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FACTORS AFFECTING CLINICAL OUTCOME AMONG TYPE 2 DIABETIC SUBJECTS ATTENDING THE OUTPATIENT DEPARTMENT OF A TERTIARY CARE HOSPITAL IN BANGLADESH

Doctoral Thesis
for the awarding of a Doctor of Philosophy (Ph.D.)
at the Medical Faculty of
Ludwig-Maximilians-Universität, Munich

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2021

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Date of Oral Defense: 21st April 2021

Abstract

Background: Diabetes care in low- and middle-income countries, such as Bangladesh, remains challenging due to limited resources. A person's self-care ability, his or her adherence to medical advice and knowledge about the disease are central to diabetes management. Furthermore, undiagnosed, diabetic secondary complications may severely affect patient outcome. Here, we, therefore, examined the adherence, knowledge, and undetected retinopathy in adults with diabetes attending the outpatient department of a tertiary care hospital in Bangladesh.

Methods: Cross-sectional, observational, monocenter study conducted at BIHS hospital in Dhaka, Bangladesh from April to August 2017; 504 participants with type 2 diabetes; questionnaires on socio-demographic parameters, adherence to medical advice, knowledge about diabetes and medical history; anthropometrics, clinical examination, laboratory chemistry, and retinal photography (n=489)**.**

Result: Adherence to the prescribed drug therapy was 52%, to recommended diet 28% and to physical activity advice 42%. Of all study participants, only 29% had good knowledge about diabetes. Factors independently associated with good knowledge about diabetes were a higher level of education, a higher family income, a duration of diabetes of 10 years or more, and controlled fasting blood glucose. In screening, diabetic retinopathy was detected in 18.8% of the study participants.

Conclusion: This study highlights possibilities for improvements of patient education, disease management and screening examinations at a diabetes care centre in Bangladesh, which are, at least in part, transferrable to other low- and middle-income countries.

Keywords: diabetes care, patient education, adherence, knowledge, type 2 diabetes, secondary complications, retinopathy, resource-limited setting

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Abbreviations

AACE	American Association of Clinical Endocrinologist
ADA	American Diabetes Association
AOR	Adjusted ODDs Ratio
BADAS	Bangladesh Diabetic Association/ Bangladesh Diabetic Somity
BDT	Bangladesh Taka
BIHS	Bangladesh Institute of Health Sciences
BIRDEM	Bangladesh Institute of Research on Diabetes, Endocrine and Metabolism
BMI	Body Mass Index
BP	Blood Pressure
BUHS	Bangladesh University of Health Sciences
CGM	Continuous Glucose Monitoring
CI	Confidence Interval
CKD	Chronic Kidney Diseases
COR	Crude ODDs Ratio
CV	Cardiovascular
CVD	Cardiovascular Diseases
DCCT	Diabetes Control and Complications Trial
DBP	Diastolic Blood Pressure
DM	Diabetes Mellitus
DPP4	Dipeptidyl peptidase-4 inhibitor
DR	Diabetic Retinopathy
EASD	European Association for the Study of Diabetes
FPF	Fasting Plasma Glucose
GDM	Gestational Diabetes Mellitus
GLUT4	Glucose Transporter Type 4
GLP	Glucagon Like Peptide
HbA1c	Haemolobin A1c or Glycated Haemoglobin

HMBG	Home Monitoring Blood Glucose
HDL	High-Density Lipoprotein
IDF	International Diabetes Federation
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
LDL	Low-density Lipoprotein
LMU	Ludwig-Maximillians University
MNT	Medical Nutrition Therapy
MODY	Maturity Onset Diabetes of the Young
NGSP	National Glycohemoglobin Standardization Program
NPDR	Non-proliferative Diabetic Retinopathy
NPH	Neutral Protamine Hagedorn
OAD	Oral Anti Diabetic
OGTT	Oral glucose tolerance test
OR	Odds Ratio
OPD	Out-Patient Department
PG	Post-Prandial
PPG	Post-Prandial Plasma Glucose
PDR	Proliferative Diabetic Retinopathy
SBP	Systolic Blood Pressure
SD	Standard Deviation
SEA	South-East Asia
SMS	Short Message Service
SPSS	Statistical Package for the Social Sciences
T2DM	Type 2 Diabetes Mellitus
TC	Total Cholesterol
UKPDS	United Kingdom Prospective Study
UAE	United Arab Emirates
WHR	Waist Hip Ratio

1 Introduction

1.1 Diabetes mellitus is a global, non-communicable epidemic

Diabetes mellitus is now one the major epidemic, non-communicable diseases leading to high mortality and morbidity worldwide. The International Diabetes Federation estimated in 2019 that 463 million people between the age of 20 and 79 years suffered from diabetes worldwide. Furthermore, this figure is expected to increase to 578 million by 2030 and 700 million by 2045. Over half of all people living with diabetes are currently undiagnosed (IDF, 2019).

About 80% of adults with diabetes are living in low- and middle-income countries and, of the total number of deaths attributable to diabetes, 58% also occur in such countries (IDF, 2019) (Akter *et al.*, 2014). The prevalence of diabetes is particularly high in the South-East Asia (SEA) Region (India, Bangladesh, Bhutan, Sri Lanka, Nepal, and Maldives) and is expected to further increase sharply in the next two decades(International Diabetes Federation, 2015).

1.1.1 Definition of Diabetes mellitus

The American Diabetes Association defines diabetes mellitus as “a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both”. Chronic hyperglycemia, in turn, can lead to failure and dysfunction of several organs, in particular the heart, the kidneys, peripheral nerves, the eyes and blood vessels. (Assoc, 2011).

1.1.2 Symptoms of diabetes mellitus

Abrupt onset of hyperglycemia can lead to polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Chronic, slowly developing hyperglycemia, on the other hand, often remains asymptomatic. In these cases, diabetes is only detected by screening examinations or when complications develop. This fact makes the disease particularly dangerous (Ramachandran, 2014).

1.1.3 Types of diabetes mellitus

Pathophysiologically, the majority of diabetes patients fall into two broad categories. The first category is type 1 diabetes, where beta cell destruction leads to an absolute deficiency of insulin secretion. This type of diabetes can be diagnosed by the detection of auto-antibodies most of the time. Specific genetic traits predispose for this condition. Individuals with type 1 diabetes depend on exogenous insulin to survive. 5-10 % of all diabetes cases fall into this category (Assoc, 2011). The second category is type 2 diabetes, where often a combination of insulin resistance and impaired insulin secretion causes the pathologic process. Again, genetic trails predispose for this disease which causes about 90% of all cases of diabetes. Despite often being asymptomatic, the degree of hyperglycemia in type 2 diabetes is sufficient to cause secondary complications in multiple target tissues (Assoc, 2011).

Early stages of type 2 diabetes, not yet meeting the diagnostic criteria for overt diabetes, are called prediabetes. Secondary complications, in particular cardiovascular disease, may already start during this period of disease development. This type of metabolic disturbance should therefore not be underestimated (Goldenberg and Punthakee, 2013).

Gestational diabetes mellitus is a condition related to type 2 diabetes with onset or first recognition during pregnancy (Goldenberg and Punthakee, 2013). Its prevalence ranges from 1 to 14% of pregnancies, depending on the population studied (Assoc, 2011). Gestational diabetes mellitus usually resolves at the end of the pregnancy but is a risk marker for the future development of type 2 diabetes.

Other forms of diabetes mellitus, often called type 3 diabetes, are due to specific causes, e.g., monogenic diabetes syndromes (e.g. maturity-onset diabetes of the young [MODY]), diseases of the exocrine pancreas (such as chronic pancreatitis and cystic fibrosis), and drug-induced diabetes (e.g. with glucocorticoid use or after an organ transplant) (Care and Suppl, 2018).

1.1.4 Risk factors of diabetes mellitus

Synergistic effects of genetics, environmental and immunological factors destroying the pancreatic beta cells are responsible for the development of type 1 diabetes mellitus (Kasper D., Fauci, A., Longo, D., Braunwald, E., Hauser, S., and Jameson, 2005). For type 2 diabetes, several risk factors

act synergistically to cause the disease. These include a number of lifestyle factors, in particular obesity, unhealthy diet, physical inactivity and rapid urbanization (Hu, 2011). Advancing age also fosters the development of type 2 diabetes mellitus, although the onset of the disease has recently moved into younger age groups due to an imbalance between energy intake and energy expenditure in modern societies (Alberti, Zimmet and Shaw, 2007).

1.1.5 Diagnostic criteria of diabetes mellitus

Diabetes mellitus can be diagnosed by measurements of plasma glucose or hemoglobin a1c (A1C) (Care and Suppl, 2018). In the absence of unambiguous hyperglycemia, results should be confirmed by repeat testing. The relevant cutoff values are given below;

Diagnostic criteria for diabetes mellitus:

FPG ≥ 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 hours.

OR

2-h PG ≥200mg/dL (11.1mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.

OR

A1C ≥6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).

1.2 Complications of diabetes mellitus

Acute, life threating complications of hyperglycemia are diabetes ketoacidosis, mostly occurring in type 1 diabetes, and the non-ketotic hyperosmolar syndrome in type 2 diabetes mellitus (Umpierrez, Murphy and Kitabchi, 2002)**.** However, long-term secondary complications constitute an even more severe burden than these acute complications. In particular, 50% of individuals with type 2 diabetes have already developed one or more diabetes-specific complication(s) at the time

of their diagnosis (Kasper D., Fauci, A., Longo, D., Braunwald, E., Hauser, S., and Jameson, 2005). The long-term secondary complications of diabetes are grouped as macrovascular (coronary artery disease, peripheral arterial disease, and stroke) and microvascular (diabetic retinopathy, nephropathy and neuropathy) (Fowler, 2008).

1.2.1 Retinopathy

In developed countries, diabetic retinopathy is the most frequent cause of acquired blindness among adults aged 20–74 years (Solomon *et al.*, 2017). Diabetic retinopathy is a neurovascular complication of both type1 and type 2 diabetes mellitus and its severity correlates with the duration of diabetes and with average glycemic control (Solomon *et al.*, 2017). Retinopathy is categorized as non-proliferative and proliferative. It is also related to diabetic macular oedema. In a pooled meta-analysis, the average prevalence of diabetic retinopathy and proliferative diabetic retinopathy was 35.4 % and 7.5 % respectively (Yau *et al.*, 2012). In one study, retinopathy developed at least seven years earlier than the clinical diagnosis of type 2 diabetes mellitus (Fong *et al.*, 2004).

1.2.2 Nephropathy

Diabetic nephropathy is the second major microvascular complication and a leading cause of kidney failure(Lim, 2014). It occurs in about 50 % of individuals with long-standing diabetes mellitus and also correlates in severity with glycemic control and the duration of diabetes (Kasper D., Fauci, A., Longo, D., Braunwald, E., Hauser, S., and Jameson, 2005)**.**

1.2.3 Neuropathy

Neuropathy causes serious morbidity and even mortality in individuals with diabetes mellitus. Typical symptoms include pain and numbness of the feet, as well as foot ulcers. (Fowler, 2008) Symptoms of autonomic neuropathy include gastroparesis, anhidrosis, bladder dysfunction, erectile dysfunction, resting tachycardia, silent ischemia, and possibly also sudden cardiac death (Boulton *et al.*, 2005).

1.2.4 Macrovascular diseases

The primary causes of death in people with diabetes mellitus is cardiovascular disease (CVD). The association of CVD with diabetes is so strong that, in risk assessment, diabetes is considered

equivalent to already established CVD, not merely a risk factor (Buse *et al.*, 2007). Diabetes mellitus is also an independent risk factor for stroke (Lehto *et al.*, 1996). Patients with type 2 diabetes have a 1.5 to 4x higher risk of stroke (Fowler, 2008).

1.3 Non-pharmacologic management of diabetes mellitus

To avoid chronic complications, blood glucose in diabetes should be maintained in a relatively narrow target range. The landmark UKPDS and DCCT trials showed that improved glycemic control is associated with a sustained decreased rate of retinopathy, neuropathy and nephropathy (Group, 1998)(Shamoon and others, 1993). To confirm that blood glucose targets are met, glucose and its long-term equivalent A1C should be measured regularly. Lifestyle measures and glucose-lowering medications can be applied to achieve blood glucose control.

In addition to glucose control, care for individuals with diabetes should include blood pressure control, lipid-lowering, evaluation of secondary complications and periodic psychologic evaluations. Whenever possible, the management of diabetes should be approached by a team of professionals. This team should include a physician, a nurse, a dietitian, a pharmacist, a podiatrist and mental health professional. A complete assessment and evaluation of co-morbidities should be done before starting the treatment plan.

1.3.1 Lifestyle Management in the treatment of diabetes

Lifestyle management is central to diabetes care. It includes diabetes self-management education, nutritional counselling, physical activity and smoking cessation advice, and psychosocial support. Lifestyle management is undertaken by providers and patients together and is relevant at all stages of the disease (‘Lifestyle management’, 2017). Patients with diabetes should participate in diabetes self-management education in order to acquire the necessary knowledge and skills. Education and counselling should be at diagnosis, annually, when complication arises, and when an alteration in care occurs (Johnson *et al.*, 2019). Education and counselling can occur in individual sessions or in group discussions, using suitable technology like an audio-visual, lecture and written material. Self-management education is aimed at active participation of the patient in the treatment process (‘Lifestyle management’, 2017).

1.3.2 Medical Nutrition Therapy (MNT)

MNT is an integral part of diabetes self-care education and diabetes mellitus management (ADA, 2002). However, this approach is complicated by the fact that it has to be individualized. A person's cultural background, individual food preferences, co-morbidities and socio-economic status, as well as the available foods, have to be acknowledged in the meal plan (Evert *et al.*, 2019).

The American Diabetes Association (ADA) emphasizes that MNT is fundamental to the overall diabetes management plan and that it should be reassessed frequently with special attention during times of changing health status (Davies *et al.*, 2018). Due to the complexity of nutrition issues, it is recommended that registered dietitians should be involved in this field (ADA, 2002). The goal of nutrition therapy is to improve or at least maintain glycemic control, achieve weight management goals, and to improve cardiovascular risk factors, e.g. blood pressure (Evert *et al.*, 2019).

1.3.2.1 Carbohydrate

A systematic review found that there is no optimal proportion of calories from carbohydrate, protein, and fat for everyone at risk for diabetes (Madelyn L. Wheeler *et al.*, 2012). Instead, macronutrient composition should individualized considering current preferences and eating patterns, as well as metabolic targets (Evert *et al.*, 2019). Research suggests that low-carbohydrate eating improves hyperglycemia and reduces anti-hyperglycemic drug requirements for type 2 diabetes patients (Johnson *et al.*, 2019). However, such a nutritional approach has to be handled with care. For individuals with diabetes, carbohydrates ideally should be from whole grains, vegetables, and milk products, less frequently also from fruit. People with diabetes or at risk to develop diabetes are also encouraged to eat a diet rich in fibre. Increasing fibre intake through vegetables, such as beans, peas, and lentils, as well as certain fruits and whole-grain products may improve glycemic control in diabetes.

1.3.2.2 Protein

Protein intake should be individualized according to the current requirements and eating habits. There is no evidence to suggest that protein adjustment will improve the glycemic status and reduce CVD risk in diabetes patient without kidney diseases (M. L. Wheeler *et al.*, 2012). Nevertheless, a slightly higher protein intake (20-30%) may contribute to satiety and thus combat

obesity (Ley *et al.*, 2014). Long term effects on nephropathy of consuming >20% energy from protein have however not been established. Therefore, it is advisable to avoid >20% energy from protein in individuals with diabetes and any stage of diabetic nephropathy (ADA, 2002).

1.3.2.3 Fat

It is recommended that diabetes patients should reduce their intake of saturated fat and *trans* fat and increase dietary omega-3 fatty acids to reduce their risk of developing CVD (Johnson *et al.*, 2019). The type and quality of fat are more important than the amount of fat with respect to CVD outcomes(Qian *et al.*, 2016). Several trials with type 2 diabetes patients have reported that a Mediterranean diet rich in monounsaturated fatty acids can improve glycemic control and serum lipids, and also reduce cardiovascular risk (Estruch *et al.*, 2013)(Brehm *et al.*, 2009). Overall, individuals with diabetes should follow the same guidelines as the general population for the recommended intake of saturated fat. Dietary cholesterol and trans-fat should be avoided.

1.3.2.4 Supplements

There is no clear evidence of a benefit of vitamin and mineral supplements in type 2 diabetes mellitus without nutritional deficiencies. Only folate supplements to prevent birth defect and calcium/vitamin D supplements for the prevention of osteoporosis should be considered (ADA, 2002).

1.3.3 Physical activity/ Exercise

Physical exercise should be one of the cornerstones of diabetes mellitus management and prevention whenever possible (Sigal *et al.*, 2006). This is particularly true for type 2 diabetes. Structured lifestyle interventions that include at least 150 min/week of physical activity in addition to dietary modifications aiming at weight loss of 5%–7% result in a reduction of type 2 diabetes incidence of about 30 percent (Colberg *et al.*, 2016). However, physical inactivity is still highly prevalent in many societies, in particular among the rising middle class in low and middle-income countries (Thent, Das and Henry, 2013). The mechanisms by which exercise positively affect type 2 diabetes are not fully understood but augmented glucose transporter 4 (GLUT-4)-mediated transport of glucose into skeletal muscle certainly plays a role. Aerobic exercise increases muscle glucose uptake by several orders of magnitude through insulin-independent mechanisms. After exercise, glucose uptake remains elevated, also by insulin-independent mechanisms, for up to 2

hours (Magkos *et al.*, 2008). Regular physical activity also boosts insulin action in the liver (Roberts, Hevener and Barnard, 2013). All types of exercise that build strength and/or endurance should be encouraged (Thent, Das and Henry, 2013). It is recommended to exercise daily or at least to allow no more than 2 days to elapse between exercise units to enhance insulin action. Children and adolescents with type 2 diabetes should be encouraged to follow the same targets as adults (Colberg *et al.*, 2016).

