Diabetes Mellitus and Retinopathy in Rural Bangladesh: A Population Based Study

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ABBREVIATIONS

ADA	American Diabetes Association
AG	After 2 hour Glucose
BADAS	Bangladesh Diabetic Association
BIRDEM	Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorder
BMI	Body Mass Index
BP	Blood Pressure
CI	Confidence Interval
DBP	Diastolic Blood Pressure
DM	Diabetes Mellitus
DR	Diabetic Retinopathy
FBG	Fasting Blood Glucose
GDM	Gestational Diabetes Mellitus
GOB	Government of Bangladesh
HbA1c	Glycosylated Hemoglobin
HC	Hip Circumference
HDL-C	High Density Lipo-protein Cholesterol
HPLC	High Performance Liquid Chromatography
ID	Identification Number
IDF	International Diabetes Federation
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance

LDL-C	Low Density Lipo-protein Cholesterol
NCDs	Non Communicable Diseases
NGO	Non Government Organization
NIDDM	Non Insulin Dependent Diabetes Mellitus
OGTT	Oral Glucose Tolerance Test
OR	Odds Ratio
SBP	Systolic Blood Pressure
SPSS	Statistical Package for Social Sciences
Sq Km	Square Kilometer
T1DM	Type 1 Diabetes Mellitus
T2DM	Type 2 Diabetes Mellitus
TC	Total Cholesterol
TG	Triglyceride
UACR	Urine Albumin Creatinine Ratio
WC	Waist Circumference
WHO	World Health Organization
WHR	Waist to Hip Ratio

ABSTRACT

Objective: The study aimed to estimate the prevalence of diabetes and retinopathy in people with normal and abnormal glucose metabolism in rural Bangladesh and to identify the associated risk factors for developing diabetes and retinopathy in this population.

Methods: This population based cross-sectional study was conducted through screening in camp settings, which included a total of 836 participants (aged ≥25 years) by following simple random procedure. Fasting blood glucose (FBG) and oral glucose tolerance test (OGTT) were performed for all participants to diagnosis diabetes according to the diagnostic criteria of World Health Organization. Retinopathy was determined by ophthalmoscopy and fundus photography. Anthropometric measurements (BMI and WHR), glycosylated hemoglobin, blood pressure, lipid profile and urine albumin creatinine ratio were also observed. Logistic regression analysis was used, without and with adjustment for potential confounders.

Results: An increased prevalence of diabetes and retinopathy was found with 7.2% (95% CI 5.4-9.0) and 5.4% (95% CI 3.9-6.9) in the present study, respectively. Moreover, the prevalence of retinopathy among the diabetic, prediabetic and nondiabetic subjects were 21.6% (95% CI 11.2-32.0), 13% (95% CI 3.4-22.6) and 3.5% (95% CI 2.2-4.8), respectively. A superior agreement was observed between FBG and OGTT (Kappa value 0.86) among the study participants. After adjusting for potential confounders BMI, WHR, serum creatinine, triglyceride, total cholesterol and UACR were found as significant independent risk indicators for the occurrence of diabetes and age, BMI, hypertension, HbA1c, serum creatinine total cholesterol and UACR were also found as significant independent risk indicators for the occurrence of retinopathy in this population.

Conclusion: The indices of obesity (increased BMI and WHR), hyperlipidemia (increased triglyceride and cholesterol), serum creatinine and urine ACR may at least in part explain the high prevalence of diabetes mellitus and retinopathy in this rural population of Bangladesh.

1 INTRODUCTION

1.1 BANGLADESH – A brief country profile

Bangladesh officially the **People's Republic of Bangladesh** is a country in South Asia. The name Bangladesh means "**Country of Bengal**" in the official Bengali language. Straddling the Ganges/Brahmaputra delta, Bangladesh is low-lying riverine land traversed by the many branches and tributaries of the Ganges and Brahmaputra rivers. It is among the most densely populated countries in the world and has a high poverty rate and vulnerable to natural disaster. As the

World Bank notes in its July 2005 Country Brief, the country has made significant progress in human development in the areas of literacy, gender parity in schooling and reduction of population growth (1). However,

Bangladesh continues to face a number of major challenges, including widespread political and bureaucratic corruption, and economic competition relative to the world.A brief overview of the country is given below:

Full name: People's Republic of Bangladesh

Term for citizen (s): Bangladeshi

Independence: 16 December 1971 (from West Pakistan); note - 26 March 1971 is the date of independence declaration from West Pakistan, 16 December 1971 is known as Victory Day and commemorates the official creation of the state of Bangladesh.

