes in clinical settings (Al-Kaabi et al., 2008). Also, lack of knowledge and understanding of the diet plan was reported to be the highest ranked barrier in the diabetic patients with diet consultation by a nutritionist (Nagelkerk, Reick, & Meengs, 2006). Since dietary recommendations often require diabetic patients to alter behaviors that have been present for a lifetime, and are based upon strong preferences (Story, Anderson, Chen, Karounos, & Jefferson, 1985), it can greatly impair their quality of life which is associated with the discontinuation of therapy

(Story et al., 1985). Earlier studies have focused on the prevention of complications and glycemic control of diabetes through diet modification, however, there is limited information on the associations with dietary behavior (Bantle et al., 2008; Brand-Miller, Hayne, Petocz, & Colagiuri, 2003) and nutrient adequacy in Korean diabetic patients and the patients' views of the burden of self-management and life satisfaction due to diet modification in this population (Cho, Shin, & Chung, 2014).

## 3.7.2 Physical Activity and Sedentary Lifestyle

Physical activity has decreased over recent decades in many populations, and this is a major contributor to the current global rise of obesity. Physical inactivity has been found to be an independent predictor of Type 2 diabetes in both cross-sectional and longitudinal studies (Hayes et al., 2002). Unfortunately South Asians have been found to be more sedentary compared to other ethnic groups (Ghosh, 2014). Increasing sedentary lifestyle is attributed to increased mechanization at workplaces and in household work. Leisure-time activities have also shifted from outdoor play to indoor entertainment such as television and computer games. Previously adolescents playing outdoor games regularly and doing household activities had lower prevalence of being overweight, compared to 3 times higher in those not participating in outdoor games (Dinsa, Goryakin,

Fumagalli, & Suhrcke, 2012). Even for equivalent degrees of obesity, more physically active subjects have a lower incidence of diabetes.

Although the "thrifty genotype" and "thrifty phenotype" hypotheses differ, they both involve a genetic susceptibility to "Western" diet and lifestyle, which is strongly associated with an increased risk of developing diabetes, both for Pacific people and for others. Due to rapid changes in lifestyle, risk factors such as obesity, diets and physical inactivity have become widespread throughout the region. This is particularly evident in the populations with the greatest social and economic changes. Pacific populations have been reported to be among the most obese populations in the world(Metcalf et al., 1998), and Bell found a higher prevalence of obesity among Pacific people living in New Zealand than in native Hawaiians or Pima Indians, with women having a higher prevalence than men(Bell et al., 2001). Bell's findings were consistent with those from previous New Zealand studies, which found that Pacific people were less involved in leisure-time activities than Maori or Caucasians with women being less active than men among Pacific Islanders. Likewise, Taylor et al reported obesity, a diet high in calorie and animal fat, decreased exercise, smoking and stress to be endemic in Pacific people (Linhart et al., 2016).

A house-to-house inquiry for patients with known diabetes was carried out in Tirupati, a town in Andhra Pradesh. 220 diabetic patients were inquired for a

detailed questionnaire regarding the type of diabetes, life style including diet, habits, heredity and exercise. Regarding life style and habit, 45 (24.5%) of the Type II patients have regular habit of both smoking and alcoholic, where 15 (8%) of the type II were either smokers or alcoholics alone. Among the total diabetic patients inquired, 92% of them were unaware about the role of other factors like smoking, alcohol, diet and exercise associated with diabetes. The study highlights a high prevalence of known type II diabetes in developing urban areas like Tirupati and these data are very important in area with most diabetic prevalence. Proper diet, life style and exercise in controlling the prevalence of diabetes must be incorporated into health services (Prasad, Kabir, Dash, & Das, 2012).

There is an increased prevalence of Type 2 diabetes in Pakistan and main risk factors identified were obesity, overweight, family history of diabetes mellitus, and hypertension (Zafar et al., 2011). A community based study showed that The proportion of diabetics was more among those who had family history of diabetes (8.6%), BMI more than 25 (24.1%) and those with sedentary lifestyle (10.4%) (Khatib, Quazi, Gaidhane, Waghmare, & Goyal, 2008).

#### 4. SUBJECTS AND METHODS

## 4.1: Study design

This was an observational analytical study based on a retrospective cohort.

## 4.2: Study area

The study was conducted at Baqai Institute of Diabetology & Endocrinology (BIDE). Baqai Institute of Diabetology & Endocrinology (BIDE) came into existence in the year 1996. It started as a single room diabetic clinic but with the untiring efforts of Prof Abdul Basit, it gradually developed into a tertiary care centre. It is now providing comprehensive services under one roof. They are pioneers in the following areas:

- First diabetes clinic with multidisciplinary approach since 1996:
  - Diabetologist
  - Dietitian
  - Educator
  - Associate diabetologist
  - Foot care assistant
- First 24hours diabetes education helpline service.
- All diabetes services available under one roof.
- J System specially designed to save multiple patient visits.
- Primary prevention of diabetes for generation.
- Full & comprehensive screening for complications in a single visit.

BIDE is situated at a middle class locality in Karachi. Most of the patients at BIDE belong to the middle class strata.

## 4.3: Study population and target population

Selected Type 2 diabetic subjects at BIDE. Data of first the visit of patients that had dietary data available were the target population.