A recent review by Pi-Sunyer et al. confirmed the strong evidence for health benefits of intensive lifestyle interventions. Weight management, fitness, glucose control, blood pressure and lipid profile normalization can all be achieved. Additionally, the number of required medications can often be reduced and participants of interventions suffer from fewer cases of diabetic complications, such as diabetic kidney disease and retinopathy. Better mobility and quality of life can also be preserved, resulting in overall lower health care costs (Pi-Sunyer, 2014).

1.4 Pharmacological management of diabetes mellitus

1.4.1 Oral hypoglycemic agents

1.4.1.1 Metformin

Metformin is the first-line drug to treat type 2 diabetes in practically all countries where it is available. It is usually well-tolerated and low in cost. Metformin should therefore be continued as long as tolerated and unless contraindicated (Marín-Peñalver *et al.*, 2016). Long term use of metformin may lead to vitamin B12 deficiency, which is especially problematic in the context of diabetic neuropathy and anaemia. Therefore, measuring serum vitamin B12 should be considered in Metformin-treated individuals.

1.4.1.2 Sulfonylureas and Meglitinides

In many countries, Sulfonylureas are still second-line medications for type 2 diabetes, despite the associated risk of hypoglycemia and weight gain. The clinical experience with these drugs is long and their cost is low. **Meglitinides** have a similar mechanism of action to the sulfonylureas but with a shorter duration of action and thus a lower risk of hypoglycemia.

1.4.1.3 Other oral anti-diabetic drugs

Alpha-glucosidase inhibitors, Thiazolidinediones, Dipeptidyl peptidase-4 inhibitors and Sodium glucose co-transporter-2 inhibitors are additional choices for the oral therapy of type 2 diabetes. The advantage of these newer drugs is that they do not cause hypoglycemia. However, specific side effects may occur and the cost of these medications is higher.

Alpha-glucosidase inhibitors: Three Alpha-glucosidase inhibitors (AGIs) are available; acarbose, miglitol, voglibose, which are widely used in the treatment of patients with type 2 diabetes. AGIs lowers the postprandial blood glucose and insulin levels by delaying the absorption of carbohydrates from the small intestine.

Thiazolidinediones (TZD): Pioglitazone and Rosiglitazone reduce plasma glucose by increasing insulin sensitivity. However, these compounds are not used anymore in many countries due to safety concern(Marín-Peñalver *et al.*, 2016) The most common adverse effects are weight gain, fluid retention, possible risk of bladder cancer, and osteoporotic bone fractures.

Dipeptidyl peptidase-4 inhibitors (DPP4i): Dipeptidyl peptidase-4 (DPP-4) inhibitors prevent the breakdown of GLP-1, thereby increasing insulin release. Available forms are sitagliptin, vildagliptin, saxagliptin and linagliptin. DPP-4i are second-line antidiabetic drugs after metformin. They can be used in combination with metformin, with sulfonylurea and with insulin. DPP4i are weight neutral and modestly reduce plasma glucose. The cost of these medicines is high.

Sodium glucose co-transporter-2 inhibitors (SGL2I): This class of antidiabetic drugs acts on the glucose co-transporter in the proximal convoluted tubules of the kidney and inhibits the re-uptake of glucose. It thereby improves glycemic control and causes weight loss. Available forms of SGL2i are dapagliflozin, empagliflozin and canagliflozin. SGL2i also demonstrated a beneficial effect on the cardiovascular system, in particular in individuals with heart failure.

1.4.2 Injectable Agents

GLP1 analogues, like exenatide and liraglutide, lower HbA1c, plasma glucose, body weight and systolic blood pressure, with practically no risk of hypoglycemia (Inzucchi *et al.*, 2015). The EASD/ADA and the AACE guidelines, therefore, recommend their use, also in combination with

metformin as dual therapy, or as triple therapy in combination with metformin and sulfonylureas, an SGL2I or insulin (Garber *et al.*, 2016).

1.4.3 Insulin

All types of diabetes mellitus can, in principle, be treated by insulin (Owens, Matfin and Monnier, 2014) and multiple different insulin formulations are available to cover both basal and prandial requirements. However, insulin regimens can be cumbersome and complicated, the risk of hypoglycemia can be high and weight gain often occurs as a result of subtle overdosing.

Type 1 diabetes should be treated with multiple daily injections of prandial and basal insulin, or with a continuous subcutaneous insulin infusion by a pump. Insulin pump and continuous glucose monitoring technology have recently advanced considerably and can contribute to a reduction in the risk of hypoglycemia (Johnson *et al.*, 2019).

For type 2 diabetes, different insulin regimens can be applied, often in combination with other glucose-lowering medications and lifestyle measures.

1.5 Self-care at the center of diabetes control

Management of diabetes exceedingly depends on an individual's self-care ability, which, in turn, is determined by adequate knowledge about the disease, regular training, trust in caregivers' advice, and a high level of motivation.

1.5.1 Non-adherence to medical advice as a major barrier to diabetes control

Non-adherence to treatment recommendations is a major barrier in the management of diabetes mellitus, all over the world and particularly in low- and middle-income countries. Adherence means adapting one's behaviour to the agreed recommendations from a health care provider (Lo, 2006). Evidence from many studies suggests that adherence to medications and lifestyle modifications have a significant impact on the treatment outcome of diabetes (García-Pérez *et al.*, 2013)(Chen, Tseng and Cheng, 2013)(Dunkley *et al.*, 2014) as well as on health care costs resulting from repeated hospitalizations, complications and subsequent rehabilitation (Adegbola *et al.*, 2016). In chronic diseases, such as diabetes, the estimated rate of non-adherence to long term therapy, according to population-based studies, ranges from 36% to 93%. It is, on average,

only 50% in high-income countries and even lower in resource-limited settings (Bailey and Kodack, 2011)(Eduardo sabate, 2010). Several studies show that poor adherence is associated with inadequate glycemic control, higher mortality rates and higher medical costs (Egede *et al.*, 2014)(Egede *et al.*, 2012)(Dibonaventura *et al.*, 2014). Quality of life is also affected (Martínez *et al.*, 2008)(Aghamollaei *et al.*, 2003)(B. *et al.*, 2007). Individuals with diabetes mellitus have to make important lifestyle changes and monitor their blood glucose, apply multiple drugs, and deal with the potential complications of their diabetes. However, one study in the United States found that only 52% of diabetic subjects followed the dietary advice they were given (Anderson and Gustafson, 1989). Another study in Alexandria showed that overall diet and physical activity compliance was also poor (Nagwa F, 2007). Non-adherence rates are also high in the South-East Asia region. One study in India found that dietary prescriptions and exercise recommendations were followed regularly by only 37% and 35% of patients, respectively (Peyrot *et al.*, 2005).

Randomized control trials involving low-cost interventions to improve patient adherence in South Asia have been conducted previously by us(S. M. S. Islam *et al.*, 2014) and others (Bhurji *et al.*, 2016). Our mid-size RCT of an automated mobile phone SMS system conducted at BIHS hospital showed very promising results, but other work involving more traditional patient education tools has not been as successful (Bhurji *et al.*, 2016).

1.5.2 Knowledge about diabetes as an essential component of self-care ability

Another important factor determining self-care ability is knowledge about the disease, its management, and its complications. Several studies have shown that good knowledge about diabetes is essential for adequate metabolic control and prevention of diabetic secondary complications (Shrivastava, Shrivastava and Ramasamy, 2013)(Murugesan *et al.*, 2007)(Fatema *et al.*, 2017)(Herath *et al.*, 2017). Poor knowledge, on the other hand, is associated with a high rate of complications and, ultimately, higher health care costs (Islam, Niessen, *et al.*, 2015a)(Islam *et al.*, 2017).

In low and middle-income countries, knowledge about diabetes among individuals affected by diabetes is often even worse than in higher-income setting because of financial constraints on patient education (Ho and Li, 2014)(Badruddin *et al.*, 2002)(Saleh *et al.*, 2012).

1.6 Diabetes in Bangladesh

Bangladesh is currently experiencing an escalation of diabetes-related health and socio-economic costs. The International Diabetes Federation estimated that in Bangladesh 8.4 million adults live with diabetes, of which an estimated 4.7 million are undiagnosed. The number of Bangladeshis with diabetes is expected to rise to 15 million in 2045 (Saeedi *et al.*, 2019). In addition, the majority of adults with diabetes in Bangladesh has poor metabolic control and is therefore prone to develop diabetic secondary complications (Islam, Alam, *et al.*, 2015).

Poor metabolic control of diabetes leads to chronic morbidity including cardiovascular disease, renal failure, stroke, blindness as a result of retinopathy, and neuropathic foot ulcers. Thereby, diabetes has a serious impact on an individual's life and function in society (Shariful Islam *et al.*, 2013). However, for countries like Bangladesh, these problems are difficult to address because their health care systems are poorly funded and ill-equipped to manage chronic conditions like diabetes.

Medication adherence is particularly low in Bangladesh, which often leads to insufficient glycemic control and avoidable life-threatening complications (S. M. S. Islam *et al.*, 2014). In one study by Farzana Saleh et al., non-adherence to regular blood glucose monitoring, diet, foot care, exercise recommendations and smoking cessation was 37%, 44.8%, 43.2%, 32.2% and 37.2%, respectively (Saleh *et al.*, 2014). Another study by Shirin Jahan Mumu et al. found that the non-adherence rates to diet, exercise, blood glucose testing, foot care, smoking and betel quid chewing cessation were 25%, 88%, 25%, 32%, 70%, and 6%, respectively (Mumu *et al.*, 2014).

1.6.1 The unique system of diabetes care in Bangladesh

The Diabetic Association of Bangladesh (Bengali acronym Bangladesh Diabetic Somiti- BADAS) was established on 28 February 1956 in Dhaka by a group of dedicated professionals and at the initiative of the late National Professor Dr Muhammad Ibrahim (1911-1989). The Association started a first, small outpatient clinic in 1957. By now, BADAS has 61 Affiliated Associations and 13 Sub-affiliated Associations over the whole country and serves millions of individuals with diabetes. Medical care at its institutions is not limited to diabetes itself but tries to address a patient's needs comprehensively.

1.6.2 The specific challenges to adequate diabetes care in Bangladesh

Bangladesh has no general health insurance and patients, therefore, have many out-of-pocket expenses. The Bangladeshi diabetes care system provides some relief in this respect, but the problem nevertheless remains. Poorer people often cannot afford the medication and other supplies they require. Additionally, physician time is extremely limited in non-private care centres.

Patient education is included in standard diabetes care in Bangladesh but is limited by financial constraints and lack of qualified personnel. Additionally, a large proportion of patients has had limited school education or is even illiterate. At the tertiary care centre, where this study was conducted, each patient at least receives an information booklet and a one-hour training session at the time of diagnosis. However, this is certainly not enough to achieve adequate patient knowledge.

Another issue is the lack of routine screening for diabetic secondary complications. These examinations, too, have to be paid for by the patient and can be, for many, prohibitively expensive. Therefore, the true extent of secondary complications is often unknown and treatment occurs too late.

2 Rationale and Objectives

The management of diabetes, like that of many chronic conditions, is complex. The patient's self-care abilities are at the centre of this process, but often adherence to medical advice is suboptimal. Further, high-quality patient education is difficult to achieve and systems to screen for and treat diabetic secondary complications are logistically challenging and expensive.

To understand the current situation of these central areas of diabetes management at a tertiary care centre in Bangladesh, this study focused on patient adherence and patient knowledge about diabetes. Additionally, screening for a common diabetic secondary complication, diabetic retinopathy, was offered as part of the study to determine how often this diagnosis was missed in regular care. Based on these assessments of the current situation, recommendations for future improvements of diabetes care in Bangladesh were developed.

2.1 Specific research questions

1. Adherence to medical advice
   1.1 Which socio-demographic factors are associated with adherence to medical advice?
   1.2 How does adherence to medical advice associate with clinical outcomes?

2. Knowledge about diabetes
   2.1 How much knowledge do patients have about diabetes, its complications and its management?
   2.2 Which socio-demographic factors are associated with poor knowledge?

3. Diabetic retinopathy
   3.1 What is the prevalence of previously undiagnosed diabetic retinopathy in the study population?
   3.2 Which socio-demographic and medical factors are associated with the presence of diabetic retinopathy?

3 Methods

3.1 Study design and site

A cross-sectional, observational study was conducted between April 2017 and August 2017 at the outpatient department of the Bangladesh Institute of Health Sciences Hospital (BIHS). BIHS is a tertiary care hospital in Dhaka and is affiliated with the Diabetic Association of Bangladesh (BADAS). All patients during the respective period, who met the inclusion criteria, were asked to participate in the study.

3.2 Sampling Technique

A total of 504 consecutive adults with type 2 diabetes who were registered at BIHS hospital and attended the outpatient department for a routine visit were recruited into the study. The sample size was determined by practical reasons.

3.3 Inclusion criteria

Adults over 25 years of age with an established diagnosis of type 2 diabetes were eligible to participate in this study. The duration of diabetes had to be more than one year and only individuals on antidiabetic medication were included in the study. They also had to be registered as patients of BIHS.

3.4 Exclusion criteria

Patients with type-1 diabetes, severe physical illness not permitting participation (e.g. end-stage renal diseases, stroke, advanced cardiovascular diseases), or a mental disorder, as well as pregnant women, were excluded from the study.

3.5 Study procedures

All data were collected by two trained research assistants during the participant's visit to the outpatient department, recorded on paper and later entered into an SPSS spreadsheet.

3.5.1 Study questionnaire

A study questionnaire in Bangla was developed after a review of the relevant literature and was used for data collection. It was translated to English and back to ensure correct representation of items in both languages. Additionally, we undertook a pretest of this questionnaire among 30 patients at the same hospital to evaluate its suitability. After pretesting, modifications were applied to finalize the questionnaire.

The questionnaire was divided into three sections. Section 1 consisted of socio-demographic information, section 2 of anthropometric measurements (i.e.; height, weight, waist and hip circumferences), and clinical examination (systolic and diastolic blood pressure measurement), section 3 of questions related to knowledge about diabetes, self-care practice and the patient's lifestyle.

To assess knowledge about diabetes, we asked a total of 16 multiple-choice questions covering 9 areas: the definition of diabetes, risk factors for diabetes, symptoms of diabetes, complications of diabetes, knowledge about adequate nutrition, physical activity requirements, diabetes management, about hypoglycemia and diabetic foot care. For questions with exactly one correct response, the correct response was assigned a score of 1 and each incorrect response got a score of 0. For questions with more than one correct response, each correct response was assigned the corresponding fraction of 1. Therefore, the maximum attainable total knowledge score was 16 and the minimum score was 0. 'Poor knowledge' was defined as a score of <50% and 'good knowledge' as a score of ≥50% (Journal and Vol, 2015).

Two-point scales were used (adherence and non-adherence) to assess patients' adherence to the diet, medication, physical activity recommendations, scheduled follow-up visits and foot care according to the guidelines by the Diabetic Association of Bangladesh (BADAS) (Mahatab H, Latif ZA, no date). Regarding dietary adherence, the patient was considered non-adherent if they did not follow the recommended diet chart (total Kcal/day ± 10%) provided by a nutritionist or dietitian. Moreover, not following specific meal times and recommended quality and quantity of food was also considered as dietary non-adherence (Saleh *et al.*, 2014). Food consumption and daily calory intake were assessed using the 72-hour dietary recall method. (Mumu *et al.*, 2020)(Schröder *et al.*, 2001).

Non-adherence to medication was measured from self-reported medication adherence using the questions below (Saleh *et al.*, 2014). Each individual medicine was checked separately according to the prescription by the attending physician.

- S/he changes the prescribed amount and dose of medicine.
- S/he doesn't observe the time the medicine should be taken.
- S/he takes more than the prescribed dose.
- S/he takes less than the prescribed dose.

A patient was considered adherent to physical activity advice if s/he reported exercise or other physical activity ≥ 30 minutes per day (Mumu *et al.*, 2014) and at least 5 days in a week, corresponding to 150 minutes per week (Mendes *et al.*, 2016).

Non-adherence to foot care recommendations was concluded if a patient reported not following one of the basic foot care principles (Saleh *et al.*, 2014). These are 'Wash feet every day.', 'Trim toenails.', 'Use lotion/cream.', 'Never walk barefoot.', 'Check inside shoe & use clean and dry socks.', Check feet with a mirror weekly to see the colour change, blisters or ulcerations', and 'Always use closed and comfortable shoes or sandals.

The health care providers write the date of the next follow-up visit and blood testing in the patient's guide book. A patient was considered non-adhered if s/he missed the prescribed date by more than ± 7 days.

Non-adherence to home monitoring of blood glucose (HMBG) was recorded if a patient did not follow the monitoring schedule recommended by his/her physician.

3.5.2 Anthropometrics and clinical examination

To assess the cardiovascular status of the patient, we measured pulse rate and blood pressure. Both readings were obtained in a sitting position after a few minutes of rest. The patient's height waist and hip circumference were measured to the nearest centimetre. The body mass index (BMI) was calculated as weight / height^2 and the waist to hip ratio (WHR) as weight circumference/hip circumference.

3.5.3 Laboratory chemistry

Laboratory chemistry parameters were copied from the patient's laboratory report, as available. Fasting plasma glucose (FPG) and 2 hours after breakfast plasma glucose (2hABF) were available from all participants, as these parameters are part of any routine visit to the BIHS outpatient department. A1C, the serum lipid profile (total cholesterol (TC), triglycerides (TG), HDL cholesterol (HDL), LDL cholesterol (LDL)), and serum creatinine have to be paid for by the patient him/herself during routine clinic visits and therefore were not available in all cases.

Uncontrolled blood glucose levels were defined as A1c > 7 %, FBG >7.2 mmol/l, or 2hABF > 10 mmol/l.