National flag: Green field with a large red disk shifted slightly to the hoist side of center; the red disk represents the rising sun and the sacrifice to achieve independence; the green field symbolizes the lush vegetation of Bangladesh.

Capital city: Dhaka

Location: Southern Asia, bordering the Bay of Bengal, between Myanmar (Burma) and India

Area: Total area 144,000 sq km (55,599 sq miles). land - 133,910 sq km and water - 10,090 sq km

Land boundaries: Total 4,246 km. Border countries: Myanmar193 km, India 4,053 km

Climate: Tropical, mild winter (October to March); hot, humid summer (March to June); humid, warm rainy monsoon (June to October)

Terrain: Mostly flat alluvial plain; hilly in southeast

Natural resources: Natural gas, arable land, timber, coal

Natural hazards: Droughts, cyclones; much of the country routinely inundated during the summer monsoon season

Population: 153,546,896 (2008 estimate)

Density: 1146/ sq km (11th position) (2008 est.)

Age structure: 0-14 years: 33.4% (male 26,364,370/female 24,859,792)

15-64 years: 63.1% (male 49,412,903/female 47,468,013)

65 years and over: 3.5% (male 2,912,321/female 2,529,502) (2008 est.)

Population growth rate: 2.022% (2008 est.)

Birth rate: 28.86 births/1,000 population (2008 est.)

Death rate: 8 deaths/1,000 population (2008 est.)

Sex ratio: Total population: 1.05 male(s)/female (2008 est.)

Infant mortality rate: Total: 57.45 deaths/1,000 live births

Male: 58.44 deaths/1,000 live births

Female: 56.41 deaths/1,000 live births (2008 est.)

Life expectancy at birth: Total population: 63.21 years

Male: 63.14 years

Female: 63.28 years (2008 est.)

Total fertility rate: 3.08 children born/woman (2008 est.)

Ethnic groups: Bengalis (98%), other 2% (includes tribal groups, non-Bengali Muslims)

Languages: Bangla (official, also known as Bengali), English and some tribal languages.

English is quite widely spoken by those with education.

Religions: Islam (83%), Hinduism (16%). Buddhists and Christians make up about 1%

of the population

Literacy: Definition: Age 15 and over can read and write.

Total population: 43.1%

Male: 53.9%

Female: 31.8% (2003 est.)

Currency: Taka (BDT)

GDP: Per capita USD 1311 (153rd position) (2007 est.)

GNI: Per capita USD 470 (2007 est.)

Major political parties: Bangladesh Nationalist Party (BNP), Bangladesh Awami League (AL), Jamaat-e-Islami Bangladesh, Jatiya Party (N) (JPN).

Government: Bangladesh is a Parliamentary Democracy with a non-executive

President elected by Parliament. Parliament and President are both elected for five years.

Head of State: President Zillur Rahman

Prime Minister: Sheikh Hasina Wazed

Membership of international groupings/organisations: Commonwealth, SAARC, UN, Organisation of Islamic Countries (OIC) (2, 3, 4).

Geography:

The area that is now Bangladesh has a rich historical and cultural past, combining Dravidian, Indo-Aryan, Mongol/Mughul, Arab, Persian, Turkic, and west European cultures. Bangladesh is bordered on the west, north, and east by Indian territory except for a short south-eastern frontier with Myanmar (Burma) and borders the Bay of Bengal in the south. Together with the Indian state of West Bengal, it makes up the ethno-linguistic region of Bengal. Most of the country is situated on deltas of large rivers flowing from the Himalayas: the Ganges, known as the Padma unites with the Jamuna (main channel of the Brahmaputra) and later joins the Meghna to eventually empty into the Bay of Bengal. To the east of the delta lie the only significant area of hilly terrain, constituting less than one-tenth of the nation's territory, is the Chittagong Hill Tracts in the narrow southeastern panhandle of the country. The highest point is located in the south-eastern extremity of Chittagong Hill Tracts. Bangladesh remains vulnerable to natural disasters and to the impact of climate change. Arable land is extremely fertile. Bangladesh's principal natural resource is natural gas (2, 4).