## 4.4: Study period

2014-2015

## 4.5: Sample population

All diabetic patients registered at BIDE from 2006 to 2014 were chosen

#### **Inclusion Criteria**

• Data of first visit of each patient that have dietary data available.

## 4.6: Data collection technique

Retrieval of data from the database (Hospital Management System) was done.

# 4.7: Data collection procedure

Data were retrieved from the Hospital Management System at BIDE. There was a total of 50,000 data among which around 35,000 were diabetes subject. Among

these subjects, 9563 had dietary data of their first visit available because the Diet and Education department at BIDE was inaugurated in 2006. The data was retrieved from the software Hospital Management System at BIDE. Patients' data is collected at different stages during their visit. The doctors, dietitians, diabetes educators and nurses have access to the HMS through their individual identities. They enter the new data and check the previous status of the patients to compare their condition. The data after its entry is managed by the IT department. I requested the IT department for providing me the data of all variables. It was found that BIDE does not collect certain variables for this reason some variables were omitted from the study. After some negotiations final data was given to me and the analysis were performed.

## 4.8: Data management and analysis

Data were compiled, edited and checked to maintain consistency using MS Excel. Repetition and omission of data was corrected before coding. Recorded data was then, exported to SPSS V.21.0 for further analysis. Descriptive and inferential statistics were used to present data. p-value less than or equal to 0.05 was considered statistically significant for most analysis. In some cases p-value of 0.01 was also used.

# 4.9: List of variables

Total	intake per day in grams &				
Calor	ies	Beha	vioral var	iables	
J	Carbohydrate	J	Smoking	Habit	
J	Proteins	J	Drinking I		
J	Fats	Demo	ographic I	Data	
Anth	ropometric variables	J	Gender		
J	Weight	J	Age		
J	Height	J	Occupation	on	
J	BMI	J	Marital St	atus	
Bioch	nemical Variables	Dura	tion	of	Diabetes
J	Fasting plasma glucose				
J	Random plasma glucose				
J	HbA1c				
J	Lipid Profile				
Clinic	cal Variables				
J	Rlood Pressure				

## 4.10: Conceptual Framework

Dietary Intake:

Total Carbohydrate

Intake /day (gm)

**Total Protein** 

Intake /day (gm)

**Total Fat** 

Intake /day (gm)



### Risk Factors:

- Dbesity (BMI)
- Hyperglycemia(FPG, RPG, HbA1c)
- Dyslipidemia (lipid profile)
- High BloodPressure (blood pressure)



### Confounders:

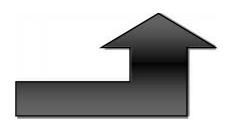
Socio-demographic variables

- ✓ Age
- ✓ Gender
- ✓ Occupation
- ✓ Marital status

Behavioral variables:

- ✓ Smoking
- ✓ Drinking

Duration of diabetes



## 5. RESULTS

Table 1 shows that male and female distribution was 53.7% and 46.3%. Mean age was  $51\pm10.9$  years. 42.9% were Housewives and 42.4% were employed. More than 90% were married.

Table 1: Characteristics of the study subjects (n=9563)

Variables	Number	Percentage
Sex		
Male	5131	53.7
Female	4432	46.3
Age in years		
<35	813	8.5
35 to 55	4958	51.8
>55	3792	39.7
Mean ± SD	51 ±	± 10.9
Occupation		
Housewife	4106	42.9
Unemployed	1104	11.6
Student	47	0.5
Employed	4055	42.4
Data Missing	251	2.7
Marital status		
Married	8771	91.7
Unmarried	442	4.6
Widow	189	2.0
Data Missing	161	1.7

Table 2 reveals that 69.4% subjects were moderately compliant, 8.7% had good compliance and 21.9% had poor compliance. More than half (60.2%) of the patients led sedentary life followed by lightly active (33.1%), moderately active (6.4%) and very active (0.3%). Almost three forth (84.7%) of the patients did not smoke and around 98.5% were non-drinkers.

Table 2: Behavioral characteristics of the study subjects (n=9563)

Variables	Number	Percentage
Dietary compliance		
Moderate Compliance	6637	69.4
Good Compliance	829	8.7
Poor Compliance	2097	21.9
Physical activity		
Sedentary	5757	60.2
Lightly Active	3165	33.1
Moderate Active	609	6.4
Very active	32	0.3
Smoking		
Yes	911	9.5
No	8101	84.7
Ex-smoker	518	5.4
Data Missing	33	0.3
Alcohol intake		
Yes	74	0.8
No	9418	98.5
Ex-drinker	15	0.2
Data Missing	56	0.6

Table 3 indicates that mean carbohydrate, protein and fat intake in grams and calories was  $230.6\pm72.2$  g &  $64\pm7.2$  cal ,  $68.1\pm23.6$  g &  $19\pm2.9$  cal, and  $27.5\pm26.3$  g &  $17\pm6.8$  cal per day respectively

Table 3: Daily intake level of Macronutrients among the subjects (n= 9563)

Macronutrients	Mean (g) ± SD	Mean Calorie Intake ± SD
Total Carbohydrate Intake	230.6±72.2	64±7.2
Total Protein Intake	68.1±23.6	19±2.9
Total Fat Intake	27.5±26.3	17±6.8

Table 4 shows that underweight, normal, overweight and obese were 1.6%, 12.9%, 34.9% and 50.6% respectively in available data for BMI.