3.5.4 Retinal fundus photography

Retinal fundus photography is not part of a routine visit at the BIHS outpatient department but was offered to all 504 participants as part of this study. In total, 489 participants completed this examination. Digital colour images were captured from each eye and the severity of diabetic retinopathy was categorized according to the international clinical retinopathy severity scales recommended by the Global Diabetic Retinopathy Project Group (Wilkinson *et al.*, 2003). A senior ophthalmologist graded the photographs as no retinopathy (no DR), mild non-proliferative retinopathy (NPDR), moderate NPDR, severe NPDR, and proliferative DR (PDR)**.**

3.6 Data Management

All paper questionnaires were verified for completeness by the principal investigator and stored in a save location. A standard data entry interface was designed using Microsoft Office Access for entering study data in a password-protected computer. Each entry was assigned anonymously by a unique identifier which could not be linked to the study participant's personal data. Data were checked and cleaned before analysis.

3.7 Statistical analysis

IBM SPSS version 24.0 was used in all analyses, which were also cross-checked by a trained statistician. Metric variables are represented as mean ±standard deviation and categorical variables as number and percentage. Univariate and multivariate logistic regression models were used to

identify factors associated with the presence of non-adherence. P-values were calculated for each of the test statistics and estimates using the appropriate method, a p-value equal to or greater than 0.05 was used as the standard to declare an estimate or test statistic to be non-significant.

3.8 Ethical Considerations

Informed written consent was obtained from all study participants after the nature, the purpose, and the procedures of the study had been explained. Participants were also informed about their right to withdraw from the study at any point and for any reason. Ethical approval was obtained from the Ethics and Research Review Committee of BUHS in Dhaka, Bangladesh. The Ethics Committee of LMU in Munich, Germany, also consented to this study.

4 Results

4.1 Socio-demographic and clinical characteristics of the study cohort

Among the 504 participants in this study, 289 were women (57.3%) and 215 were men (42.7%). The age of the participants was 52.4±11.2 years. Only 2.2% of the study participants had a normal Waist to Hip ratio (WHR) whereas the remaining 97.8% had a waist to hip ratio in the health risk group, defined as > 0.90 for men and > 0.85 for women. Most of the participants were from the middle-income group (52.6%), 31.5% from the lower-income and 16% from the high-income group. More than 50% of the study subjects were housewife (51.4%). 20.2% of the study population were obese, 47.2% were overweight and 1.4% were underweight. 17.1% were illiterate, while 37.9% had higher secondary education or above. Of all participants,64.1% had a family history of diabetes mellitus. 32.5% of the participants had chronic kidney disease (CKD) and 18.8% had diabetic retinopathy. The mean duration of Diabetes was 9.64±6.97 years. **(Table 4.1)**.

Table 4.1: Baseline characteristics of the study participants.

Characteristics	N	(%)
Gender		
Male	215	42.7
Female	289	57.3
Age		
<=40 years	88	17.5
41-55 years	221	43.8
56+ years	195	38.7
(Mean ± SD)	*(52.4 ± 11.2)*	
Residence		
Urban	409	81.2
Rural	95	18.8
Marital status		
Unmarried	7	1.4
Married	443	87.9
Widow/divorced	54	10.7
BMI		
Underweight	7	1.4
Normal	157	31.2
Overweight	238	47.2

Obese	102	20.2
Mean ± SD	26.97± 3.93	
WHR (Health risk, male > 0.90 & female > 0.85)		
Normal	11	2.2
Health risk	493	97.8
(Mean ± SD)	*(0.99±0.06)*	
Education		
Illiterate	86	17.1
Secondary	227	45.0
Higher Secondary & above	191	37.9
Occupation		
Unemployed/Retired	85	16.9
Service	92	18.3
Business	68	13.5
Housewife	259	51.4
Family income		
Low-middle Income (< Tk.21271)	159	31.5
Upper-middle Income (Tk. 21271- Tk.65761)	265	52.6
High Income (> Tk.65761)	80	15.9
(Mean ± SD)	*(44353.57±41793.54)*	
Family history of diabetes		
Yes	323	64.1
No	181	35.9
HbA1c (n=301)		
Good Control (≤7)	44	14.6
Poorly Control (7-8)	68	22.5
Uncontrolled (≥8)	189	62.9
(Mean ± SD)	*(8.97±1.85)*	
Fasting Blood Sugar		
Uncontrolled (>7.2)	352	69.8
Control (≤ 7.2)	152	30.2
(Mean ± SD)	*(9.30±3.80)*	
Two hours after breakfast		
Uncontrolled (> 10)	361	71.6
Control (≤ 10)	143	28.4
(Mean ±SD)	*(12.78±4.44)*	
Total Cholesterol (n=188)		
High (> 200)	64	34.0
Normal (≤ 200)	124	66.0
HDL (n=145)		
Normal (≥ 40 for male and ≥ 50 for female)	43	29.7
Low (< 40 for male and < 50 for female)	102	70.3
LDL (n=174)		
High (> 100)	89	51.1

Normal (≤ 100)	85	48.9
TG (n= 200)		
Normal	120	60.0
Abnormal	80	40.0
eGFR (n=329)		
CKD (eGFR ≤ 60mL/min/1.73 m²)	107	32.5
No CKD (eGFR>60mL/min/1.73 m²)	222	67.5
(Mean ± SD)	*(67.74±21.27)*	
Diabetic Retinopathy (n=489)		
NDR	397	81.2
NPDR mild	57	11.7
NPDR moderate	28	5.7
NPDR severe	4	0.8
PDR	3	0.6
Systolic Blood Pressure (SBP) (n= 504)		
Uncontrolled (>140 mm of Hg)	125	24.8
Control	379	75.2
(Mean ± SD)	*(127.86±15.34)*	
Diastolic Blood Pressure (DBP) (n= 504)		
Uncontrolled (<90 mm of Hg)	100	19.8
Control	404	80.2
(Mean ± SD)	*(79.87 ± 8.51)*	
Duration of Diabetes		
< 10 years	291	57.7
>= 10 years	213	42.3
(Mean ± SD)	*(9.64 ± 6.97)*	
Total Knowledge Score		
Good Knowledge	147	29.2
Poor Knowledge	357	70.8
(Mean± SD)	*(6.84±2.16)*	

4.2 Anthropometric characteristics

The mean (95% CI) BMI of all study subjects was 26.97 kg/m^2 (24.16 to 29.78). More than half of the study participants were overweight and obese (67.4%). The BMI range in women was higher than that in men (**Figure 4.1**).

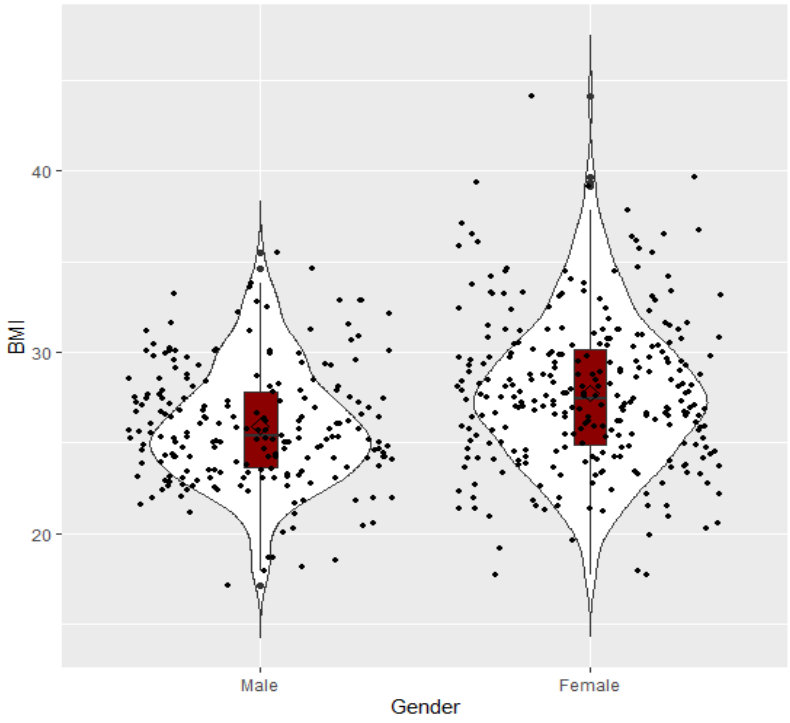


Figure 4.1: Body Mass Index (BMI) of study participants by gender

The mean waist to hip ratio of the study participants correlated with age in a linear fashion. Older participants, on average, also had a longer duration of diabetes. These findings are visualized in **Figure 4.2**.

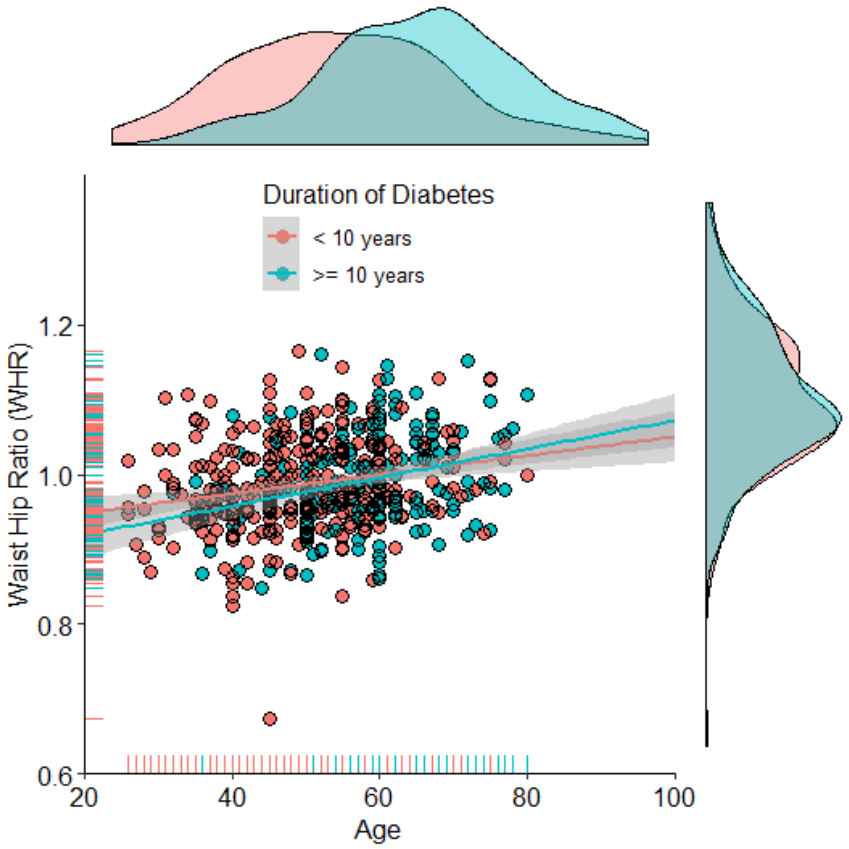


Figure 4.2: Waist Hip Ratio (WHR), age and diabetes duration of the study participants

4.3 Biochemical characteristics

Study participants were categorized as having or not having controlled diabetes according to the cutoff values described in chapter 3. Based on FPG, 69.8% had uncontrolled diabetes. 71.6% had uncontrolled diabetes according to the 2hABG and even 85.4% had uncontrolled diabetes based on A1C (**Figure 4.3**).

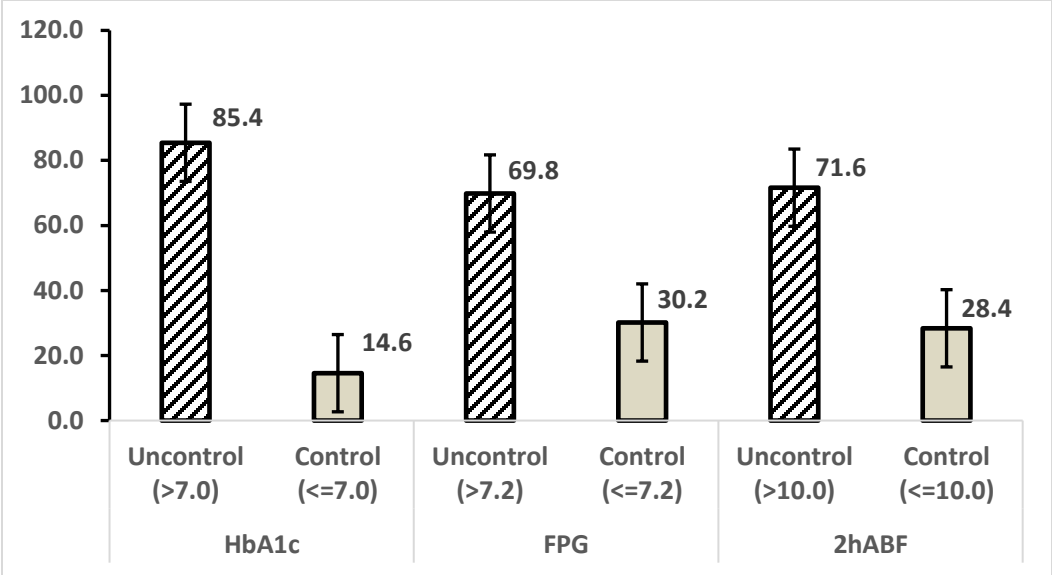


Figure 4.3: Blood sugar profile of the study participants

4.4 Comorbidities and diabetic secondary complications

Figure 4.4 depicts the percentages of study participants with individual comorbidities according to hospital records. Hypertension (40.08%) and eye problems (30.95) were the most common problems in this area.

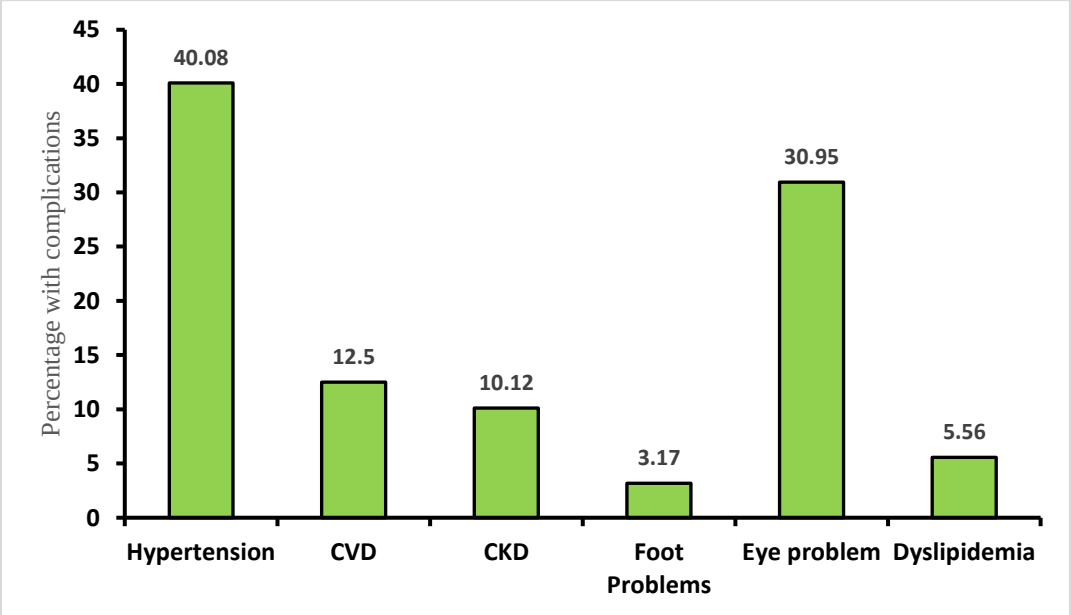


Figure 4.4: Other complications of the study participants

4.5 Adherence to medical advice

To study adherence to medical advice in detail, we first assessed the overall adherence rates. Overall drug adherence was 52.4% (**Table 4.2**). Among the insulin treated subgroup (n=260), the adherence rate was in a comparable range (51.9%). 211 participants were on oral drugs. In the Sulphonylurea group, the adherence rate was 72.5%, it was 75.5% for Metformin and 74.2% for DPP4 inhibitors (**Figure 4.6**).