Climate

Traditionally Bangladeshis subdivide the year into six seasons: Grismo (summer), Barsha (rainy), Sharat (autumn), Hemanto (cool), Sheet (winter), and Bashonto (spring). For practical purposes, however, three seasons are distinguishable: summer, rainy, and winter. Bangladeshi climate is tropical and governed by the monsoon winds with a mild winter from October to March; a hot, humid summer from March to June. A warm and humid

monsoon season lasts from June to October and supplies most of the country's rainfall. In summer (March to September) the monsoon winds bring very heavy rainfall (up to 200 inches), often accompanied by cyclonic storms. The short winter is relatively dry. In winter the mean temperature is about 16 degrees centigrade (53F) and in summer 33 degrees centigrade (91F).

Bangladesh is now widely recognized to be one of the countries most vulnerable to climate change. Natural calamities, such as floods, tropical cyclones, tornadoes and tidal bores occur almost every year, combined with the effects of deforestation, soil degradation and erosion. Flooding is normal and life has adapted to take account of this almost in each year. But occasionally excessive flooding, as in 1988, 1998, and 2004 causes widespread destruction and loss of life. There were several reasons for the severity of the flooding. Firstly, there were unusually high monsoon rains. Secondly, the Himalayas shed off an equally unusually high amount of melting water. Trees that usually intercept rain water were cut down for firewood or to make space for animals. Natural hazards that come from increased rainfall, sea level rise, and tropical cyclones are expected to increase as climate change, each seriously affecting agriculture, water & food security, human health and shelter. It is believed that in the coming decades the rising sea level alone will create more than 25 million climate refugees (2, 5-8).

Land

Bangladesh is a land of rivers that crisscrossed throughout the mostly flat territories of the country. A humid, low-lying, alluvial region, Bangladesh is composed mainly of the great combined delta of the Padma, Jamuna and Meghna, with a network of numerous rivers and canals. Except for the Chittagong Hills along the Myanmar border, most of the country is no more than 300 ft (90 m) above sea level. Vast green fields are hounded by low hills in the northeast and the southeast with an average elevation of 244 and 610 metres respectively. Bangladesh is laced with numerous streams, distributaries, and tidal creeks, forming an intricate network of waterways

that constitutes the country's chief transportation system. Along the southwestern coast is the Sundarbans, a mangrove swamp area with numerous low islands. The low-lying delta region is subject to severe flooding from monsoon rains, cyclones (hurricanes), and storm surges that bring major crop damage and high loss of life. The cyclones of 1970 and 1991 and the monsoon floods of 1988, 1998, and 2004 were particularly devastating.

People

Bangladesh is one of the world's ten most populated countries and has one of the highest population densities (about 1146 people per sq km). Regionally, the eastern districts have a slightly higher density than the western ones. On average, a household consists of 5.6 persons. The level of urbanization is low at 20% but it has a predominantly rural population, with over 75% which primarily depend on a poorly developed agriculture for livelihood. The capital city of Dhaka has an estimated population of 8.58 million. The annual growth rate of the population has come down to around 2% with the acceptance of family planning practices rising to 48.7%. The tribal people, who lead a simple life, are generally self-reliant, producing their own food and drinks and weaving their own clothes. The great majority of Bangladesh's population is Bengali, although Biharis and several tribal groups constitute significant minority communities. About 83% of the population is Sunni Muslim and 16% is Hindu. Bangla (Bengali) is the nation's official language, and English is used in urban centers.

Economy

Bangladesh is one of the world's poorest nations, with overpopulation adding to its economic woes, and it is heavily reliant on foreign aid. Major impediments to growth include frequent cyclones and floods, the inefficiency of state-owned enterprises, a rapidly growing labor force that cannot be absorbed by agriculture, delays in exploiting energy resources (natural gas), and inadequate power supplies. The country's economy is based on agriculture. Rice, jute, tea, wheat, sugarcane, and tobacco are the chief crops.