Table 4: Pattern of the Nutritional Status of the study subjects (n= 9354)

Nutritional status (kg/m²)	Frequency	Percentage
Underweight (<18.5)	154	1.6
Normal (18.5 - 23)	1207	12.9
Overweight (23 - 27.5)	3265	34.9
Obese (>27.5)	4736	50.6

Table 5 shows 75.9%, 65% and 93.9% patients had 7 mmol/l FPG, 11.1 mmol/l RPG and 6.5% HbA1c blood sugar respectively among the patients whose data for each variable was available.

Table 5: Pattern of glycemic status of the study subjects

Glycemic Groups	Frequency	Percentage
FPG (n=995)		
<7 mmol/l	240	24.1
7 mmol/l	755	75.9
Mean ± SD	$184.0 \pm 75.2$	
RPG (n=512)		
<11.1 mmol/l	179	35.0
11.1 mmol/l	333	65.0
Mean ± SD	$253.4 \pm 113.3$	
HbA1c (n=6734)		
<6.5%	410	6.1
6.5%	6323	93.9
Mean ± SD	$9.7 \pm 2.4$	

Table 6 shows that among the patients with available data for each variable 72.8% and 27.2% patients had total cholesterol <200 mg/dl and 200 mg/dl respectively followed by 57.8% with triglyceride <150 mg/dl and 42.1% with 150 mg/dl and LDL-C <100 mg/dl 46.4% and 100 mg/dl 53.6%. Regarding HDL male and female distribution was 78.2% had <40 mg/dl and 89.3% had <50 mg/dl respectively.

Table 6: Pattern of lipid profile of the study subjects

Variables	Frequency	Percentage
Total Cholesterol (n=4222)		
<200 mg/dl	3073	72.8
200 mg/dl	1148	27.2
Mean ± SD	$173.7 \pm 46.8$	
Triglycerides (n=4136)		
<150 mg/dl	2392	57.8
150 mg/dl	1744	42.1
Mean ± SD	$159.0 \pm 102.3$	
LDL-C (n=4283)		
<100 mg/dl	1985	46.4
100 mg/dl	2296 53.6	
Mean ± SD	$105.8 \pm 39.3$	
Male HDL-C (n=2302)		
40 mg/dl	502	21.8
<40 mg/dl	1801	78.2
Mean ± SD	$33.6 \pm 8.7$	
Female HDL-C (n=1903)		
50 mg/dl	204	10.7
<50 mg/dl	1699 89.3	
Mean ± SD	$37.8 \pm 9.5$	

Table 7 shows that in the data available for blood pressure 56.5% of study subjects had systolic pressure above 120 mm Hg whereas prevalence of diastolic pressure above 80 mm Hg was 31.3%.

Table 7: Blood Pressure status of the study subjects (n=9513)

Variables	Frequency	Percentage
Systolic BP		
120 mm Hg	4138	43.4
>120 mm Hg	5375	56.5
Mean ± SD	$130.3 \pm 20.4$	
Diastolic BP		
80 mm Hg	6539	68.7
>80 mm Hg	2974	31.3
Mean ± SD	$80.7 \pm 10.7$	

Table 8 shows that in available data Mean carbohydrate, protein and fat intake among underweight, normal, overweight and obese groups was  $227.3\pm85.9$ ,  $64.8\pm25.0$ ,  $26.3\pm25.2$ ;  $225.7\pm70.5$ ,  $65.3\pm23.0$ ,  $26.2\pm24.2$ ;  $233.2\pm70.4$ ,  $68.6\pm23.3$ ,  $27.5\pm26.1$  and  $231.2\pm73.3$ ,  $68.7\pm24.0$  and  $28.1\pm27.4$  respectively and statistical significance was found in case of carbohydrate (p=0.018) and protein (p=0.001). In group comparison normal vs overweight and normal vs obese groups also showed statistical significance.

Table 8: Level of macronutrient intake according to the nutritional status of the study subject (n=9362)

Nutritional Status	n	Carbohydrate	Protein	Fat
Underweight (<18.5 kg/m²)	154	$227.3 \pm 85.6$	$64.8 \pm 25.0$	26.3 ± 25.2
Normal (18.5 - 23 kg/m²)	1207	$225.7 \pm 70.5$	$65.3 \pm 23.0$	$26.2 \pm 24.2$
Overweight (23 - 27.5 kg/m²)	3265	$233.2 \pm 70.4$	$68.6 \pm 23.3$	$27.5 \pm 26.1$
Obese (>27.5 kg/m <sup>2</sup> )	4736	$231.2 \pm 73.3$	$68.7 \pm 24.0$	$28.1 \pm 27.4$
F/p		3.376/0.018*	8.410/0.001*	1.80/0.145
Group comparison				
Normal vs overweight		- 7.553/0.011*	- 3.342/0.001*	
Normal vs obese			- 3.480/0.001*	

Results are expressed in mean  $\pm$  SD. One way ANOVA (Post-HOC Bonferroni) was performed as the test of significance. p 0.05 was considered as level of significance

Table 9 shows macronutrients intake has no significant association with FBG, RBG and HbA1c with one exception; fat and HbA1c that show significant association at p=0.042.