Only some participants were adherent to dietary advice (28.2%). Of the 479 participants who received advice for physical activity, 42.4% were adherent. Of the 456 participants who had been given a date for a scheduled follow-up visit by their physician, 58.6% were adherent. Regarding home monitoring of blood glucose (HMBG), 270 participants had received the advice to do so, 88.2 % were adherent. 254 participants had been given advice for foot care, and 68.1% were adherent to this advice (**Table 4.2; Figure 4.5**)

Table 4.2: Frequency of adherence to medical advices among the study subjects

Characteristics	**N**	**(%)**
Overall Drug Adherence		
Yes	264	52.4
No	240	47.6
Insulin Adherence (n=260)		
Yes	135	51.9
No	125	48.1
Sulphonylurea Adherence (n=211)		
Yes	153	72.5
No	58	27.5
Metformin Adherence (n=261)		
Yes	197	75.5
No	64	24.5
DPP4 Inhibitor Adherence (n=306)		
Yes	227	74.2
No	79	25.8
Advice for Diet	504	100 %
Adherence to Dietary Advices		
Yes	142	28.2
No	362	71.8

Advice for physical exercise (n=504)		
Yes	479	95.0
No	25	5.0
Adherence of Physical Activities (n=479)		
Adherence	203	42.4
Non-Adherence	276	57.6
Advice for follow-up visit by Physician		
Yes	456	90.5
No	48	9.5
Adherence of Follow-up visit (Physician)		
Adherence	267	58.6
Non-Adherence	189	41.4
Advice to HMBG		
Yes	271	53.8
No	233	46.2
Adherence to HMBG		
Yes	239	88.2
No	32	11.8
Advice of Foot care from physician		
Yes	254	50.4
No	250	49.6
Adherence of Foot care from physician		
Yes	173	68.1
No	81	31.9

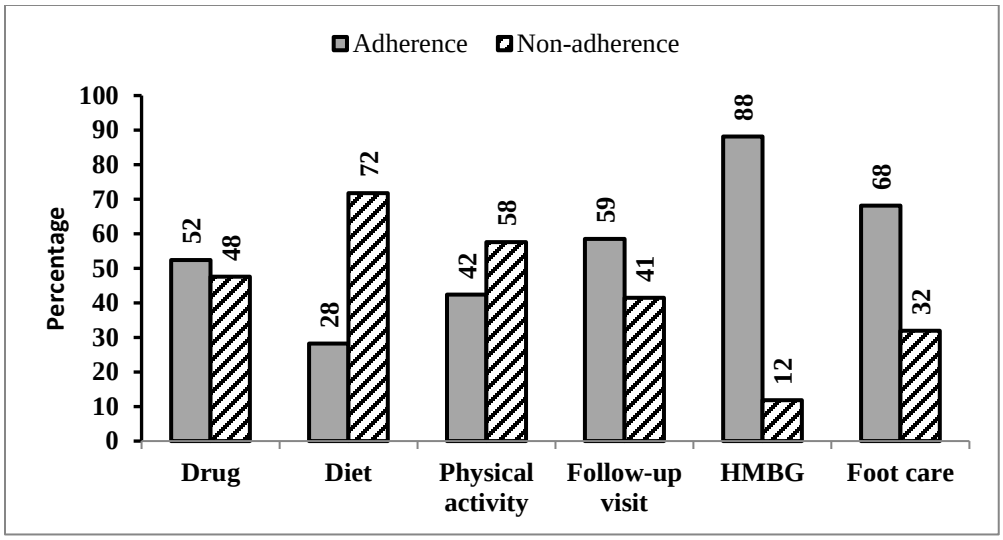


*Figure 4.5**:** Adherence (solid grey) and non-adherence rate (striped) of the study subjects regarding drug therapy, diet, physical activity, scheduled follow-up visits and foot care*

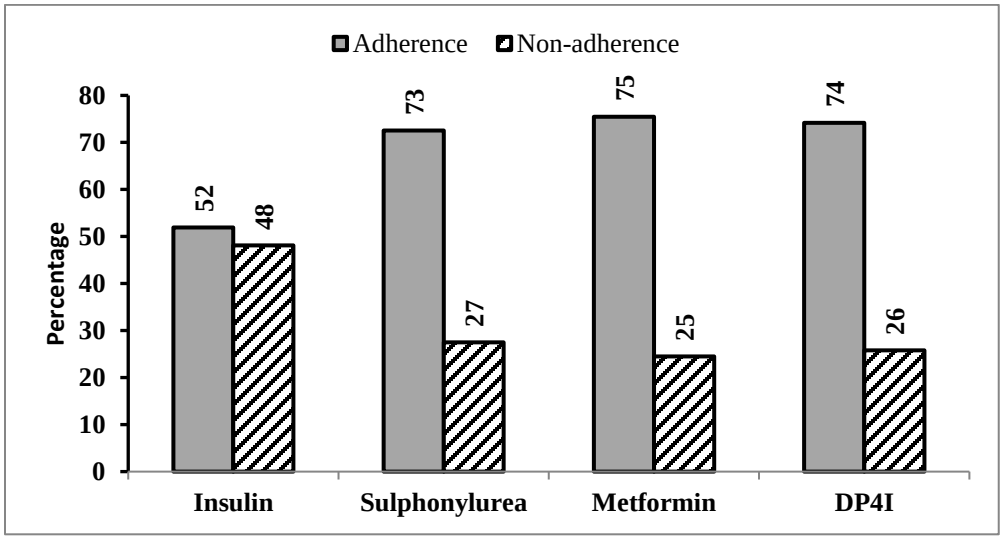


Figure 4.6: Adherence (solid grey) and non-adherence rates (striped) among users of different antidiabetic drugs

4.5.1 Factors for non-adherence

To identify factors associated with adherence versus non-adherence to medical advice, we next applied logistic regression models. We focused on adherence to drug therapy, dietary and physical activity advice. First, we ran univariate analyses to identify individual associations. Those with a p-value of less than 0.05 were then included in the multivariate analysis. The univariate analyses are shown in the left part of the data table, the combined multivariate model is shown on the right.

4.5.1.1 Drug adherence

In univariate analyses, drug adherence was higher among the age group of 41-55 years and among those with hypertension. It was lower in the insulin treated group compared to those with oral medications and in those with an eye problem. In the multivariate analysis, age of 41 years or more, coexisting hypertension, and oral medication versus insulin were independently associated with higher drug adherence (**Table 4.3**). Eye problems were associated with lower adherence.

Table 4.3: Factors associated with drug adherence

Characteristics	Non-adherence	Adherence	COR [95% CI]	p-value	AOR [95% CI]	p-value
	N (%)	N (%)				
Age						
<= 40 years	50(56.8)	38(43.2)	Ref.		Ref.	
41-55 years	**108(48.9)**	**113(51.1)**	**1.81[1.09-3.02]**	**0.022**	**2.31[1.34-3.98]**	**0.003**
56+ years	82(42.1)	113(57.9)	1.32[0.89-1.94]	0.164	**1.60[1.06-2.42]**	**0.027**
Gender						
Male	105(48.8)	110(51.2)	Ref.			
Female	135(46.7)	154(53.3)	1.09[0.76-1.55]	0.637		
Residence						
Urban	191(46.7)	218(53.3)	Ref.			
Rural	49(51.6)	46(48.4)	0.82[0.53-1.29]	0.391		
Occupation						
Unemployment/ Retired	37(43.5)	48(56.5)	Ref.			
Service	49(53.3)	43(46.7)	0.91[0.55-1.49]	0.698		

Business	35(51.5)	33(48.5)	1.34[0.83-2.16]	0.228		
Housewife	119(45.9)	140(54.1)	1.25[0.73-2.13]	0.417		
Education						
Illiterate	43(50)	43(50)	Ref.			
Secondary	112(49.3)	115(50.7)	1.25[0.75-2.08]	0.396		
Higher Secondary & Above	85(44.5)	106(55.5)	1.21[0.83-1.79]	0.324		
Marital status						
Unmarried	4(57.1)	3(42.9)	Ref.			
Married	215(48.5)	228(51.5)	0.71[0.16-3.2]	0.653		
Widow/Divorced	21(38.9)	33(61.1)	0.48[0.1-2.35]	0.363		
Monthly family income						
low and lower middle income	94(49.7)	95(50.3)	Ref.			
upper middle income	123(48.2)	132(51.8)	1.59[0.88-2.88]	0.125		
high income	23(38.3)	37(61.7)	1.35[0.81-2.24]	0.168		
Family type						
Nuclear	158(46.5)	182(53.5)	Ref.			
Joint	82(50)	82(50)	0.87[0.6-1.26]	0.457		
Family history						
No	158(48.9)	165(51.1)	Ref.			
Yes	82(45.3)	99(54.7)	1.16[0.8-1.67]	0.436		
Duration of diabetes mellitus						
<10 years	134(46)	157(54)	Ref.			
>= 10 years	106(49.8)	107(50.2)	0.86[0.6-1.23]	0.409		
Complication-HTN						
No	155(51.3)	147(48.7)	Ref.			
Yes	**85(42.1)**	**117(57.9)**	**1.45[1.01-2.08]**	**0.042**	**1.49[1.02-2.18]**	**0.04**
Complication-CKD						
No	220(48.6)	233(51.4)	Ref.			
Yes	20(39.2)	31(60.8)	1.46[0.81-2.64]	0.207		
Complication-Eye						
No	153(44)	195(56)	Ref.			
Yes	**87(55.8)**	**69(44.2)**	**0.62[0.43-0.91]**	**0.014**	**0.61[0.41-0.91]**	**0.015**
Complication-DL						
No	229(48.1)	247(51.9)	Ref.			
Yes	11(39.3)	17(60.7)	1.43[0.66-3.12]	0.366		
Complication-CVD						
No	209(47.4)	232(52.6)	Ref.			
Yes	31(49.2)	32(50.8)	0.93[0.55-1.58]	0.787		
Complication-Foot						
No	231(47.3)	257(52.7)	Ref.			
Yes	9(56.3)	7(43.8)	0.70[0.26-1.91]	0.484		

Treatment type						
OAD	96(39.0)	150(61.0)	Ref.			
Insulin	17(44.7)	21(55.3)	**0.47[0.32-0.68]**	**<0.001**	**0.38[0.26-0.57]**	**<0.001**
OAD & Insulin	127(57.7)	93(42.3)	0.59[0.3-1.19]	0.139	0.50[0.24-1.04]	0.064
BMI						
Normal	6(85.7)	1(14.3)	Ref.			
Under weight	67(42.7)	90(57.3)	0.12[0.01-1.06]	0.056		
Over weight	113(47.5)	125(52.5)	0.15[0.02-1.27]	0.082		
Obase	54(52.9)	48(47.1)	0.19[0.02-1.61]	0.127		
WHR						
Normal	5(45.5)	6(54.5)	Ref.			
Health risk	235(47.7)	258(52.3)	1.09[0.33-3.63]	0.884		
Overall knowledge						
Poor	174(48.7)	183(51.3)	Ref.			
Good	66(44.9)	81(55.1)	0.86[0.58-1.26]	0.433		

4.5.1.2 Dietary adherence

As mentioned above, adherence to dietary advice was the lowest among all categories examined (28%), but we found no specific factor associated with adherence in this category (**Table 4.4**).

Table 4.4: Factors for dietary non-adherence

Characteristics	Non-adherence	Adherence	COR [95% CI]	p-value	AOR [95% CI]	p-value
	N (%)	N (%)				
Age						
<= 40 years	47(54.0)	40(46.0)	Ref.			
41-55 years	100(45.9)	118(54.1)	1.19[0.71-1.97]	0.507		
56+ years	96(49.7)	97(50.3)	0.86[0.58-1.26]	0.433		
Gender						
Male	109(51.7)	102(48.3)	Ref.			
Female	134(46.7)	153(53.3)	1.22[0.85-1.74]	0.273		
Residence						

Urban	200(49.4)	205(50.6)	Ref.	
Rural	43(46.2)	50(53.8)	1.13[0.72-1.78]	0.584
Occupation				
Unemployment/Retired	43(51.2)	41(48.8)	Ref.	
Service	47(51.1)	45(48.9)	1.24[0.75-2.02]	0.401
Business	35(53.8)	30(46.2)	1.23[0.76-1.98]	0.394
Housewife	118(45.9)	139(54.1)	1.37[0.8-2.37]	0.254
Education				
Illiterate	38(44.2)	48(55.8)	Ref.	
Secondary	108(48.2)	116(51.8)	0.74[0.44-1.24]	0.256
Higher Secondary & Above	97(51.6)	91(48.4)	0.87[0.59-1.29]	0.494
Marital status				
Unmarried	2(28.6)	5(71.4)	Ref.	
Married	217(49.5)	221(50.5)	2.45[0.47-12.79]	0.286
Widow/Divorced	24(45.3)	29(54.7)	2.07[0.37-11.63]	0.409
Monthly family income				
low and lower middle income	84(44.7)	104(55.3)	Ref.	
upper middle income	131(52.2)	120(47.8)	0.93[0.54-1.6]	0.785
high income	28(47.5)	31(52.5)	1.05[0.63-1.75]	0.842
Family type				
Nuclear	164(49.1)	170(50.9)	Ref.	
Joint	79(48.2)	85(51.8)	1.04[0.71-1.51]	0.845
Family history				
No	154(48.1)	166(51.9)	Ref.	
Yes	89(50)	89(50)	0.93[0.64-1.34]	0.688
Duration of diabetes mellitus				
<10 years	142(49.3)	146(50.7)	Ref.	
>= 10 years	101(48.1)	109(51.9)	1.05[0.74-1.5]	0.790
Complication-HTN				
No	146(49)	152(51)	Ref.	
Yes	97(48.5)	103(51.5)	0.98[0.69-1.4]	0.914
Complication-CKD				
No	221(49.4)	226(50.6)	Ref.	
Yes	22(43.1)	29(56.9)	1.29[0.72-2.31]	0.394
Complication-Eye				
No	177(51.5)	167(48.5)	Ref.	
Yes	66(42.9)	88(57.1)	1.41[0.96-2.07]	0.077
Complication-DL				
No	230(48.9)	240(51.1)	Ref.	
Yes	13(46.4)	15(53.6)	1.11[0.51-2.37]	0.797
Complication-CVD				

No	214(49.2)	221(50.8)	Ref.	
Yes	29(46)	34(54)	1.14[0.67-1.93]	0.639
Complication-Foot				
No	238(49.3)	245(50.7)	Ref.	
Yes	5(33.3)	10(66.7)	1.94[0.65-5.77]	0.232
Treatment type				
OAD	125(51.2)	119(48.8)	Ref.	
Insulin	19(54.3)	16(45.7)	1.27[0.88-1.84]	0.196
OAD & Insulin	99(45.2)	120(54.8)	1.44[0.7-2.95]	0.319
BMI				
Normal	4(57.1)	3(42.9)	Ref.	
Under weight	71(45.8)	84(54.2)	0.63[0.14-2.93]	0.559
Over weight	121(51.1)	116(48.9)	0.78[0.17-3.57]	0.751
Obese	47(47.5)	52(52.5)	0.68[0.14-3.19]	0.623
WHR				
Normal	6(60)	4(40)	Ref.	
Health risk	237(48.6)	251(51.4)	0.63[0.18-2.26]	0.478
Overall knowledge				
Poor	170(48)	184(52)	Ref.	
Good	73(50.7)	71(49.3)	1.11[0.76-1.64]	0.589

4.5.1.3 Physical activity adherence

In univariate analyses, physical activity advice was followed less often by women, and by participants with eye problems, CVD and insulin treatment. Individuals with higher secondary & above education, who were widowed or divorced, and who had dyslipidemias followed the advice more often. In the multivariate analysis, female gender, married and having an eye problem were independently associated with less adherence. Having dyslipidemia associated with higher adherence (**Table 4.5**).

Table 4.5: Factor for physical activity non-adherence

Characteristics	**Non-adherence**	**Adherence**	**COR**	**p-value**	**AOR**	**P-value**
	N (%)	**N (%)**	**[95% CI]**		**[95% CI]**	
Age						

<= 40 years	46(54.8)	38(45.2)	Ref.			
41-55 years	124(58.5)	88(41.5)	0.88[0.52-1.48]	0.628		
56+ years	106(57.9)	77(42.1)	1.02[0.69-1.53]	0.909		
Gender						
Male	105(51.2)	100(48.8)	Ref.		Ref.	
Female	171(62.4)	103(37.6)	**0.63[0.44-0.91]**	**0.014**	**0.27[0.09-0.78]**	**0.016**
Residence						
Urban	222(57.2)	166(42.8)	Ref.			
Rural	54(59.3)	37(40.7)	0.92[0.58-1.46]	0.712		
Occupation						
Unemployment/Retired	40(51.3)	38(48.7)	Ref.			
Service	52(57.1)	39(42.9)	0.66[0.4-1.1]	0.112		
Business	31(50.8)	30(49.2)	0.84[0.51-1.36]	0.473		
Housewife	153(61.4)	96(38.6)	0.65[0.37-1.14]	0.132		
Education						
Illiterate	51(63)	30(37)	Ref.		Ref.	
Secondary	132(61.1)	84(38.9)	1.63[0.95-2.78]	0.075	1.28[0.67-2.44]	0.451
Higher Secondary & Above	93(51.1)	89(48.9)	**1.5[1.01-2.24]**	**0.045**	1.36[0.86-2.14]	0.188
Marital status						
Unmarried	1(14.3)	6(85.7)	Ref.		Ref.	
Married	238(56.7)	182(43.3)	7.85[0.94-65.75]	0.058	0.04[0.019-0.049]	**0.011**
Widow/Divorced	37(71.2)	15(28.8)	**14.8[1.64-133.62]**	**0.016**	0.63[0.32-1.25]	0.187
Monthly family income						
low and lower middle income	103(56)	81(44)	Ref.			
upper middle income	143(60.3)	94(39.7)	0.98[0.56-1.71]	0.936		
high income	30(51.7)	28(48.3)	1.04[0.62-1.75]	0.890		
Family type						
Nuclear	181(55.2)	147(44.8)	Ref.			
Joint	95(62.9)	56(37.1)	0.73[0.49-1.08]	0.112		
Family history						
No	172(56)	135(44)	Ref.			
Yes	104(60.5)	68(39.5)	0.83[0.57-1.22]	0.346		
Duration of diabetes mellitus						
<10 years	156(56.5)	120(43.5)	Ref.			
>= 10 years	120(59.1)	83(40.9)	0.9[0.62-1.3]	0.571		
Complication-HTN						
No	163(58.2)	117(41.8)	Ref.			
Yes	113(56.8)	86(43.2)	0.94[0.65-1.36]	0.755		
Complication-CKD						

No	250(58)	181(42)	Ref.			
Yes	26(54.2)	22(45.8)	1.17[0.64-2.13]	0.610		
Complication-Eye						
No	180(54.4)	151(45.6)	Ref.			
Yes	96(64.9)	52(35.1)	**0.65[0.43-0.96]**	**0.032**	**0.65[0.43-0.98]**	**0.041**
Complication-DL						
No	268(59)	186(41)	Ref.			
Yes	8(32)	17(68)	**3.06[1.29-7.24]**	**0.011**	**3.03[1.24-7.42]**	**0.015**
Complication-CVD						
No	233(55.9)	184(44.1)	Ref.			
Yes	43(69.4)	19(30.6)	**0.56[0.32-0.99]**	**0.047**	0.55[0.30-1.01]	0.056
Complication-Foot						
No	270(58.1)	195(41.9)	Ref.			
Yes	6(42.9)	8(57.1)	1.85[0.63-5.41]	0.263		
Treatment type						
OAD	125(53.2)	110(46.8)	Ref.		Ref.	
Insulin	15(51.7)	14(48.3)	**0.66[0.45-0.96]**	**0.031**	0.74[0.49-1.12]	0.152
OAD & Insulin	136(63.3)	79(36.7)	0.62[0.29-1.36]	0.233	0.68[0.30-1.53]	0.348
BMI						
Normal	5(71.4)	2(28.6)	Ref.			
Under weight	71(49.3)	73(50.7)	0.39[0.07-2.07]	0.268		
Over weight	133(58.1)	96(41.9)	0.55[0.11-2.92]	0.486		
Obase	67(67.7)	32(32.3)	0.84[0.15-4.55]	0.837		
WHR						
Normal	4(36.4)	7(63.6)	Ref.			
Health risk	272(58.1)	196(41.9)	2.43[0.7-8.41]	0.161		
Overall knowledge						
Poor	201(59.8)	135(40.2)	Ref.		Ref.	
Good	75(52.4)	68(47.6)	0.74[0.5-1.1]	0.136	1.18[0.77-1.82]	0.453

4.5.2 Clinical outcome and non-adherence

Several adverse clinical outcomes associated with drug non-adherence. These were higher A1C, FPG, and 2hAPG, as well as the presence of diabetic retinopathy. The estimated eGFR was also higher in individuals with drug non-adherence (**Table 4.6**). No clinical outcomes were associated with dietary non-adherence (**Table 4.7**). Higher BMI, A1C, FPG, and 2hAPG were the adverse clinical outcomes associated with physical activity non-adherence (**Table 4.8**).