Bangladesh is the world's largest producer of jute. Fishing is also an important economic activity, and beef, dairy products, and poultry are also produced. Except for natural gas (found along its eastern border), limited quantities of oil (in the Bay of Bengal), coal, and some uranium, Bangladesh possesses few minerals.

Dhaka and Chittagong (the country's chief port) are the principal industrial centers; clothing and cotton textiles, jute products, newsprint, and chemical fertilizers are manufactured, and tea is processed. In addition to clothing, jute, and jute products, exports include tea, leather, fish, and shrimp. Remittances from several million Bangladeshis working abroad are the second largest source of foreign income. Capital goods, chemicals, iron and steel, textiles, food, and petroleum products are the major imports. Western Europe, the United States, India, and China are the main trading partners.

History

Before the independence of India and Pakistan, the territory formed part of the Indian provinces of Bengal and Assam. Following partition in 1947, East Bengal, with a Muslim majority population, emerged as the eastern wing of Pakistan. During the period of East and West Pakistan there was a growing sense of Bengali nationalism, stimulated in part by the insensitivity of the central Government in West Pakistan, particularly on language (Urdu was declared the official language although few in East Pakistan spoke it).

In the 1970 general elections the Awami League (AL), a Bengali nationalist party led by Sheikh Mujibur Rahman, won a landslide victory in East Pakistan. Since the East had the larger population this gave it an absolute majority in the national parliament. After West Pakistan failed to recognise the AL's majority, Sheikh Mujib launched a secessionist uprising. The Pakistan Government responded with vicious military tactics, including the targeted murder of “intellectuals” (including many Hindus) and mass rape. This eventually led to the intervention of the Indian army and the new state of Bangladesh was declared independent on 16 December 1971.

Government

Bangladesh is a parliamentary democracy with Islam as the state religion. Direct elections involving all citizens over the age 18 are held every five years for the unicameral parliament known as Jatiyo Sangshad. The parliament building is known as the Jatiyo Sangshad Bhaban designed by architect Louis Kahn and currently has 345 members including 45 reserved seats for women, elected from single-member constituencies. The Prime Minister, as the head of the government, forms the cabinet and runs the day-to-day affairs of state. He or she must be a member of parliament who commands the confidence of the majority of parliament. The President is the head of the state, a largely ceremonial post elected by the parliament.

However the President's powers are substantially expanded during the tenure of a Caretaker Government, which is responsible for the conduct of elections and transfer of power. The officers of the caretaker government must be non-partisan and are given three months to complete their task. This transitional arrangement is an innovation that was pioneered by Bangladesh in its 1991 election and then institutionalized in 1996 through its 13th constitutional amendment.

Bangladesh went ahead with its general election in December 2008. It was the first general election since the army-backed caretaker government took power in January 2007. The Awami League, headed by Sheikh Hasina, won in a landslide, taking 262 of 299 seats in Parliament. The vote was considered fair and largely free of scandal. Sheikh Hasina was sworn in as prime minister in January 2009.

Health status & Health service delivery

Although Bangladesh had a basic health care infrastructure in the 1980s, much remained to be done, particularly in rural areas, where health care is inaccessible for many people and the majority of the people faced critical health problems. The incidence of communicable disease was extensive, and there was widespread malnutrition. Poor standards of hygiene and sanitation,

inadequate sewage disposal, and inadequate supplies of safe drinking water cause up to 80% of diseases. Flood prone areas are subject to waterborne diseases. High levels of maternal and infant mortality are experienced and adherence to traditional home births practices is common. Infants suffered from chronic malnutrition. There is a risk of dengue and malaria fever throughout Bangladesh. There are significant geographical variations in the incidence and prevalence of disease.

The Ministry of Health and Family Planning was responsible for developing, coordinating, and implementing the national health and mother-and-child health care programs. Less than 40 percent of the population has access to the basic health care services, and overall health care performance remained unacceptably low by all conventional measurements. Program implementation, however, was limited by severe financial constraints, insufficient program management and supervision, personnel shortages, inadequate staff performance, and insufficient numbers of buildings, equipment, and supplies. Immunization and family planning programmes have been successful but Bangladesh is still the world's most densely populated country. Improving health care in Bangladesh will be an enormous task.