Table 9: Level of macronutrient intake according to the glycemic status of the study subjects

Variables	n	Carbohydrate	Protein	Fat
Fasting Blood Glucose (n=995)				_
<7 mmol/l	240	229.3±82.5	$67.5 \pm 29.3$	$25.6 \pm 19.0$
7 mmol/l	755	$233.9 \pm 72.9$	$70.4 \pm 23.8$	29.2±28.2
t/p		ns	ns	ns
Random Blood Glucose (n=512)				
<11.1 mmol/l	179	214.6±64.8	$62.5 \pm 20.5$	$24.0 \pm 20.1$
11.1 mmol/l	333	$213.7 \pm 69.6$	$62.0 \pm 21.4$	23.2±18.1
t/p		ns	ns	ns
HbA1c (n=6734)				
<6.5%	410	$229.4 \pm 73.1$	$66.7 \pm 21.8$	$25.6 \pm 19.6$
6.5%	6323	$231.4 \pm 73.7$	$67.9 \pm 24.0$	$27.7 \pm 27.5$
t/p		ns	ns	2.04/0.042*

Results are expressed in mean  $\pm$  SD. Independent t-test was performed as the test of significance and p 0.05 was taken as significance level

Table 10 reveals that intake of macronutrients was not significant in most cases except triglycerides and proteins, and LDL-C and protein.

Table 10: Level of macronutrients intake according to the lipid status of the study subjects

Variables	n	Carbohydrate	Protein	Fat
Total Cholesterol (n=4222)				
<200 mg/dl	3073	$234.4 \pm 75.4$	$69.9 \pm 25.4$	$27.5 \pm 22.7$
200 mg/dl	1148	234.5±75.3	69.3±25.0	$28.4 \pm 28.4$
t/p		ns	ns	ns
Triglycerides (n=4136)				
<150 mg/dl	2392	$232.6 \pm 74.7$	$68.5 \pm 24.3$	$27.3 \pm 23.1$
150 mg/dl	1744	$235.8 \pm 76.0$	$71.1 \pm 26.5$	$28.3 \pm 26.0$
t/p		ns	-3.166/0.002*	ns
LDL-C (n=4283)				
<100 mg/dl	1985	$233.3 \pm 74.4$	$68.8 \pm 24.8$	$27.4 \pm 23.9$
100 mg/dl	2296	$235.1 \pm 76.0$	$71.0 \pm 25.6$	$28.0 \pm 24.8$
t/p		ns	-2.251/0.024*	ns
Male HDL-C (n=2302)				
40 mg/dl	501	$259.3 \pm 74.6$	$77.5 \pm 27.0$	$30.0 \pm 21.9$
<40 mg/dl	1801	$262.9 \pm 77.1$	$79.0 \pm 26.4$	$31.6 \pm 27.2$
t/p		ns	ns	ns
Female HDL-C (n=1930)				
50 mg/dl	204	195.0±52.5	$57.6 \pm 15.5$	$23.2 \pm 20.3$
<50 mg/dl	1699	$201.4 \pm 58.7$	$59.0 \pm 18.8$	$23.6 \pm 21.6$
t/p		ns	ns	ns

Results are expressed in mean±SD. Independent t-test was performed as the test of significance and p 0.05 was taken as significance level

Table 11 shows that according to the available data there is no significant association between macronutrient intake and, systolic and diastolic blood pressures

Table 11: Level of macronutrients intake according to the status of the blood pressure of the study subjects (n=9513)

Variables	n	Carbohydrate	Protein	Fat
Systolic Blood Pressure				
120 mm/Hg	4138	$231.4 \pm 73.1$	$68.3 \pm 23.9$	$27.3 \pm 24.9$
>120 mm/Hg	5375	$230.1 \pm 71.6$	$67.8 \pm 23.4$	$27.7 \pm 26.5$
t/p		ns	ns	ns
Diastolic Blood Pressure				
80 mm/Hg	6539	231.3±72.6	$68.3 \pm 24.1$	$27.6 \pm 25.8$
>80 mm/Hg	2974	$229.1 \pm 71.4$	$67.5 \pm 23.8$	$27.3 \pm 27.5$
t/p		ns	ns	ns

Results are expressed in mean±SD. Independent t-test was performed as the test of significance and p 0.05 was taken as significance level

Table 12 shows that no relation was found between macronutrients intake and BMI.

Table 12: Correlation between body mass index (BMI) and macronutrient intake (n=9354)

Variables	Total Carbohydrate		Total Protein		Total Fat intake	
	inta	ake	intake			
	r	р	r	р	r	р
BMI	-0.018	0.076	0.016	0.128	0.012	0.228

<sup>\*\*</sup> Correlation is significant at the 0.01 level (2-tailed).