Table 4.6: Association between clinical outcome and drug adherence

Variables	**Drug Adherence**	**Drug Non-adherence**	**P-value**
BMI	26.82 ± 3.85	27.13 ± 4.02	0.361
WHR	0.99 ± 0.06	0.99 ± 0.06	0.746
HbA1c (n=301)	7.97 ± 1.40	10.05 ± 1.70	**<0.001**
FPG	7.99 ± 2.24	10.73 ± 4.00	**<0.001**
2hABF	11.06 ± 3.27	14.67 ± 4.78	**<0.001**
eGFR (n=329)	64.41 ± 19.47	71.38 ± 22.60	**0.003**
Retinopathy			
NDR	218 (54.91%)	179 (45.09%)	
DR	34 (36.96%)	58 (63.04%)	**0.002**
SBP	127.71 ± 16.17	128.03 ± 14.40	0.813
DBP	79.85 ± 8.65	79.90 ± 8.38	0.950
Total Cholesterol	181.53 ± 50.42	178.10 ± 47.45	0.632
HDL	40.19 ± 8.95	38.27 ± 9.85	0.223
LDL	102.77 ± 37.49	105.16 ± 33.74	0.658
TG	181.73 ± 98.34	210.65 ± 125.83	0.071

Table 4.7: Association between clinical outcome and dietary adherence

Variables	Diet Adherence	Diet Non-adherence	P-value
BMI	26.91 ± 3.91	27.01 ± 3.94	0.769
WHR	0.99 ± 0.07	0.99 ± 0.06	0.287
HbA1c (n=301)	9.01 ± 1.79	8.96 ± 1.96	0.792
FPG	9.24 ± 3.3	9.36 ± 3.7	0.697
2hABF)	12.68 ± 4.15	12.88 ± 4.76	0.617
eGFR (n=329)	66.99 ± 22.17	68.43 ± 20.4	0.542
Retinopathy			
NDR	131 (33.0%)	266 (67.0%)	0.280

DR	25 (27.17%)	67 (72.83%)	
SBP	128.93 ± 16.31	126.67 ± 14.24	0.100
DBP	80.43 ± 8.72	79.28 ± 8.38	0.134
Total Cholesterol	185.45 ± 45.48	174.08 ± 50.96	0.115
HDL	39.26 ± 9.39	39.09 ± 9.61	0.911
LDL	107.58 ± 33.64	99.55 ± 36.54	0.137
TG	181.07 ± 84.04	211.19 ± 133.47	0.057

Table 4.8: Association between clinical outcome and adherence to physical activity

Variables	**Physical Activity Adherence**	**Physical Activity Non-adherence**	**P-value**
BMI	26.49 ± 3.57	27.46 ± 4.16	**0.008**
WHR	0.98 ± 0.06	0.99 ± 0.06	0.221
HbA1c (n=301)	8.48 ± 1.67	9.38 ± 1.94	**<0.001**
FPG	8.45 ± 2.67	9.89 ± 3.76	**<0.001**
2hABF	11.96 ± 3.75	13.28 ± 4.71	**0.001**
eGFR (n=329)	68.54 ± 19.58	67.24 ± 22.66	0.602
Retinopathy			
NDR	164 (43.39%)	214 (56.61%)	0.396
DR	33 (38.37%)	53 (61.63%)	
SBP	127.55 ± 15.43	128.15 ± 15.15	0.671
DBP	79.75 ± 8.17	80.11 ± 8.66	0.650
Total Cholesterol	172.93 ± 49.44	184.06 ± 48.43	0.134
HDL	39.43 ± 9.64	39.15 ± 9.75	0.868
LDL	99.68 ± 35.72	109.66 ± 35.69	0.079
TG	186.85 ± 101.40	199.06 ± 122.59	0.462

4.5.3 Reasons for non-adherence

In the study questionnaire, we also asked the study participants for their reasons to not follow the medical advice they were given.

4.5.3.1 Drugs

The most common reasons given for drug non-adherence were ‘forgot to take medication’ (59.1%), ‘too busy with work or family’ (43.8%), and financial constraints (29.3%). Less frequently given reasons were ‘was not sick enough to take medicine’ (18.8%), ‘away from home’ (10.6%), ‘adverse effects’ (12.5%), ‘taking other drugs like herbal, homeopath, ayurvedic or traditional medicine’ (5.3%), ‘could not take Insulin without the help of another person’ (2.9%), and ‘taking different medicine according to the advice of physician other than attending physician’ (6.3%). (**Table 4.9**)

Table 4.9: Reasons for non-adherence to prescribed drug therapy

Reasons	**N**	**%**
Forgot to take	123	59.1%
Too busy (work/ Family)	91	43.8%
Too expensive/ Cost of medicine	61	29.3%
Patient away from home	22	10.6%
Wasn't sick enough	35	16.8%
Doesn't like due to adverse effects	26	12.5%
Prefers herbal/ homeo/ ayurvedic/ traditional drugs	11	5.3%
Could not take Insulin without help of another person	6	2.9%
Taking different medicine according to the advice of another physician	13	6.3%

4.5.3.2 Diet

The reasons given for dietary non-adherence were ‘lack of willingness or laziness to make recommended food’ (55.3%), ‘too busy to take recommended food’ (15.6%),

'nutritionist/physician did not explain the diet properly' (15.3%), 'felt hungry with recommended food' (12.3%), 'forgot to take recommended food' (5.8%). **(Table 4.10)**

Table 4.10: Reasons for non-adherence to dietary advice

Reasons	**N**	**%**
Forgot to take recommended food	21	5.8%
Too busy (work/family)	57	15.6%
Patient felt hungry with this recommended amount of food	45	12.3%
Lack of willingness/laziness to make recommended food	202	55.3%
The nutritionist /physician did not explain the recommended diet properly	56	15.3%

4.5.3.3 Physical activity

The reasons given for non-adherence to physical activity advice were 'physical discomfort' (46.4%), 'too busy' (33.6%), 'lack of willingness or laziness' (20.0 %), 'educator or physician did not explain properly' (10.9%), and 'forgot to do' (3.4 %) (**Table 4.11**).

Table 4.11: Reasons given for non-adherence to physical exercise.

Reasons	**N**	**Percentage**
Forgot to do	9	3.4%
Too busy	89	33.6%
Physical discomfort	123	46.4%
Lack of willingness/laziness to do	53	20.0%
Educator/physician was not properly instructed	29	10.9%

4.5.3.4 Foot care

The most common reasons given for non-adherence to foot care were ‘not properly instructed’ (56.2%), ‘too busy’ (13.1%) and ‘don’t like it’ (12.1%). Reasons given less often are listed in **Table 4.12**.

Table 4.12: Reasons for non-adherence to foot care

Reasons	**N**	**%**
Forgot to do	26	8.3%
Too busy	41	13.1%
Doesn't like to do	38	12.1%
Did not feel to do so	11	3.5%
Feeling physically discomfort	21	6.7%
Educator/ Physician did not instruct me properly	176	56.2%

4.5.3.5 Follow up visits

The reasons given for not appearing for the recommended follow up visit were ‘too busy’ (30.8%), ‘lack of willingness/laziness to come’ (24 %), ‘lack of money’ (16.3 %), ‘was not feeling sick enough’ (14.5%), ‘forgot to visit’ (6.3%), and ‘poor structure of health care facility (1.8%) (**Table 4.13**).

Table 4.13: Reasons for non-adherence to the Follow-up visit

Reasons	N	%
Forgot to go	14	6.3%
lack of money	36	16.3%
Too busy	68	30.8%

Was not feeling sick enough	32	14.5%
Poor structure of health care facility	4	1.8%
Lack of willingness/laziness to come	53	24.0%

4.5.3.6 Home monitoring of blood glucose

The reasons given for not following the recommended home monitoring of blood glucose (HMBG) regimen were 'don't have monitoring device' (32.4%), 'negligence' (32.4%), physical discomfort (26.4%), and 'not properly instructed' (26.5%). Other reasons given are listed in **Table 4.14**

Table 4.14: Reasons for non-adherence to home monitoring of blood glucose

Reasons	**N**	**Percentage**
Don't have a monitoring device	11	32.4%
Forgot to do	6	17.6%
Fear to test	5	14.7%
Too busy	4	11.8%
Absence of helping person	5	14.7%
Physically discomfort	9	26.5%
Negligence	11	32.4%
Educator/Physician were not properly instructed	9	26.5%

4.6 Knowledge about diabetes

As part of the study questionnaire, we also examined the participants knowledge in nine areas of diabetes itself and the care for this disease.

The mean total knowledge score covering all nine areas of knowledge about diabetes was 6.8±2.2 out of the maximum possible score of 16. One hundred forty-seven participants (29%) had good

knowledge (a score of at least 8), whereas 357 participants (71%) had poor knowledge (a score of less than 8; (**Figure 4.7**).

4.6.1 Individual knowledge areas

Regarding the individual knowledge areas, the proportion of subjects with good knowledge was lowest in the areas of diabetic symptoms (18%), risk factors for diabetes (20%), foot care (22%), hypoglycemia (27%) and complications (28 %). It was highest in the areas of recommended physical activity (79%) and recommended diet (60%) (**Figure 4.8**)

4.6.2 Factors associated with good knowledge about diabetes

Factors associated with good knowledge, in univariate logistic regression analyses, were male gender, a higher level of education, having learned an occupation, a higher family income, a duration of diabetes of 10 years or more. With multivariate adjustment, a higher level of education, a higher family income, a duration of diabetes of 10 years or more, and controlled fasting blood glucose remained independently associated with good knowledge (**Table 4.15**).

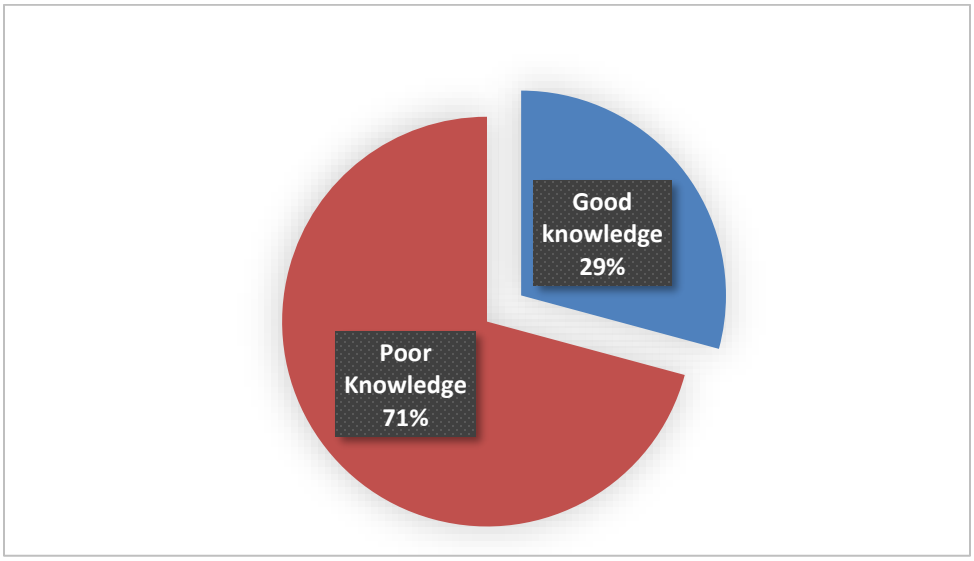


Figure 4.7: Proportions of study participants with good vs. poor knowledge about diabetes

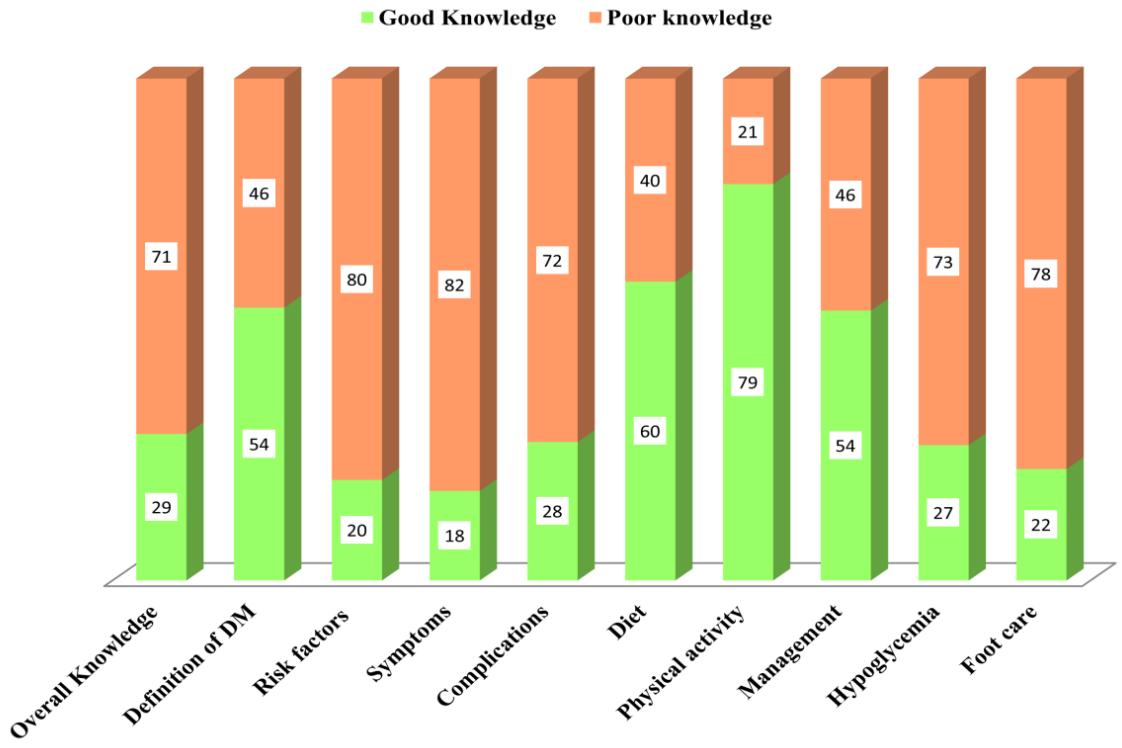


Figure 4.8: Proportions of participants with good vs. poor knowledge about diabetes in the nine different areas of knowledge examined in this study

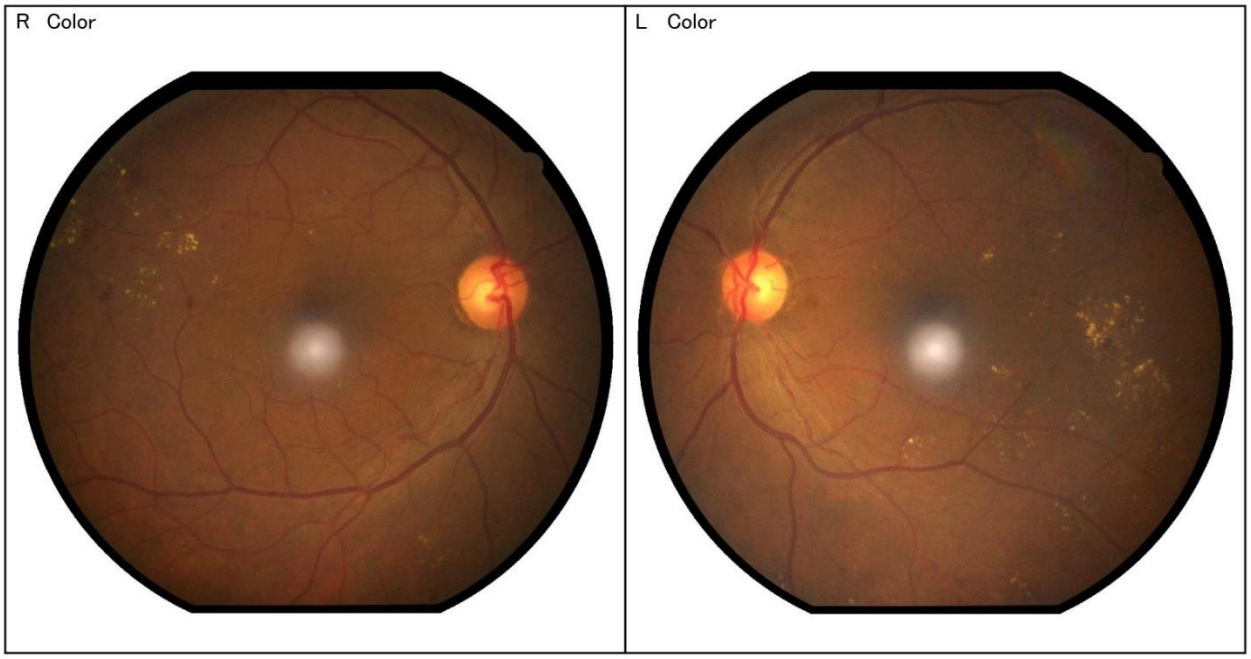
Table 4.15: Factors associated with good knowledge about diabetes