1.2 Global Burden of Diseases

Non-communicable Diseases

Bangladesh has been experiencing an epidemiological transition from communicable diseases to non-communicable diseases (NCDs). NCDs are important cause of disease burden, morbidity and mortality. At least 25% of the deaths in primary and secondary government health facilities are caused by these diseases. Presently, Bangladesh does not have a community-based public health program for NCDs. Only hospital-based information, although poor, is available. However, exact situation in the country is not known because of lack of representative data, lack of advocacy, lack of logistic and other facilities for initiation of efficient surveillance system on NCDs, as well

as difficulties in the generating resources for newer initiatives. Surveillance for a few communicable diseases is known to exist although it needs major improvement. Unfortunately there is no national surveillance system for non-communicable diseases. The Health, Nutrition, Population Sector Programme (HNPSP) has identified three NCDs- cancer, cardiovascular diseases and diabetes mellitus- as major public health problems. Therefore surveillance of these diseases should be started to assist in formulating country policies and programmes. They have a few common risk factors for which Bangladesh does not have representative data to be addressed for primary prevention. Tertiary level hospital data indicate that cardiovascular diseases have already appeared as one of the leading causes of mortality. Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) and its sister organizations has initiated surveillance of diabetes mellitus all over the country.

1.3 Diabetes Mellitus

Diabetes mellitus (DM) is a group of metabolic disorder with multiclinical features characterized by high blood glucose levels, with disturbances of carbohydrate, fat and protein metabolism, resulting from insulin secretion, or insulin action or both. Diabetes mellitus, commonly referred to as diabetes, means “sweet urine”. Elevated levels of blood glucose (hyperglycemia) lead to spillage of glucose into the urine, hence the term sweet urine. Glucose is the main source of energy for the body's cells. Normally, the levels of glucose in the blood are tightly controlled by a hormone called insulin, which is made by the pancreas. Insulin helps glucose enter the cells and thus lowers the blood glucose level. When blood glucose elevates (for example, after eating food), insulin is released from the pancreas to normalize the glucose level. In patients with diabetes, the pancreas does not make enough insulin or the body can't respond normally to the insulin that is made. This causes glucose levels in the blood to rise, leading to symptoms such as increased urination, extreme thirst, and unexplained weight loss. Diabetes mellitus is also an important factor in accelerating the hardening and narrowing of the arteries,

leading to coronary heart diseases, strokes, and other blood vessel diseases. Diabetes mellitus is a chronic medical condition, meaning that although it can be controlled, it lasts a lifetime. Uncontrolled and poorly controlled diabetes increase the risk of macro-and micro vascular disorders, infections, dysfunction and other associated problems. Long-term DM may lead to complications in any organ of the body, but main target organs are heart, kidney, nerves and eyes.

Classification of Diabetes Mellitus

According to World Health Organization (WHO) diabetes mellitus has been classified into two types: type 1 diabetes mellitus and type 2 diabetes mellitus (WHO, 1999). Beside that gestational diabetes mellitus is another known type of diabetes.

Type 1 diabetes: It was previously called insulin dependent diabetes or juvenile onset diabetes. This is immune mediated diabetes. Type 1 diabetes mellitus results from an absolute deficiency of insulin due to autoimmune destruction of the insulin producing pancreatic beta cell (9). This type of diabetes can affect generally in early stage of life and insulin is required for survival. It has multiple genetic predispositions and has also been said to be related to environmental factors, though still poorly defined. This type of diabetes, account for 5-10% of those with diabetes.

Type 2 diabetes: Type 2 diabetes mellitus, the commonest form of diabetes is also called non-insulin dependent diabetes mellitus or adult onset diabetes. This type of diabetes is characterized by insulin resistance and/or abnormal insulin secretion, either of which may predominate (10, 11). Type 2 diabetes mellitus, account for approximately 90-95% of those with diabetes. Type 2 diabetes mellitus is a disorder entirely separate from type 1 diabetes mellitus. Relative beta-cell insufficiency is, by definition, present in all individuals with type 2 DM. The disorder, in most cases, is also characterized by insulin resistance detected at the level of skeletal muscle, adipose tissue, and the liver. Insulin resistance at the former site results in decreased peripheral glucose

disposal, while the latter, in increased hepatic glucose production. In many individuals, the natural history of type 2 DM begins with a period of insulin resistance with preserved, indeed augmented, pancreatic insulin secretion, as the insensitivity to insulin action in peripheral tissues is overcome by hyperinsulinemia. As a result, plasma glucose concentrations remain relatively normal. As the disease progresses, however, pancreatic islet cell function falters and it is no longer able to meet the peripheral demand. As a result, insulin levels fail to keep up with requirements, and hyperglycemia ensues.