Table 13 shows that there is no correlation between macronutrient intake and blood glucose measuring variables. Only fat intake shows slight relation with fasting blood glucose at a highly significant level (p<0.01)

Table 13: Correlation between blood glucose and macronutrient intake

Variables	n	Total Carbohydrate intake		Total Protein intake		Total Fat intake	
		r	р	r	р	r	р
FBS	995	0.031	0.33	0.043	0.172	0.101	0.001**
RBS	512	-0.003	0.952	-0.021	0.635	-0.054	0.226
HbA1c	6733	0.041	0.001**	0.018	0.136	0.027	0.029*

<sup>\*\*</sup> Correlation is significant at the 0.01 level (2-tailed); \* correlation is significant at the 0.05 level (2-tailed)

Table 14 shows carbohydrate and protein intake didn't have any relation with lipid variables but in case of fat slightly positive correlation can be seen with total cholesterol and triglycerides, whereas slightly negative relation can be seen between fat intake and HDL-C among males. But all are insignificant.

Table 14: Correlation between cholesterol and macronutrient intake

Variables	n	Total Carbo intak	•	Total Protein intake		Total Fat intake	
		r	р	r	р	r	р
Total Cholesterol	4221	0.008	0.613	0.016	0.307	0.22	0.162
Triglycerides	4136	0.047	0.002**	0.082	0.0001**	0.34	0.27
LDL-C	4281	-0.002	0.890	0.022	0.156	0.024	0.124
Male HDL-C	2302	-0.018	0.392	-0.028	0.174	-0.25	0.230
Female HDL-C	1902	-0.013	0.563	-0.016	0.473	-0.012	0.590

<sup>\*\*</sup> Correlation is significant at the 0.01 level (2-tailed); \*correlation is significant at the 0.05 level (2-tailed)

Table 15 shows there is no correlation in any case.

Table 15: Correlation within systolic, diastolic and macronutrient intake (n=9513)

Variables	Total Carb	,			Total Fa	it intake
	inta	ke	intake			
	r	р	r	р	r	р
Systolic BP	0.010	0.310	0.006	0.583	0.021	0.450*
Diastolic BP	0.003	0.803	-0.002	0.829	-0.001	0.917

<sup>\*</sup>Correlation is significant at the 0.05 level (2-tailed)

Significant association has been found between duration of diabetes (p=0.001), physical activity (p=0.001) total carbohydrate intake (p=0.001) and total protein intake (p=0.001) with body mass index of the respondents.

Table 16: Multiple linear model for identify the predictors of Body Mass Index

				95.0%	95.0% CI of B	
Variables	Unstandardized	Standardized	p-value	Lower Bound	Upper Bound	
Age	-0.006	-0.013	0.225	-0.017	0.004	
Duration of diabetes	-0.044	-0.067	0.001	-0.058	-0.030	
Physical Activity	-1.108	0.052	0.001	-1.539	-0.676	
Total CHO Intake (gm)	-0.006	-0.074	0.001	-0.008	-0.003	
Total Protein Intake (gm)	0.013	0.061	0.001	0.006	0.021	
Total Fat Intake (gm)	0.002	0.009	0.424	-0.003	0.006	

Significant association has been found between age (p=0.013), duration of diabetes (p=0.001) and total fat intake (p=0.004) with fasting plasma glucose of the respondents.

Table 17: Multiple linear model for identifying the predictors of Fasting Plasma Glucose

asina eracese					
		Chandand's ad		95.0% CI of B	
Variables	Unstandardized	Standardized	p-value	Lower	Upper
				Bound	Bound
Age	-0.580	-0.082	0.013	-1.037	-0.123
Duration of diabetes	1.620	0.153	0.001	0.936	2.303
Physical Activity	-17.495	-0.060	0.059	-35.645	0.654
Total CHO Intake (gm)	-0.011	-0.017	0.829	-0.112	0.090
Total Protein Intake (gm)	0.076	0.029	0.633	-0.237	0.390
Total Fat Intake (gm)	0.286	0.096	0.004	0.090	0.483

No association was found in case of random plasma glucose.

Table 18: Multiple linear model for identifying the predictors of Random Plasma Glucose

				95.0% CI of B	
Variables	Unstandardized	Standardized	p-value	Lower Bound	Upper Bound
Age	-0.462	-0.045	0.340	-1.433	0.496
Duration of diabetes	0.712	0.043	0.362	-0.833	2.276
Physical Activity	-13.216	-0.028	0.528	-54.377	27.945
Total CHO Intake (gm)	0.041	0.025	0.735	-0.199	0.281
Total Protein Intake (gm)	-0.055	-0.010	0.896	-0.885	0.775
Total Fat Intake (gm)	-0.322	-0.054	0.285	-0.913	0.269

Significant association has been found between age (p=0.001), duration of diabetes (p=0.001), physical activity (p=0.001) and total carbohydrate intake (p=0.002) with HbA1c of the respondents.

Table 19: Multiple linear model for identifying the predictors of Heamoglobin A1c

		0		95.0% CI of B	
Variables	Unstandardized	Standardized	p-value	Lower Bound	Upper Bound
Age	-0.027	-0.126	0.001	-0.032	-0.022
Duration of diabetes	0.030	0.101	0.001	0.022	0.037
Physical Activity	-0.470	-0.049	0.001	-0.699	-0.241
Total CHO Intake (gm)	0.002	0.061	0.002	0.001	0.003
Total Protein Intake (gm)	-0.004	-0.036	0.072	-0.007	0.001
Total Fat Intake (gm)	0.002	0.024	0.075	0.001	0.004

Significant association has been found between age (p=0.001) and duration of diabetes (p=0.001) with Total Cholesterol of the respondents.