Variables		**univariate**		**with multivariate adjustment**	
		OR [95% CI]	**p-value**	**OR [95% CI]**	**p-value**
Age (in years)	≤40 years	Ref.			
	41-55 years	0.86[0.49-1.51]	0.610		
	>56 years	0.94[0.62-1.43]	0.770		
Gender	Male	**2.04[1.38-3.01]**	**<0.001**	0.92[0.41-2.08]	0.840
	Female	Ref.			
Education	Illiterate	Ref.			
	Under Secondary	**10.17[3.1-33.37]**	**<0.001**	**8.55[2.56-28.55]**	**<0.001**
	Higher Secondary and	**21.26[6.49-**	**<0.001**	**13.73[3.98-**	**<0.001**

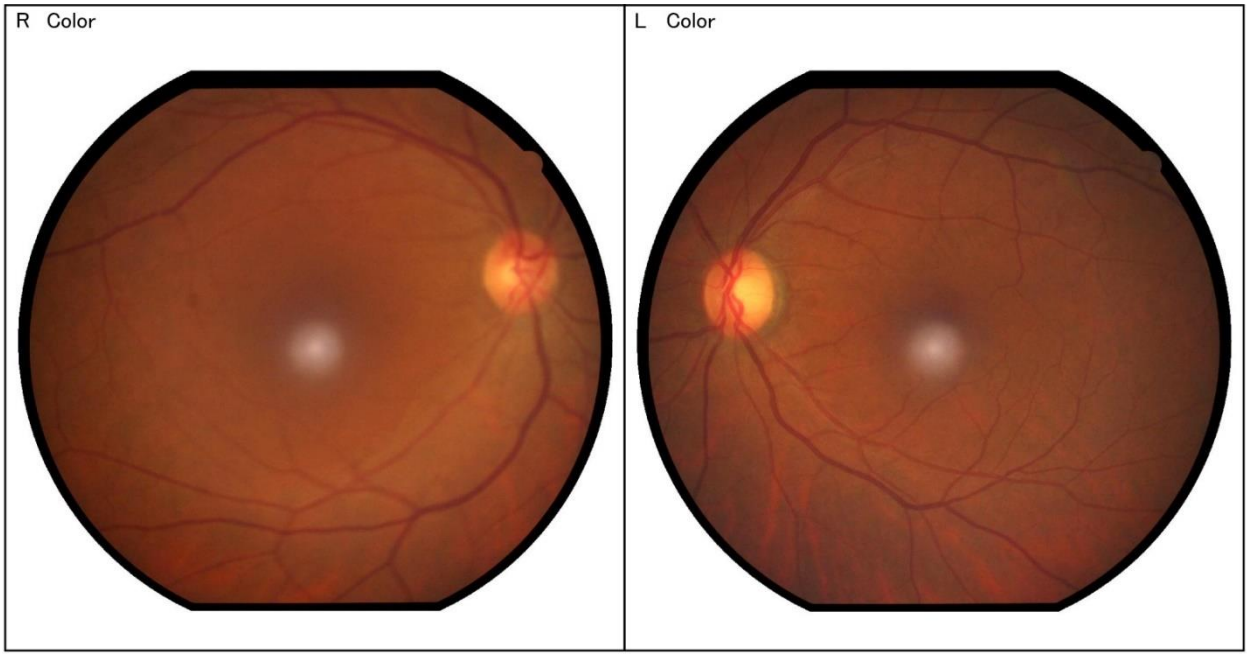
Occupation	Unemployment/Retired	**2.47[1.45-4.19]**	**0.001**	1.34[0.52-3.44]	0.545
	Service	**2.50[1.49-4.19]**	**0.001**	1.40[0.57-3.41]	0.460
	Business	**2.26[1.27-4.03]**	**0.006**	1.67[0.62-4.53]	0.312
	Housewife	Ref.		Ref.	
Monthly Family Income (in BDT)	Lower- middle income (TK.≤20,000)	Ref.			
	Upper- middle income (TK.20,001 – TK.65,000)	**2.75[1.66-4.55]**	**<0.001**	**2.14[1.25-3.65]**	**0.006**
	Higher income (TK. >65,000- ≥25001)	**4.6[2.48-8.54]**	**<0.001**	**3.12 [1.61-6.07]**	**0.001**
BMI	Underweight	Ref.			
	Normal	0.91[0.17-4.89]	0.915		
	Overweight	0.96[0.18-5.07]	0.961		
	Obese	1.42[0.26-7.7]	0.682		
Waist Hip Ratio (Health risk, male > 0.90 &	Normal	Ref.			
	Health risk	0.33[0.1-1.11]	0.074		
Family history of diabetes	Yes	Ref.			
	No	0.75[0.5-1.13]	0.166		
Duration of Diabetes	<10 years	Ref.			
	>= 10 years	**1.86[1.26-2.74]**	**0.002**	**1.71[1.12-2.62]**	**0.013**
Fasting Blood Sugar	Uncontrolled (n=352)	Ref.			
	Controlled (n=152)	**1.54[1.02-2.31]**	**0.040**	**1.63[1.04-2.54]**	**0.034**
Blood sugar two hours after breakfast	Uncontrolled (n=361)	0.78[0.52-1.19]	0.251		
	Control (n=143)	Ref.			
eGFR	CKD	0.71[0.42-1.18]	0.189		
	No CKD	Ref.			
HbA1C	Good control	1.66[0.86-3.20]	0.132		
	Uncontrolled	Ref.			
Retinopathy	NDR (n=397)	0.76[0.47-1.24]	0.276		
	DR (n=92)	Ref.			

4.7 Diabetic Retinopathy

Because screening for diabetic retinopathy is not routinely done at BIHS hospital, we offered the study participants a free of charge retinal examination described in the methods section, retinal photographs were taken from both eyes (**Figure 4.9**) and a senior ophthalmologist graded them as no retinopathy (no DR), mild non-proliferative DR (mild NPDR), moderate NPDR, severe NPDR, proliferative DR (PDR).



(a) (b)



(c) (d)

Figure 4.9: Examples of retinal photographs; (a) & (b) with diabetic retinopathy, (c) & (d) without

The baseline characteristics of the 489 study participants who also agreed to retinal photography are listed in **Table 4.16**.

Table 4.16: baseline characteristic of the study subjects with a retinal photograph (n= 489)

Characteristics	**N**	**%**
Gender		
Male	209	42.7
Female	280	57.3
Age		
<=40 years	88	18.0
41-55 years	211	43.1
56+ years	190	38.9
(Mean ± SD)	*(52.4 ± 11.2)*	
Education		
Illiterate	85	17.4
Primary	87	17.8
Secondary	132	27.0
Higher Secondary	59	12.1
Graduate & above	126	25.8
Occupation		
Unemployed	17	3.5
Service	89	18.2
Business	66	13.5
Retired	67	13.7
Housewife	250	51.1
Family income		
Low-middle Income (< Tk.21271)	154	31.5
Upper-middle Income (Tk. 21271- Tk.65761)	257	52.5
High Income (> Tk.65761)	78	16.0
(Mean ± SD)	*(19970.6 ±11.2)*	
Body mass index (BMI)		
Underweight (<18.5 kg/m^2)	7	1.4
Normal (18.5-24.99 kg/m^2)	154	31.5
Overweight (24.99-29.99 kg/m^2)	232	47.5
Obese (≥ 30.0 kg/m^2)	96	19.6
(Mean ± SD)	*(26.9 ± 3.9)*	
Waist Hip Ratio (WHR)		
Normal (male ≤ 0.90 and female ≤ 0.85)	11	2.2

Health risk (male > 0.90 and female > 0.85)	478	97.8
Family history of diabetes (n=533, multiple response)		
Grand Parents	7	1.3
Parents	181	34.0
Uncle/Aunt	7	1.3
Siblings	99	18.6
Others	62	11.6
No one	177	33.2
HbA1c (n=302)		
Good Control (≤7%)	44	14.6
Uncontrolled (>7%)	258	85.4
(Mean ± SD)	*(9.0 ± 1.9)*	
Fasting blood sugar		
Uncontrolled (>7.2)	339	69.3
Control (≤ 7.2)	150	30.7
(Mean ± SD)	*(9.3 ± 3.5)*	
Two hours after breakfast		
Uncontrolled (> 10)	351	71.8
Control (≤ 10)	138	28.2
(Mean ± SD)	*(12.8 ± 4.5)*	
Total cholesterol (n=186)		
High (> 200)	63	33.8
Normal (≤ 200)	123	66.2
(Mean ± SD)	*(180 ± 177.5)*	
HDL (n=144)		
Normal (≥ 40 for male and ≥ 50 for female)	43	29.9
Low (< 40 for male and < 50 for female)	101	70.1
(Mean ± SD)	*(39.2 ± 9.5)*	
LDL (n=171)		
High (> 100)	87	50.9
Normal (≤ 100)	84	49.1
(Mean ± SD)	*(103.9 ± 35.6)*	
TG (n=292)		
Normal	119	60.4
Abnormal	78	39.6
(Mean ± SD)	*(197.0 ± 114.0)*	
eGFR (n=322)		
CKD (eGFR ≤ 60mL/min/1.73 m²)	106	32.9
No CKD(eGFR > 60mL/min/1.73 m²)	216	67.1
(Mean ± SD)	*(67.8 ± 35.6)*	

Systolic blood pressure		
Uncontrolled (>140 mm of hg)	123	25.2
Control (≤140 mm of hg)	366	74.8
(Mean ± SD)	*(128 ± 15.5)*	
Diastolic blood pressure		
Uncontrolled (>90 mm of hg)	98	20.0
Control (≤90 mm of hg)	391	80.0
(Mean ± SD)	*(79.9 ± 8.5)*	
Duration of diabetes		
<10 years	280	57.3
>10 years	209	42.7
(Mean ± SD)	*(9.7 ± 7.0)*	
Drug adherence		
Adherence	252	51.5
Non-adherence	237	48.5
Physical activities (n=464)		
Adherence	197	42.5
Non-adherence	267	57.5
Dietary adherence (10% variation from diet chart) (n=484)		
Adherence	133	27.5
Non-adherence	351	72.5
Diabetic Retinopathy		
NDR	397	81.2
DR	92	18.8

4.7.1 Prevalence of previously undiagnosed diabetic retinopathy

We detected diabetic retinopathy in 92 individuals (18.8%; **Table 4.16**). The Prevalence of different grades of diabetic retinopathy were 11.7% for mild NPDR, 5.7% for moderate NPDR, 0.8% for severe NPDR, and 0.60% for PDR 0.60% (**Figure 4.10**). The prevalence of retinopathy increased with the known duration of diabetes, from 3% with less than 3 years to 40% with 15 years or more (**Figure 4.11**).

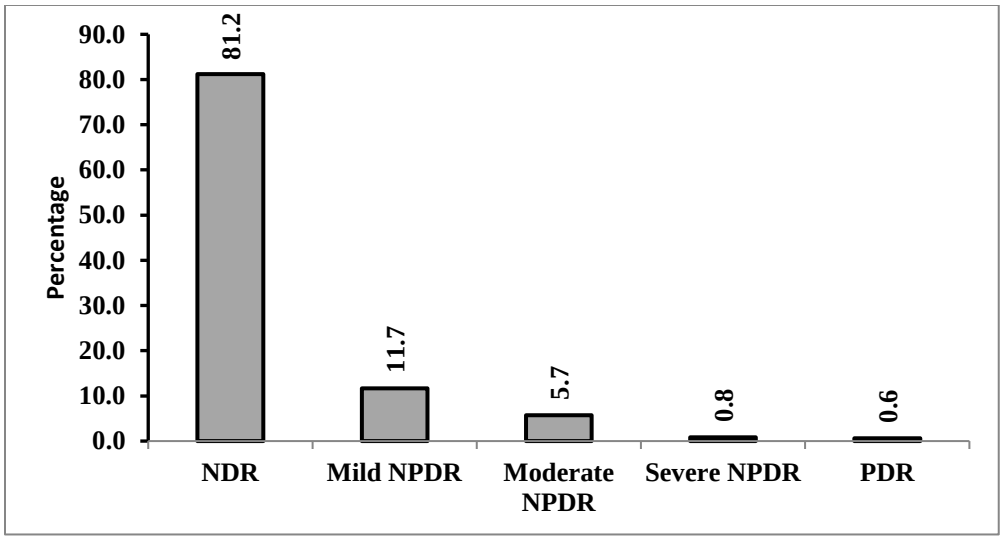


Figure 4.10: Prevalence rate of NDR and mild NPDR, moderate NPDR, severe NPDR and PDR

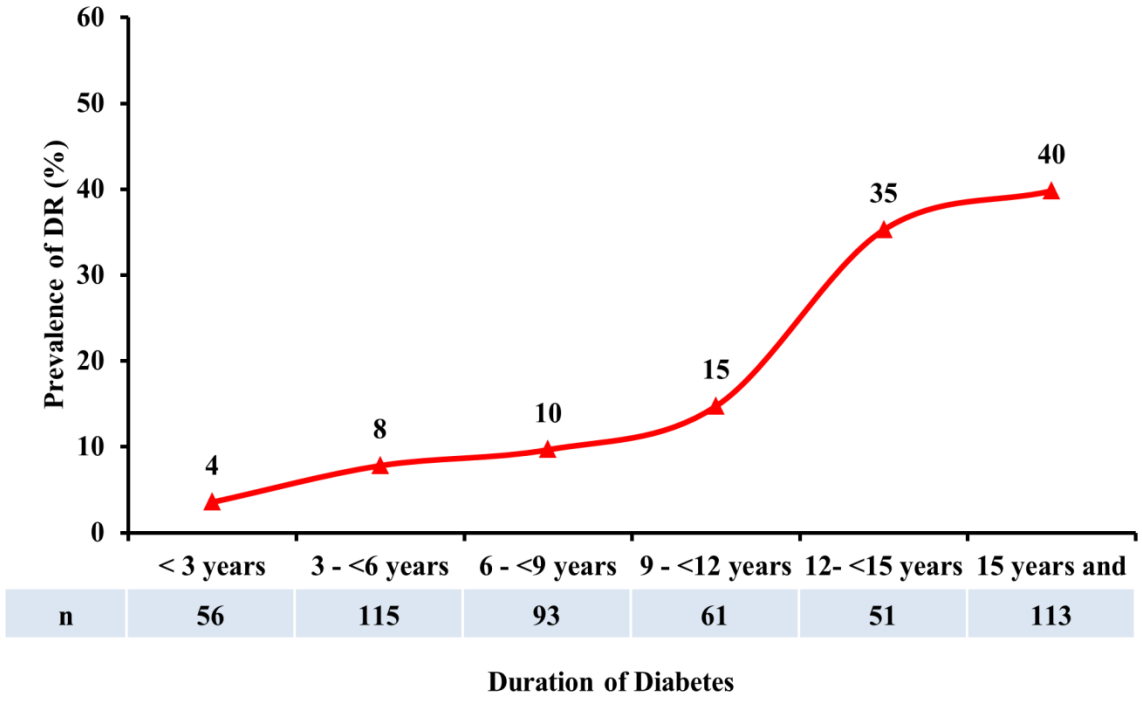


Figure 4.11: Relationship between prevalence of DR and diabetes duration

4.7.2 Factors associated with the presence of diabetic retinopathy

In univariate logistic regression analyses, higher age, FPG, PPG, HbA1c and duration of diabetes, as well as the presence of chronic kidney disease, uncontrolled blood pressure and non-adherence to drug therapy were associated with diabetic retinopathy (**Table 4.17**). In a multivariate logistic regression analysis, uncontrolled fasting plasma glucose [adj. OR 2.57(1.3-5.08); p=0.007], a known diabetes duration of 10 years or more [adj. OR 9.51(3.85-23.46) ;< 0.001] and non-adherence to drug therapy [adj. OR 1.82(1.07-3.10); p=0.027] remained independently associated with diabetic retinopathy (**Table 4.18**).