Gestational diabetes mellitus: Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. The definition applies regardless of whether insulin or only diet modification is used for treatment or whether the condition persists after pregnancy. It does not exclude the possibility that unrecognized glucose intolerance may have begun along with the pregnancy. GDM complicates 4% of all pregnancies in the U.S., resulting in 135,000 cases annually. The prevalence may range from 1 to 14% of pregnancies, depending on the population studied. Deterioration of glucose tolerance occurs normally during the 3rd trimester of pregnancy.

1.4 Global Trend of Diabetes Mellitus

In recent years, diabetes mellitus (DM) appears to be a global health problem. It is one of the leading causes of death, disability and economic loss through out the world. Diabetes affects persons of all ages and races. The disease reduces both a person's quality of life and life expectancy and imposes a large economic burden on the health care system and on families.

According to the World Health Organization (WHO) Report there were 171 million people worldwide with DM in 2000 and predicted that 366 million people will have DM by 2030 (P1: 1). The International Diabetes Federation has estimated that another 314 million persons have impaired glucose tolerance and that number will increase to 472 million by 2030 (12). In 2003,

the worldwide prevalence of diabetes mellitus was estimated at 5.1 percent among people age 20 to 79. By 2025, the worldwide prevalence is projected to be 6.3 percent, a 24 percent increase compared with 2003 (13).

The prevalence of DM is reaching epidemic proportions. The prevalence of diabetes was higher in developed countries than in developing countries (13). However, it is estimated that the developing countries will bear the brunt of this epidemic in the 21st century, with 80% of all new cases of diabetes expected to appear in the developing countries by 2025 (P1: 2). In the developing world, the prevalence was highest in Europe and Central Asia and lowest in Sub-Saharan Africa. Some of these variations may reflect differences in the age structures and level of urbanization of the various populations. The largest increase in prevalence by 2025 is expected to be in the Middle-East, Sub-Saharan Africa, South Asia, and Latin America (P1: 1). In terms of those affected, the biggest increase in the developing countries is projected to take place among adults of working age.

The World Health Organization (WHO) estimates that, in 2001, worldwide approximately 1.6 percent of all deaths caused by diabetes mellitus, and approximately 3 percent of all deaths caused by non-communicable diseases. More recent estimates by WHO suggests that the actual number may be triple this estimate and that about two-thirds of these deaths occur in developing countries (14). Within the developing regions, most deaths caused by diabetes occurred in East Asia and the Pacific and the fewest in Sub- Saharan Africa. Diabetes-related complications include microvascular diseases; for example, retinopathy, blindness, nephropathy, and kidney failure and macrovascular diseases; like, coronary heart disease, stroke, peripheral vascular disease, and lower-extremity amputation. Those complications result in disability. In the United States, a much higher proportion of people with diabetes than of people without diabetes have physical limitations: 66 percent compared with 29 percent (15). Disabilities are even more pronounced among older people

(16). Cardiovascular disease (CVD) causes up to 65 percent of all deaths in developed countries of people with diabetes (17).

1.5 Literature Review: Diabetes Mellitus

Diabetes mellitus (DM) is becoming a pandemic worldwide. WHO listed 10 countries to have the highest numbers of people with diabetes in 2000 and 2030 (P1: 1). Bangladesh appears in the list for both 2000 and 2030 with India, Pakistan, China, Japan and USA etc. According to the report, Bangladesh has 3.2 million of diabetic subjects, and the number is expected to increase to a staggering 11.1 million by 2030. Several small-scale population based studies conducted in Bangladesh at different time points have revealed an increasing trend of diabetes prevalence in rural and urban communities (P1: 3-10). A recent population based study (P1: 4) showed a significant increase in the prevalence of DM in rural Bangladesh from 2.3% to 6.8% over 5 years. This prevalence was higher than found in the previous rural studies of Bangladesh (P1: 6, 8). However, the association of obesity and diabetes in this population is unconventional. Some studies showed that BMI and WHR were important predictors of diabetes in rural Bangladeshi population, although the population was considered as lean (P1: 4, 6), while the others did not (P1: 3, 5).