Table 20: Multiple linear model for identifying the predictors of Total Cholesterol

				95.0% CI of B	
Variables	Unstandardized	Standardized	p-value	Lower	Upper
				Bound	Bound
Age	-0.334	-0.078	0.001	-0.469	-0.199
Duration of diabetes	-0.476	-0.083	0.001	-0.659	-0.294
Physical Activity	-1.994	-0.010	0.505	-7.859	3.872
Total CHO Intake (gm)	-0.019	-0.030	0.229	-0.049	0.012
Total Protein Intake (gm)	0.010	0.006	0.827	-0.083	0.104

Total Fat Intake	0.038	0.020	0.245	-0.026	0.102
(gm)					

Significant association has been found between age (p=0.001), duration of diabetes (p=0.001), total carbohydrate intake (p=0.001) and total protein intake (p=0.001) with serum triglycerides of the respondents.

Table 21: Multiple linear model for identifying the predictors of Serum

Triglycerides

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				95.0% CI of B			
Variables	Unstandardized	Standardized	p-value	Lower Bound	Upper Bound		
Age	-1.117	-0.120	0.001	-1.413	-0.821		
Duration of diabetes	-0.444	-0.035	0.029	-0.842	-0.045		
Physical Activity	-2.798	-0.007	0.672	-15.758	10.162		
Total CHO Intake (gm)	-0.091	-0.067	0.007	-0.157	-0.025		
Total Protein Intake (gm)	0.465	0.115	0.001	0.259	0.670		
Total Fat Intake (gm)	-0.007	-0.002	0.919	-0.148	0.134		

Significant association has been found between age (p=0.001), duration of diabetes (p=0.001) and total carbohydrate intake (p=0.014) with LDL cholesterol of the respondents.

Table 22: Multiple linear model for identifying the predictors of LDL-C

				95.0% CI of B		
Variables	Unstandardized Standardized p-va	p-value	Lower Bound	Upper Bound		
Age	-0.217	-0.061	0.001	-0.330	-0.105	
Duration of diabetes	-0.431	-0.089	0.001	-0.583	-0.279	
Physical Activity	-4.340	-0.026	0.086	-9.301	0.621	
Total CHO Intake (gm)	-0.034	-0.060	0.014	-0.057	-0.006	
Total Protein Intake (gm)	0.063	0.038	0.138	-0.019	0.137	
Total Fat Intake (gm)	0.029	0.020	0.244	-0.022	0.086	

No association was found in male HDL cholesterol and any predictors.

Table 23: Multiple linear model for identifying the predictors of male HDL-C

Variables	Unstandardized	Standardized	p-value	95.0% CI of B	
				Lower Bound	Upper Bound
Age	0.010	0.013	0.557	-0.024	0.044
Duration of diabetes	0.016	0.016	0.483	-0.029	0.063
Physical Activity	0.946	0.029	0.160	-0.373	2.264
Total CHO Intake (gm)	0.001	0.006	0.855	-0.006	0.008
Total Protein Intake (gm)	-0.007	-0.022	0.511	-0.029	0.014
Total Fat Intake (gm)	-0.006	-0.017	0.464	-0.021	0.010

Significant association has been found between physical activity and HDL cholesterol of the respondents (p=0.017)

Table 24: Multiple linear model for identifying the predictors of female HDL-C

able 24. Multiple linear model for identifying the predictors of remaie fibe-c					
Variables	Unstandardized	Standardized	p-value	95.0% CI of B	
				Lower Bound	Upper Bound
Age	-0.003	-0.003	0.887	-0.045	0.039
Duration of diabetes	0.003	0.002	0.929	-0.054	0.059
Physical Activity	2.771	0.055	0.017	0.489	5.052
Total CHO Intake (gm)	0.000	-0.004	0.914	-0.011	0.010
Total Protein Intake (gm)	-0.006	-0.011	0.742	-0.041	0.029
Total Fat Intake (gm)	-0.004	-0.008	0.735	-0.025	0.018

Significant association has been found between physical activity with systolic blood pressure of the respondents (p=0.01).

Table 25: Multiple linear model for identifying the predictors of Systolic Blood Pressure

Variables	Unstandardized	Standardized	p-value	95.0% CI of B	
				Lower	Upper
				Bound	Bound
Age	0.032	0.017	0.121	-0.009	0.074
Duration of diabetes	-0.030	-0.012	0.287	-0.085	0.025
Physical Activity	2.121	0.25	0.016	0.403	3.840
Total CHO Intake (gm)	0.006	0.020	0.210	-0.003	0.015
Total Protein Intake (gm)	-0.025	-0.028	0.090	-0.055	0.004
Total Fat Intake (gm)	0.017	0.022	0.056	0.001	0.035

No association was found between any of the predictors and diastolic blood pressure

Table 26: Multiple linear model for identifying the predictors of Diastolic Blood Pressure