Table 4.17: Univariate logistic regression with the presence (DR) vs. absence (NDR) of diabetic retinopathy as the dependent variable

Variable	**DR N (%)**	**NDR N (%)**	**p-value**
Gender			
Male	45(21.53)	164(78.47)	0.184
Female	47(16.79)	233(83.21)	
Age			
<= 40 years	9(10.23)	79(89.77)	**0.002**
41-55 years	33(15.64)	178(84.36)	
56+ years	50(26.32)	140(73.68)	
Education			
Illiterate	12(14.12)	73(85.88)	0.436
Secondary and below	45(20.55)	174(79.45)	
Higher secondary & above	35(18.92)	150(81.08)	
Occupation			
Unemployment	20 (23.81)	64(76.19)	0.343
Service	17(19.1)	72(80.9)	
Business	15(22.73)	51(77.27)	
Housewife	40(16.0)	210(84.0)	
Monthly Family Income			
Low Income	0(0)	0(0)	0.125
Low-middle Income	37(24.03)	117(75.97)	
Upper-middle Income	41(15.95)	216(84.05)	
High Income	14(17.95)	64(82.05)	
Body Mass Index (BMI)			
Underweight	2(28.57)	5(71.43)	0.117
Normal	38(24.68)	116(75.32)	
Overweight	37(15.95)	195(84.05)	

Obese	15(15.63)	81(84.38)	
Weist Hip ratio			
Normal	2(18.18)	9(81.82)	0.999
Health risk	90(18.83)	388(81.17)	
Family history of diabetes			
Yes	51(19.92)	205(80.08)	0.511
No	41(17.6)	192(82.4)	
HbA1c			
Good Control	2(4.55)	42(95.45)	**0.004**
Uncontrolled	60(23.26)	198(76.74)	
Fasting blood sugar			
Uncontrolled	78(23.01)	261(76.99)	**<0.001**
Control	14(9.33)	136(90.67)	
Blood sugar after 2h of breakfast			
Uncontrolled	81(23.08)	270(76.92)	**<0.001**
Control	11(7.97)	127(92.03)	
eGFR			
CKD	31(29.25)	75(70.75)	**0.029**
No CKD	40(18.52)	176(81.48)	
Systolic blood pressure			
Uncontrolled	31(25.2)	92(74.8)	**0.036**
Control	61(16.67)	305(83.33)	
Diastolic blood pressure			
Uncontrolled	19(19.39)	79(80.61)	0.871
Control	73(18.67)	318(81.33)	
Duration of diabetes			
< 5 years	7(5.19)	128(94.18)	**<0.001**
5-10 years	20(11.05)	161(88.95)	
>= 10 years	65(37.57)	108(62.43)	
Drug adherence			
Adherence	34(13.49)	218(86.51)	**0.002**
Non-adherence	58(24.47)	179(75.53)	
Physical adherence			
Adherence	33(16.75)	164(83.25)	0.396
Non-adherence	53(19.85)	214(80.15)	
Dietary adherence (10% variation from advice)			
Adherence	24(18.05)	109(81.95)	0.904
Non-adherence	65(18.52)	286(81.48)	

Table 4.18: Multivariate logistic regression the presence (DR) vs. absence (NDR) of diabetic retinopathy as the dependent variable

Variable	Unadjusted OR [95% CI]	p-value	Adjusted OR [95% CI]	p-value
Gender				
Male	1.00			
Female	0.74[0.47-1.16]	0.185		
Age				
<=40 years	1.00			
41-55 years	1.63[0.74-3.56]	0.223	0.98[0.41-2.35]	0.968
56+ years	**3.14[1.46-6.71]**	**0.003**	1.16[0.47-2.87]	0.748
Education				
Illiterate	0.70[0.35-1.44]	0.336		
Secondary and below	1.11[0.68-1.81]	0.682		
Higher secondary and above	1.0			
Occupation				
Unemployed/ Retired	1.64[0.9-3.01]	0.109		
Service	1.24[0.66-2.32]	0.502		
Business	1.54[0.79-3.01]	0.202		
Housewife	1.00			
Family income				
Low-middle Income (< Tk.21271)	1.45[0.73-2.87]	0.293		
Upper-middle Income (Tk. 21271-Tk.65761)	0.87[0.45-1.69]	0.677		
High Income (> Tk.65761)	1.00			
Body mass index (BMI)				
Underweight (<18.5 kg/m^2)	1.22[0.23-6.55]	0.816	1.68[0.25-11.22]	0.595
Normal (18.5-24.99 kg/m^2)	1.00		1.0	
Overweight (24.99-29.99 kg/m^2)	**0.58[0.35-0.96]**	**0.035**	0.59[0.33-1.03]	0.065
Obese (≥ 30.0 kg/m^2)	0.57[0.29-1.10]	0.091	0.71[0.34-1.48]	0.363
Waist Hip Ratio (WHR)				
Normal (male ≤ 0.90 and female ≤ 0.85)	1.00			
Health risk (male > 0.90 and female > 0.85)	1.04[0.22-4.91]	0.957		
Family history of diabetes				
Yes	1.17[0.74-1.84]	0.511		
No	1.00			
Fasting blood sugar				
Uncontrolled (>7.2)	**2.9[1.58-5.32]**	**0.001**	**2.57[1.3-5.08]**	**0.007**
Control (≤ 7.2)	1.00			
Two hours after breakfast				
Uncontrolled (> 10)	3.46[1.78-6.73]	**<0.001**		
Control (≤ 10)	1.00			
Systolic blood pressure				

Uncontrolled(>140 mm of hg)	1.68[1.03-2.75]	**0.037**	1.1[0.63-1.92]	0.746
Control(≤140 mm of hg)	1.00			
Diastolic blood pressure				
Uncontrolled(>90 mm of hg)	1.05[0.60-1.84]	0.871		
Control (≤90 mm of hg)	1.00			
Duration of diabetes				
< 5 years	1.00			
5-10 years	2.27[0.93-5.54]	0.071	2.03[0.81-5.09]	0.130
>= 10 years	**11.00[4.84-25.00]**	**<0.001**	**9.51[3.85-23.46]**	**<0.001**
Drug adherence				
Adherence	1.00			
Non-adherence	**2.08[1.30-3.31]**	**0.002**	**1.82[1.07-3.10]**	**0.027**
Physical activities				
Adherence	1.00			
Non-adherence	1.23[0.76-1.99]	0.396		
Dietary adherence (10% variation from diet chart)				
Adherence	1.00			
Non-adherence	1.03[0.62-1.73]	0.904		

5 Discussion

5.1 High burden of uncontrolled diabetes and comorbidities

The consecutively recruited study cohort depicts typical features of the patient population of a non-private hospital in Bangladesh and other South-East Asian countries. With a mean age of 53 years, this population is young compared to individuals type 2 diabetes in western countries. Additionally, the mean BMI of 27 kg/m^2 is relatively low and highlights the propensity of South-East Asians to develop type 2 diabetes already in the normal weight or overweight range. **Figure 4.1** specifically highlights this point, which also raises a number of unresolved questions regarding pathophysiology.

Another relevant observation is the low overall education level of this population. With 17% illiterate individuals it poses a grave challenge for all efforts targeted at higher levels of patient knowledge. A further challenge is illustrated by the fact that only 30% of the study participants had adequate metabolic control based on plasma glucose measurements. Based on A1C, the proportion was even lower. Finally, the proportion of participants with significant comorbidities was also high.

5.2 Low adherence to medical advice

5.2.1 Lifestyle advice

Adherence to dietary advice was the lowest of all categories in our study (28%). This result is comparable to a previous study in Bangladesh (Mumu *et al.*, 2014). It highlights the global problem of dietary patterns incompatible with cardiometabolic diseases, such as type 2 diabetes (Serour *et al.*, 2007)(Khan *et al.*, 2012)(Divya and Nadig, 2015) (Howteerakul *et al.*, 2007), but also underscores the need for better patient education in Bangladesh and at the treatment center, where this study was conducted. The dietary recommendations not being properly explained by the nutritionist or physician was one of the most cited reasons for dietary non-adherence and this aspect could certainly be improved.

With 42.4%, adherence to physical activity advice was also low and similar to previous studies in Nepal and Hungary (Parajuli *et al.*, 2014) (Hankó *et al.*, 2007). Women were less adherent than man in our study, which may be due to cultural and religious barriers for women in Bangladesh. Similar result was found in previous studies (Hickey and Mason, 2017)(Van Uffelen, Khan and Burton, 2017). It is well established that to control dyslipidemia physical activity is very important. In this study, we found that dyslipidemic patients were more likely to adhere to physical activity advice, which may be due to the fact that more emphasis was put on physical activity in the presence of dyslipidemia (Sigal *et al.*, 2006). Physical discomfort was the reason most often given for non-adherence to physical activity advice, as found previously (Serour *et al.*, 2007). This result warrants further investigation because, while physical activity may cause discomfort in some individuals, this should not be such a common issue. Rather, inadequate training plans and recommendations, as well as cultural issues, may play a role. Adverse clinical outcomes associated with non-adherence to physical activity advice were a higher BMI and higher plasma glucose values and A1C. All these parameters point to the paramount importance of physical activity in diabetes management and should prompt reconsideration of current motivational approaches.

Adherence to foot care advice, recommended follow up visits and home monitoring of blood glucose also was suboptimal. Foot care, in particular, did not seem to have been explained properly to the patients, as this was mentioned as one of the main reasons for non-adherence. Similarly, education about the other two areas could be improved further.

5.2.2 Drug therapy

As expected, adherence to medical advice was low. Only 52% of participants fulfilled the criteria for adherence to the prescribed drug therapy. Adherence to physical activity advice, foot care advice and scheduled follow-up visits was in a similar range, while adherence to dietary advice was still significantly lower (28%). The best category was adherence to prescribed home monitoring of blood glucose (88%), which was, however, only prescribed to 290 out of the 504 individuals in the study.

As already mentioned in the introduction, non-adherence to chronic drug therapy is common around the globe and has a significant negative impact on treatment outcomes (Kasznicki, Głowacka and Drzewoski, 2007) (Mukherjee *et al.*, 2013). In our study, individuals with insulin

therapy were less compliant than those with oral therapies, which is an expected finding among type 2 diabetic patients. Unlike in type 1 diabetes, omission of insulin injections in type 2 diabetes usually not result in severe symptoms but only impair long-term metabolic control. Hence, since insulin injections are cumbersome, adherence tends to be low. Fear, pain and discomfort with needling could be other possible reasons for non-adherence with insulin (Aminde *et al.*, 2019). Moreover, the price of insulin is higher than that of oral medications and thus remains a challenge with affordability (Gill, 2014). Interestingly, older individuals were more adherent in our study. This is in agreement with in studies conducted at a hospital at Cameron (Aminde *et al.*, 2019) and elsewhere (Krousel-Wood *et al.*, 2005). Non-adherence is common in younger group usually due to lack of knowledge, burden of therapy and fear of side effects (Van Der Wal *et al.*, 2006), while older patients seem to be more aware of the importance of glycemic control (Abebaw *et al.*, 2016). Another factor related to higher adherence was concomitant hypertension, but we can only speculate, why this was the case. One possibility is that they take all medications at once and thus the two indications booster each other.

Not surprisingly, several adverse clinical outcomes were associated with non-adherence to the prescribed medication. Foremost, these related to glucose control but also diabetic retinopathy was more common with non-adherence (see also below). The higher eGFR, which we observed in the non-adherent group, could be related to the observation, that non-adherent individuals tended to be younger. It also could result from the fact that blood pressure medications, such as ACE inhibitors, were also not taken and thus their eGFR-lowering effect was weaker in the non-adherent group.

The most common reason cited for not taking the prescribed medicines was forgetfulness (59.1%). Similar findings were reported in several studies in Ethiopia, Cameron, UAE, Nigeria and India (Gelaw *et al.*, 2014)(Aminde *et al.*, 2019) (Arifulla *et al.*, 2014)(Adisa, Alutundu and Fakeye, 2009)(Mukherjee *et al.*, 2013). Busy for work/family was the second most cited reason for non-adherence to drug therapy in our study (43.8%), which is in agreement with a previous examination from Ethiopia (Wabe, Angamo and Hussein, 2011). Finally, the high price of medicines was the third most commonly given reason (29%). This issue remains central to chronic care in Bangladesh

and other low- and middle-income countries (Kalyango, Owino and Nambuya, 2008)(Hjelm and Nambozi, 2008).

5.3 Knowledge about Diabetes

Diabetes management largely depends on an individual's self-care ability, which in turn is affected by a number of factors. One important factor is knowledge about the disease, its management, and its complications. Several studies have shown that good knowledge about diabetes is required for adequate metabolic control and thus the prevention of diabetic secondary complications(Shrivastava, Shrivastava and Ramasamy, 2013)(Murugesan *et al.*, 2007). On the other hand, poor knowledge is associated with a high rate of complications and higher health care costs(Islam, Niessen, *et al.*, 2015b).

An individual's level of education is the factor most strongly linked to knowledge about diabetes in our study. This result is not unexpected, as it is in line with several other publications from different countries(Hawthorne and Tomlinson, 1999)(Siddique *et al.*, 2017)(Ozcelik *et al.*, no date)(Rafique and Azam, 2006). Illiterate subjects had particularly low knowledge about diabetes in our sample, which may be due to the fact that currently part of the information about diabetes is conveyed in writing. To reach the illiterate and poorly educated, a more comprehensive approach to patient training, beyond the current booklet and one-hour training session, seems necessary. This is particularly relevant because it has been shown that a comprehensive diabetes support program can be disproportionally effective for illiterate individuals(Rothman *et al.*, 2004). The independent association of a low family income with poor knowledge about diabetes that we observed has also been demonstrated in other studies(Jasper *et al.*, 2014)(Fenwick *et al.*, 2013)(Ding and Teng, 2006). We can only speculate about the reasons for this association, which goes beyond the effect of education. One explanation may be that the more affluent have a higher exposure to health-related information through the media. The observed higher knowledge about diabetes with a longer time since diagnosis has also been shown previously(Ozcelik *et al.*, no date)(Fenwick *et al.*, 2013). It is reassuring that individuals with diabetes learn more about their disease as time progresses.

Regarding the different areas of knowledge about diabetes, our first observation was that many study participants had poor knowledge in all the areas examined. Among the five areas least known to the study participants, symptoms and management of hypoglycemia, complications, as well as foot care, are the ones directly important to the individual with diabetes. Finally, our study confirmed the independent association of poor knowledge about diabetes with insufficient metabolic control. This has been shown previously in studies from Bangladesh and other countries(F. M. A. Islam *et al.*, 2014)(Al-maskari *et al.*, 2013)(Al-adsani, Moussa and Al-jasem, 2019) and reaffirms the importance of adequate patient training.

5.4 Diabetic Retinopathy

Diabetic Retinopathy (DR) is the most common microvascular complication of diabetes and the leading cause of blindness worldwide. It is not routinely examined in Bangladesh and thus the number of undetected or uncertain cases is high. Although 31% of the patients in our study reported 'an eye problem', a current retinal examination was not available. Our screening study revealed an overall prevalence of diabetic retinopathy of 18.8 %, which is in line with one population based study in rural Bangladesh (21.6%) (Akhter *et al.*, 2013). Our result is also comparable to studies in neighboring countries; Nepal (19.3%)(Paudyal *et al.*, 2008), Sri Lanka (15%)(Weerasuriya *et al.*, 1998), and Pakistan (15%)(Iqbal and Zafar, 2009). The prevalence of proliferative retinopathy, which usually requires treatment, was still low (0.6%) in this relatively young cohort. Nevertheless, our findings highlight the necessity to include retinopathy screening into the regular follow up examinations of diabetic patients in Bangladesh – as this is routine in many other countries.

Uncontrolled diabetes, a known disease duration of over 10 years and non-adherence to the recommended drug therapy were the factors associated to diabetic retinopathy. These confirm previous findings (Akhter *et al.*, 2013) and may also serve as risk markers to identify individuals with diabetes who should be screened preferentially.

5.5 Strengths and limitations of this study

A strength of this study is its consecutive recruitment of a large cohort of type 2 diabetic individuals. This approach reduced the selection bias and provided sufficient statistical power. Data collection and processing were also standardized and retinal photographs were evaluated by an independent specialist. The main weakness of this study is that, in many aspects, it relied on self-reported information. Counting pills or tracking physical activity may have provided more accurate results in some cases but such approaches were financially not feasible in this project. An additional weakness was the fact that not all laboratory parameters, in particular not A1C, were available from all participants; again, due to financial constraints. However, as far as we can tell from the consistency of our results, this fact did not introduce significant bias. Given the monocenter setting of this study, it may also not be representative for diabetes in Bangladesh in general. More affluent patients may be treated in private hospitals and receive a higher level of care, while the rural population may still lack specialized diabetes care at all.

6 Conclusions

This study shows that low adherence to medical advice remains a major problem among diabetic patients in Bangladesh. This problem concerns both drug therapy and lifestyle advice. Similarly, knowledge about diabetes, its complications and management is often insufficient. To improve diabetes-related knowledge and motivation for adherence, new training programs should be established. These should primarily target the uneducated, the illiterate and the poor. Therefore, written information is probably of little use and training should focus on the information with the highest practical value. Contemporary tools, such as training videos available online, should be explored for their usefulness in this setting. Cultural issues, particularly those affecting women, should also be addressed.

The screening done for diabetic retinopathy during this study illustrates how, even today, dangerous and preventable complications of diabetes develop unrecognized, if one does not actively look for them. Better, regular screening programs are therefore needed in Bangladesh, not only for retinopathy, but also for other silent complications, where the situation probably is not any better.

Finally, the proportion of cases with uncontrolled diabetes was still way too high in this study population. Every effort should be made, to improve the access to specialized diabetes care and medication in Bangladesh, irrespective of a person’s wealth and societal standing.

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8 Annex

8.1 Statement on pre-release and contribution

A manuscript on Knowledge on Diabetes and its Determinants among type 2 Diabetic subjects has been submitted for publication and is under review.

Mohammad Wahiduzzaman was responsible for the design and develop of the study protocol. As the Principal Investigator, he supervised data collection and data entry, performed data cleaning and data analysis, and wrote the first draft of the manuscript and the monographic thesis. Andreas Lechner, Liaquat Ali and Friederike Banning were responsible for guiding the development of the study protocol, provided expert opinion and feedback, supported data analysis and reviewed the draft manuscript and thesis. Md. Sahidul Islam and Sharmin Hossain gave advice on conducting the statistical analyses. Mostary Zannath and Archana Dev Karmakar helped with data collection.

8.2 Dedication

This thesis is dedicated to my parents for their love, blessing and support. I dedicate this work to my beloved children Rahid Zaman and Ashfak Zaman and my lovely wife Nazmun Nahar Trisha. Lastly, I dedicate this work to my brother and sister, especially to my brother Abul Basher.

They always encourage me and they do their best to have a better life and my education.

8.3 Acknowledgements

First of all, my heartiest thanks to all my PhD supervisors- PD Dr. Andreas Lechner, Dr. med. Friederike Banning and Professor Liaquat Ali for their outstanding guidance and support all through the journey of my PhD studies. I have been fortunate to work under your direct supervision, learn from you and complete my PhD thesis, for which I remain ever grateful. Without your support, my dream would never have been fulfilled.

I am grateful to all the faculty and colleagues at the Center for International Health (CIH), Institut für Medizinische Informationsverarbeitung, Biometrie und Epidemiologie (IBE), Department of

Infectious Diseases and Tropical Medicine and several other departments at LMU for the excellent teaching and support.