Blastollo Bl	00011033010				
Variables	Unstandardized	Standardized	p-value	95.0% CI of B	
				Lower Bound	Upper Bound
Age	0.014	0.014	0.204	-0.008	0.036
Duration of diabetes	-0.002	-0.001	0.910	-0.028	0.031
Physical Activity	0.729	0.016	0.120	-0.189	1.646
Total CHO Intake (gm)	0.003	0.017	0.281	-0.002	0.008
Total Protein Intake (gm)	-0.012	-0.024	0.142	-0.027	0.004
Total Fat Intake (gm)	0.001	0.001	0.935	-0.009	0.010

#### 6. DISCUSSION

In this study a total of 9563 diabetic subjects' data out of 50,000 were collected retrospectively from the hospital software namely Hospital Management System. The BIDE is the leading specialized diabetes care center and a nonprofit good quality hospital in Karachi, Pakistan. Usually, all types of people come from nearby area. For that reason, this study could not be generalized but this large number of data may give us a preliminary idea about macronutrient intake and the risk factors of micro- and macrovascular complications among Pakistani population in general.

Analysis of the descriptive data suggests that substantial proportion of newly registered BIDE patients; suffer from a high degree of risk of micro- and macrovascular diabetic complications.

In the present study, uncontrolled hyperglycemia is one of the most important risk factors and it is seen that 75%, 65% and 94% suffer from hyperglycemia at a level of FPG 7.0 mmol/l or RPG 11.1 mmol/l and HbA1c 7.0% respectively. One Indian study, which was conducted in different out-patient facilities found 34.7% patient had uncontrolled diabetes (Joshi et al., 2012) which is more than double in the present study. In other studies among Bangladeshi population (Latif, Jain, & Rahman, 2011; Rahman et al., 2015) found 92% and 76.9% uncontrolled diabetic subjects respectively which is almost similar to the present study. In case of uncontrolled hyperglycemia among the respondents, we observed in this study that the respondents consume relatively more carbohydrate; that can be a reason why more than 84% were reported to be overweight and obese. In addition, evidence shows that obesity has a strong relation with insulin resistance (Kahn & Flier, 2000; Tewari, Awad, Macdonald, & Lobo, 2015) which may lead to hyperglycemia. On the other hand, other possible reasons for the uncontrolled hyperglycemia among the respondents could be lack of their awareness due to lack of dietary educational intervention, their dietary habit; physical inactivity, and unaware regarding the complication of hyperglycemia. On Pearson's correlation analysis the level of hyperglycemia did not show any significant relationship with the intake of individual macronutrients and the lack of association was further confirmed in the multiple regression analysis on adjusting the effects of potential confounders like age, duration of diabetes and physical activity. A similar result was obtained when HbA1c was used as a marker of the glycemic status. This is in contrast to findings of a systematic review on effect of different dietary approaches on adults with T2DM and it revealed that with lower carbohydrate diets the levels of the risk factors of CVDs were improved (Ajala, English, & Pinkney, 2013). Another study conducted on the Iranian population showed that low glycemic load diet (low-carbohydrate 41%, high fat 36% from good fats and high protein 22%) is appropriate for diabetic patients who manage their diabetes poorly and it improved their CVD risk factors also (Afaghi, Ziaee, & Afaghi, 2012).

According to US Food and Drug Administration (USFDA) and US Department of Agriculture (USDA) guideline; at least 45 percent and not exceed to 65 percent of calories per day should be consumed from dietary carbohydrate for an adult. In the present study we observed that respondents were consumed more than 64% calorie from the carbohydrate which is just in border line of the recommendation and reported more than FAO (63%) data. A report on a general group of healthy subjects shows that the contribution of carbohydrate of total calorie among Pakistani people is 63% (FAO, 2011). Another important fact regarding distributions of calories is related to fat. In the present study protein and fat contributed 19 and 17 percent respectively to the total calorie of the diabetic subjects. In the same report on healthy subjects the respective contribution by protein and fat were 10 and 27 percent respectively. Thus among Pakistani general population fat intake seems to be higher than the diabetic patients at BIDE. It seems that the diabetic patients become little more aware about fat intake, but not regarding carbohydrate intake. The principal source of carbohydrate in Pakistan is wheat and people are used to take wheat in every meal. The possible reasons for consumed more carbohydrate could be that they have limited purchasing capacity (according to World Bank 2015, almost half of the Pakistani are lies in lower or lower middle economic class) of meat, fish, fruits and vegetables. All this reflect poor awareness as well as practice among Pakistani diabetic subjects regarding their datary habits. Although the exact distribution in an individual patient may vary, the diabetic patients, in general should have much lower proportion of calories from carbohydrate sources. It seems that the Health Education and Nutrition Department at BIDE has a great challenge to educate and train these patients for modifying their dietary practices and lifestyle. It could be interesting to see the outcome of the BIDE intervention through prospective studies.

As per the present study, proportion of overweight and obesity among these BIDE patients was 35% and 51% respectively which is higher than a Yemen study which reported 43.5% overweight and 11% obesity (Al-Sharafi & Gunaid, 2014). Another study conducted among Bangladeshi diabetic women where 22% overweight and 48% obesity are reported (Akter et al., 2014). Reported high carbohydrate and fat intake, and higher proportion of sedentary work might be the reasons for overweight and obesity.