A special thank you to all my colleagues from BIHS Hospital, Dr Mohammad Yousuf, Dr Farhad Newaz and Dr Amimul Ehsan. I am also extremely grateful to Professor Khurshida Khanom and Sharmin Hossain of the Department of Health Promotion and Health Education of Bangladesh University of Health Sciences (BUHS)for their support and engouement throughout the study, I am very grateful to Shahidul Islam, from WHO and Sharmin Hossain from BUHS for their help and suggestions regarding statistical analysis and providing valuable comments and contribution on the manuscripts. I am also grateful to Dr Manir Hossain Mollah and S. M. Samiul Hoque Chowdhury, from the Department of Biostatistics of BUHS. Special thanks to Dr Sheikh Mohammed Shariful Islam and Dr Rizwanul Bari who encouraged me to undertake the PhD CIH[LMU.]

I am grateful to the Vice-Chancellor of BUHS Professor Dr Faridul Alam for the support of my studies. I also thank Dr Mostari Zannat and our data collection and data management team a for their excellent work, dedication and sincerity in helping with this study.

This PhD study was supported by The German Federal Ministry of Economic Cooperation and Development (BMZ)) and BUHS. I am grateful to CIH [LMU,] BUHS and BIHS, DAAD, BMZ and Exceed to support our study.

Finally, I am grateful to my wonderful family; I cannot ever thank you enough for all your endless, unconditional love, sacrifice and support.

8.4 Affidavit

Mohammad Wahiduzzaman

Name

Street

Zip code, town

Country

I hereby declare, that the submitted thesis entitled

Factors affecting clinical outcome among Type 2 diabetic subjects attending the outpatient department of a tertiary care hospital in Bangladesh

is the result of my own work. I have only used the sources indicated and have not made unauthorised use of services of a third party. Where the work of others has been quoted or reproduced, the source is always given.

The submitted thesis or parts thereof have not been presented as part of an examination degree to any other university.

I further declare that the electronic version of the submitted thesis is congruent with the printed version both in content and format.

Dhaka,30/09/2020	Mohammad Wahiduzzaman
Place, Date	Signature of PhD Candidate

8.5 Study questionnaire

Study Title: Factors Affecting Clinical Outcome among Type 2 Diabetic Subjects Attending OPD of A Tertiary Care Hospital in Bangladesh

1. Primary Information

1.1	Date	
1.2	Participant ID	
1.3	Name	
1.4	Address	Current residence…… Permanent residence……
1.5	Contact No	Mobile 1……. Mobile 2…….
1.7	Name & Signature of the interviewer	Name …… Signature……

2. Socio-demographic Information

Sl no	Questionnaire	Answer (Encircle appropriate response)	Code
2.1	Age	……years……	
2.2	Gender	1= Male 2= Female	
2.3	Education	1= Illiterate 2= Primary 3= Secondary school 4= Higher secondary /College 5= Graduate and above	
2.4	Religion	1= Muslim 2= Non-Muslim	
2.5	Marital status	1=Unmarried 2=Married 3=Widow/widower 4=Divorced	
2.6	Occupation	1= Unemployed 2= Service 3= Business	

		4= Retired 5= Housewife 6=Self employed 7= Others	
2.7	Income (Personal)	Monthly in Taka= ……. [Enter 00 if None]	
2.8	Total Family members	No= ……..	
2.9	Total Family Income	Monthly in Taka= ……. [Enter 00 if None]	
2.10	Family type	1=Nuclear 2=Join	

3. Diabetes Related Information

Sl no	Questionnaire	Answer(Encircle appropriate response)	Code
3.1	Duration of Diabetes	…….. Years	
3.2	How do you control your diabetes	1= by OAD 2= by Insulin 3= OAD & Insulin both 88= Others specify……..	
3.3	Duration of Diabetes treatment?	Months= Years=	
3.4	Problem other than diabetes (Take a snapshot from patients last prescription)	1= Hypertension 2= Kidney problem 3= Eye problem 4 = Dyslipidemia 5 = Cardiovascular diseases 6 = Problem in foot 7 = Problem in mouth 8= Problem in skin 9 = Neuropathy (nerve damage) 10 = Hearing problem 88 = Others (specify)…….	
3.5	Who is in your family is/are suffering from Diabetes?	1 = Grandparents 2 = Parents	

		3 = Uncle/ Aunt 4 = Siblings 5= No one 88= Others (specify)……	

4. Knowledge Related to diabetes

Sl no	Questionnaire	Answer *(Encircle appropriate response)*	Code
4.1	What do you mean by diabetes?	1= Increased blood glucose above normal level 2= Insufficient insulin in body 3= Body not respond to insulin 4= don't know 88= Others ……..	
4.2	What are the risk factors to develop diabetes? (more than one answer may be correct)	1= Obesity 2= family history of diabetes 3= lack of exercise 4= unhealthy food 5= excessive sweets and sweet products 6= Lack of insulin 7=Don't know	
4.3	What is the good level for fasting blood sugar?	1= 4- 6 mmol/l 2= 6- 8 mmol/ 3= 8- 10 mmol/l 4= 10-12 mmol/l 5= don't know	
4.4	What is the good level for the blood sugar 2 hours after breakfast?	1= 4- 6 mmol/l 2= 6- 8 mmol/l 3= 8- 10 mmol/l 4= 10-12 mmol/ 5= d0n't know	
4.5	What are the symptoms of diabetes? (Interviewer: do not mention the answers to the respondents)	1 = Excess urination 2 = Excess hunger 3 = Excess thirst 4 = Loss of body weight	

		5 = Slow healing process of wound 6 = Tiredness 7 = Weakness 8 = Blurred vision 9 = Infections 10 = Skin problem 11 = Tingling or numbness in hands or feet 88= Others	
4.6	Which of these are possible complications of diabetes? (more than one answer may be correct)	1=Heart attack 2=Stroke 3=kidney diseases 4=Amputations or foot ulcer 5=Blindness 6= Nerve diseases 7= Hypertension 88= Others	
4.7	What are the causes that Increase blood glucose level? (Interviewer: do not mention the answers to the respondents)	1 = Excess carbohydrates intake 2= Intake of sweets and sweet products 2 = Not intake medicine properly 3 = Stress 4 = Lack of exercise 5 = Infection, illness, or surgery 6= Effect of other drug 88 = Others (specify)	
4.8	Do you know the main components of diabetes management?	1 = Eat recommended and well balanced food timely 2 = Avoid sugar-sweetened beverages 3 = Do physical exercise regularly (at least 30 minutes per day and 5 days per week) 4 = Take medicines on time, including insulin (if necessary) as prescribed by the doctor 5 = Check blood sugar frequently, as	

		advised by the doctor and maintain a diary of all the readings 88 = Others (specify	
4.9	What is hypoglycemia?	1= low level of blood glucose 2= high level of blood glucose 3= Don't know	
4.10	What are the Symptoms of hypoglycemia?	1 = excessive Hunger 2 = Excessive Sweating 3 = Palpitation 4 = Dizziness and discomfort 5 = Tiredness and drowsiness 7 = Nausea /vomiting 88 = Others (specify)	
4.11	Level of blood sugar for hypoglycemia?	1= …….mm/l 2= Don't know	
4.12	What the foods or drinks used to manage hypoglycemia?	1 = Sugar 2 = Glucose or glucose tablet 3 = Soft drink 4 = Fruit juice 5 = Banana 6 = Apple 7 = Honey 8 = Milk 88 = Others (specify)	
4.13	How many times food intake is essential for diabetic patient?	1 = 3 times 2= 3-5 times 3= >5 times 0= Any other answers	
4.14	How many days in a week a diabetic patient should do physical exercise?	1 = All days in a week 2 = 5 days in a week 0=other answers	
4.15	How much times in a day a diabetic patient should do physical exercise?	1 = <30 minutes/ day 2= >30 minutes/ day 0=other answers	
4.16	Do you know what are the advices regarding foot care?	1 = Wash feet every day 2 = Trim toenails 3 =Use lotion/cream 4 = Never walk barefoot	

		5= Check inside shoe & use clean and dry socks 6 = Check feet with a mirror weekly to see color change, blister or ulceration 7=Always use closed and comfortable shoes or sandals. 88 = Others (specify)	

5. Anthropometric and Biochemical Measurement

SL No.	Questionnaire	Answer *(Encircle appropriate response)*	Code
5.1	Weight (kg) *(*Interviewer will measure by weight		
5.2	Height (cm) (Interviewer will measure by height measurement scale)		
5.3	Waist circumference (cm) (Interviewer will measure by measurement tap)	……..	
5.4	Hip circumference (cm) *(*Interviewer will measure by measurement tap)	……..	
5.5	Waist to Hip ratio	……	
5.6	Blood Pressure (mm/Hg) (Interviewer will measure by the measurement machine)	a. Systolic b. Diastolic	
5.7	Blood Glucose (mg/dl) (Interviewer: please fill in from patient book)	c. Fasting blood glucose d. Blood glucose 2 hours after breakfast	
5.8	Fundus Photography	NDR NPDR 1.Mild 2.Moderate 3. Severe PDR	

5.9	Other biochemical tests (if available)	HbA1C S. Creatinine… Cholesterol….. HDL…… LDL……. TG……. Others……..	
5.11	Pulse rate	……	

6. Adherence to Drug Advices

SL no	**Questions**	**Response**	**Code**
		Drug name/ Generic name	
6.1	Do you take medicine according to physician's recommendation as follows? (Mention the name of the prescribed drug- See the prescription) a. Changed prescribed dose of medicine? b. Don't observe the time? c. Take more amount of medicine? d. Take less amount of prescribed medicine? (If any of the option is positive, patient will mark as nonadherent)	1…… (1= No/2= Yes)	
		2…… (1= No/2= Yes)	
		3…… (1= No/2= Yes)	
		4…… (1= No/2= Yes)	
		5…… (1= No/2= Yes)	
		6…… (1= No/2= Yes)	
		7…… (1= No/2= Yes)	
		8…… (1= No/2= Yes)	
		9…… (1= No/2= Yes)	
6.2	When you find that your blood sugar is controlled, what do you do (please select one answer)?	1= Stop medicine/insulin 2= Decrease the dose of medicine/insulin 3= Increase the dose of medicine/insulin 4= no change at all	

6.3	Do you have any barrier to take insulin? If yes mention the reasons behind it	1= No 2= Fear of needling 3= Insulin is too costly 4= Fear of hypoglycemia (low blood sugar) 5= Insulin my cause harm to your health	

	Reasons for nonadherence to drug advices.	Name of Medicine										Code
SL No 6.4		1	2	3	4	5	6	7	8	9	10	
	Patient factors 1= Forgot to take 2= Too busy (work/ Family) 3= Too expensive/ Cost of medicine 4= Patient away from home 5= Wasn't sick Enough 6= Doesn't like due to adverse effects 7= Prefers herbal/ homeopathy/ ayurvedic/ traditional drugs 8= Could not take Insulin without help of others person 9= Taking different medicine according to the advice of another physician 88= Others(specify)……											

	Provider factors 1= Unavailability of drugs 2= Too much medicine 3= Pharmacy is too far 4= Unreadable prescription 5= Not properly explained by the doctor 88= Others (specify)……											

7. Adherence to Dietary Advices

Question		Response	Code
7.1	According to diabetic book, diet chart No **(please see the guide book**)	1 = No. # 1(1000 kcal) 2 = No. # 2 (1200 kcal) 3 = No. # 3 (1400 kcal) 4 = No. # 4 (1600 kcal) 5 = No. # 5 (1800 kcal) 6 = No. # 6 (2000kcal) 7 = No. # 7 (2200kcal) 8 = No. # 8 (2400 kcal) 9 = No. # 9 (2600kcal) 10 = No. # 10 (2800 kcal)	
7.2	Do you follow the diet chart as per recommendation?	1=Yes 2=No	
7.3	If you are not taking any of the recommended diet, please mention the following reasons? 1=Forgot to take 2=Too busy (work/family) 3=Too expensive 4=Lack of money 5=Unavailability of food in market 6=Unavailability of food at home 7=Not cooked 8=Doesn't like the recommended food	Breakfast= Midmorning= Lunch=	

	9= Patient felt physically discomfort with this 10=Patient felt hungry with this recommended amount of food 11=Lack of willingness/ laziness to make recommended amount of food 12= The Nutritionist/ Physicians advices regarding diet were not properly explained 88=Others (specify)……	Evening snacks= Dinner=	
7.4	Yesterday, how many times did you take food? (Interviewer: If yesterday was any special day for patient, then record dietary history of another day)	1 = 1 time 2 = 2 times 3 = 3 times 4 = 4 times 5 = 5 times 6 = 6 times 7 = More than 6 times	

Please do mention the food items that you took in last 72 hours

Time and frequency of food intake		**Description of Food items**	**Quantity/Amount of Food**			**Code**
			Day 1	**Day 2**	**Day 3**	
7.5	Pre-breakfast	1= Biscuit 2= Muri 3= Raw Tea 4=Others				
7.6	Breakfast (…….)	1 = Bread/handmade bread (ruti) small & thin 2 = Rice 3 = Egg 4 = Leaves & vegetables 5 = Dal 6= Fruits 7= Milk 88 = Others (specify)				

7.7	Morning Snack (…….)	1 = Cookies 2 = Muri/khoi 3 = Noodles 4 = Singara/ Samosa 5 = Fruits 6 = Leaves & vegetables 88 = Others (specify)				
7.8	Lunch (…….)	1 = Rice 2 = Hand made bread (ruti) - small & thin 3 = Fish/meat 4 = Dal 5 = Leaves & vegetables 6 = Fruits 88=Others (specify)				
7.9	Afternoon Snack (…….)	1 = Cookies 2 = Muri/khoi 3 = Noodles 4 = Barley 5 = Fruits 88 = Others (specify)				
7.10	Dinner (…….)	1 = Handmade bread (ruti)- small & thin 2 = Rice 3 = Fish/meat 4 = Dal 5 = Leaves & vegetables 6 = Fruits 88 = Others (specify)				
7.11	Bedtime snack (……..)	1 = Milk 2 = Biscuits 88 = Others (specify				

8. Adherence to physical activity

SL No.	**Question**	**Response** *(Encircle appropriate response)*	**Code** *(Write code no)*
8.1	Advice for physical exercise? (from guide book)	1 = Yes 2 = No	
8.2	Recommended physical activity from guide book)	1 = Walking 2 = Cycling 3 = Jogging 4= Swimming 88 = Others (Specify)	
8.3	Recommended days per week	1= <3 days 2= <5 days 3= >5 days 4= Not specified	
8.4	Recommended minutes per day	1= …… Hours 2= ……. Minutes	
8.5	Do you always do it as recommended?	1 = Yes 2 = No 3= Sometimes	
8.6	What types of physical activity are you doing?	1 = Walking 2 = Cycling 3 = Jogging 4= Swimming 88 = Others (specify	
8.7	How many days per week are you performing?	**……** day	
8.8	How many minutes per day are you Performing?	1=……. Hours 2= ……..Minutes	
8.9	Reasons for not follow the recommended Physical activity?	1=Forgot to do 2=Too busy 3=Bad weather 4=Doesn't like to do 5=Physically discomfort 6= Not enough space	

		7=Previous bad experience 8=Doing more physical activity 9=Lack of willingness/laziness to do 10= Educator/ Physician were not properly instructed	

9. **Adherence to Follow-up visit Advice**

SL no	**Questions**	**Response** ***(Encircle appropriate response)***		**Code** ***(Write code no)***
9.1	Any advice for follow-up visit by Physician?	1 = Yes 2 = No		
9.2	Any advice for follow-up visit by Nutritionist?	1 = Yes 2 = No		
9.3	Please mention the last recommended date of follow-up	1= Physician: Date…… 2= Nutritionist: Date…….		
9.4	Did you visit (due date/ within 7 days) last time according to recommendations?	1 = Physician (Yes/No) 2 = Nutritionist (Yes/No)		
9.5	Reasons for not follow the recommended follow up visit- 1=Forgot to go 2= Lack of money 3=Too far 4=Too busy 5=Bad weather 6= Absence of accompanying person 7= Was not sick enough 8= Poor structure of health facility 9= Bad attitude of staff	<u>Physician</u>	<u>Nutritionist</u>	

	10= Staff are usually missing 11= No transport 12= Long waits 13= Prefers self-treatment 14= Prefers herbal/homeopathy/ ayurvedic/ traditional treatment 15= Was sick 16= Lack of willingness/ laziness to Come 88 = Others (specify)			

10. Adherence to Home monitoring blood glucose (HMBG)

SL No.	Question	Response	Code
10.1	Any advice regarding your blood glucose monitoring at home?	1 = Yes 2 = No	
10.2	Mention how many times per day/week/month?	Numbers…….. ./ day/week/ month	
10.3	Do you monitor your blood glucose at home according to your physician's recommendation?	1 = Yes 2 = No	
10.4	Mention how many times you do HMBG per day/week/month?	Numbers…….. ./ day/week/month	
10.5	Why you don’t follow recommended HMBG?	1= Don't have monitoring device 2= Forgot to do 3= Fear to test 4= Too busy 5= Absence of helping person 6= Physically discomfort 7= Negligence 8= Educator/ Physician were not properly instructed 88= Others (specify)	

11. Adherence to foot care advices

SL No.	**Questions**	**Response** *(Encircle appropriate response*	**Code** *(Write code no)*
11.1	Do you have any advices regarding the foot care from your physician?	1= Yes 2= No	
11.2	Please mention the advices?	1 = Wash feet every day 2 = Trim toenails 3 =Use lotion/cream 4 = Never walk barefoot 5= Check inside shoe & use clean and dry socks 6 = Check feet with a mirror weekly to see color change, blister or ulceration 7=Always use closed and comfortable shoes or sandals. 88 = Others (specify)	
11.3	How many days did you wash your feet in last seven?	……..Days	
11.4	How many days did you inspect your feet by mirror in last seven days?	……..Days	
11.5	How many days ago did you last trim your toenails?	……..Days	
11.6	Do you follow the recommended foot care advices?	1 = Yes 2 = No	
11.7	If not, please mention the reasons behind it?	1=Forgot to do 2=Too busy 3=Doesn't like to do 4= Did not feel to do so 5=Feeling physically discomfort 6= Educator/ Physician were not properly instructed 88 = Others (specify)	