Obesity and overweight are important risk factors of vascular complications of diabetes. In the present study people with higher BMI were found to consume higher amount of calories from all the macronutrients, not from any specific one. Univariate analysis did not show any significant association between BMI and level of individual macronutrient intake but multivariate analysis showed that the BMI decreased with higher intake of carbohydrates and increasing with higher intake of protein. This is consistent with the findings of a case-control study that was performed on the data collected over nine years period; it concluded that a protein-rich diet is not inversely related to BMI, and a carbohydrate-rich diet is not directly related to BMI (Randi et al., 2007). Fat intake in the present study did not show any association with BMI neither in univariate nor in multivariate analysis. A study done on British population revealed that high fat consumers

tend to have a higher BMI than low fat consumers, but not all high fat consumers are overweight or obese (Macdiarmid, Cade, & Blundell, 1996). This may be the reason why we cannot find any significant association between the higher BMI and fat intake among the study subjects. The type of fats also have to play an important part in this regard as studies suggest that unsaturated fat intake has an inverse effect on CVD risk factors where as intake of trans fats increases the chances of CVD (Oh, Hu, Manson, Stampfer, & Willett, 2005). It can be assumed that the fat intake among the subjects is low but the kind of fat they consume might be dangerous (there is no data available on the type of fate). The positive association of BMI with protein intake may be explained by general high consumption of red meat among the Pakistani population. The red meat has high proportion of animal fat and can cause overweight and obesity among the subjects. It should be noted that proper information on the most important confounder (i.e. level of physical exercise) is missing in the present database. Accordingly, it is difficult to draw more meaningful conclusion in this respect and this emphasizes the need to expand the patient information base in Baqai in relevant areas.

Hypertension is an important risk factor of cardiovascular diseases which are increased by nearly four times in type 2 diabetic patients. Blood pressure has previously, time and again, been shown to be positively associated with quantity and type of carbohydrate and fat intake. The OmniHeart randomized trial revealed that the substitution of carbohydrate with either protein or monounsaturated fat can lower blood pressure, improve lipid levels, and reduce suspected cardiovascular risk (Appel et al., 2005). In another article it was mentioned that a more healthy diet, that is a diet with much less salt and increased potassium through an increase in fruit and vegetable consumption, a reduction in fat intake with substitution of saturated by monounsaturated fat, a reduction in meat and dairy products with an increase in fish consumption will have large effects on blood pressure. At the same time, it will decrease other cardiovascular risk factors, particularly cholesterol and glucose intolerance

(MacGregor, 1999; Parkin, 2011). In the present study, neither the group difference nor the correlation and multiple regression analysis showed any significant association between the level of blood pressure and individual macronutrient intake in the diabetic subjects.

In the present study more than two-third (73%) were reported to have hypercholesterolemia and more than half (58%) had hypertriglyceridemia. Of adults aged 18 years or older with diagnosed diabetes, 65% had blood LDL cholesterol greater than or equal to 100 mg/dl or they used cholesterol-lowering medications (ADA, 2014). The level of serum cholesterol among the patients in the present study showed no significant correlation with any macronutrient intake, but it showed a marginally significant (p<0.05) association with fat intake on regression analysis. In contrast serum triglyceride showed a highly significant association with carbohydrate intake (p<0.002) (positive) and total protein intake (p<0.001). Paradoxically serum triglycerides showed no association with fat intake. It may be noted that intake among Pakistani people is mainly in the forms of red meats which are rich in fats and it may happen that this issue is not given proper attention during assessment of the intake. Accordingly, association of hypertriglyceridemia with protein intake may be a reflection of increased fat intake mixed with red meat. Neither LDL- nor HDL-cholesterol showed any association with any of the macronutrients.

## Conclusion

- The prevalence of macro- and microvascular diseases risk factors are fairly high among the Pakistani diabetic patients who were outside any comprehensive care. Vast majority of them have uncontrolled diabetes, almost fifty percent have overweight, obesity and hypertension, and more than two-third had dyslipidemia.
- The proportion of macronutrient intake among general diabetic subjects in Pakistan substantially differs from the generally recommended proportions applicable for diabetic subjects. In particular, the proportion of carbohydrate as a source total daily calorie is around 20% higher than the usually recommended proportion for diabetic patients.
- ) Intake of carbohydrate and protein are important determinants of overweight and obesity among Pakistani diabetic subjects
- Except overweight and obesity, there seems to be no micro- or macro vascular risk factor which is associated with any individual macronutrient intake at a significant level.

## Recommendations

- People, Policy Makers and Service Providers should be made aware about the high prevalence micro- and macrovascular risk factors among diabetic subjects in Pakistan
- Appropriate dietary proportions for macronutrients should urgently be promoted among Pakistani diabetic subjects. Longitudinal studies should be conducted at BIED to evaluate the impact of patient education in the center

## Limitations

- Only one hospital of Karachi was approached so we cannot generalized the results of this study for the Pakistani population.
- 24 hour recall cannot be considered as a thorough dietary assessment tool to evaluate patients' common everyday dietary habits
- Some important data could not be found in the database. Addition of some more data, for e.g. type of meat and, type and duration of physical activity may lead to some difference at the time of analysis and would have given meaningful results.

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