The risk for developing diabetes is higher in people with a family history of diabetes (18). This finding strongly suggests that genetic determinants play a role, but so far few genes have been associated with type 2 diabetes. Environmental factors include prenatal factors, obesity, physical inactivity, and dietary and socioeconomic factors.

The strongest and most consistent risk factors for diabetes and insulin resistance among different populations are obesity and weight gain (19) for each unit increase in body mass index, the risk of diabetes increases by 12 percent (20). The distribution of fat around the trunk region, or central obesity, is also a strong risk factor for diabetes (21). Cardiovascular disease, atherosclerosis, hypertension, and stroke are common problems affecting

individuals with diabetes, all of which correlate highly with the presence of obesity (22, 23). Cardiovascular disease (CVD) is the leading cause of death among diabetics, and is responsible for much of the increase in diabetes-related morbidity and mortality. CVD-related mortality is 2–4 times higher among diabetics (22).

Diabetes risk may be reduced by increasing physical activity. Conversely, a sedentary lifestyle and physical inactivity are associated with increased risks of developing diabetes (24). Some studies report a positive relationship between dietary fat and diabetes, but specific types of fats and carbohydrates may be more important than total fat or carbohydrate intake. Increased affluence and Westernization have been associated with an increase in the prevalence of diabetes in many indigenous populations and in developing economies (25, 26). Conversely, in developing countries, those in lower socioeconomic groups have a higher risk of obesity and consequently of diabetes (27).

1.6 Retinopathy

Retinopathy is a general term for all disorders of the retina, the light-sensitive membrane at the back of the eye. It is a microvascular disorder affecting the small blood vessels in the retina, which includes microaneurysms, retinal hemorrhages, and hard exudates. In some people with retinopathy, blood vessels may swell and leak fluid. In other people, abnormal new blood vessels grow on the surface of the retina. The progression of retinopathy is gradual, advancing from mild abnormalities, characterized by increased vascular permeability, to moderate and severe nonproliferative retinopathy, characterized by vascular closure, to proliferative retinopathy, characterized by the growth of new blood vessels on the retina and posterior surface of the vitreous (28). Retinal microvascular abnormality is the leading cause of visual disability or acquired blindness. Someone having retinopathy, at first may not notice the changes of vision. But over the time, it can get worse and cause vision loss. Retinopathy usually affects both eyes.

Types of Retinopathy

The type of retinopathy is often specified. Arteriosclerotic retinopathy is retinal disease due to arteriosclerotic ("hardening of the arteries"). Hypertensive retinopathy is retinal disease due to high blood pressure. Diabetic retinopathy is retinal disease associated with diabetes, etc.

Arteriosclerotic retinopathy: It is retinal disease caused by arteriosclerotic. In this condition, the arterioles (small arteries) in the retina become partially blocked because of thickening of their walls. Using an ophthalmoscope, a doctor can see the thickened arterioles and other indications of diminished blood supply to the retina. (The characteristic features include narrowed tortuous arterioles with a "copper wire" appearance, scattered small hemorrhages and sharp-edged deposits with no edema around them.) As a general rule, arteriosclerotic retinopathy does not damage vision, although it is a danger signal that the blood vessels in the body are arteriosclerotic and that steps are badly needed to prevent the progression of the disease process.

Hypertensive Retinopathy: In addition to causing heart and kidney problems, untreated hypertension can also affect the eyesight. Hypertension can cause damage to the blood vessels in the retina, the area at the back of the eye where images focus. This condition is known as hypertensive retinopathy. The damage can be serious if hypertension is not treated. Signs of retinopathy include, narrowing of blood vessels, fluid oozing from the blood vessels, spots on the retina known as cotton wool spots and hard exudates, swelling of the macula and optic nerve and bleeding in the back of the eye. The professional uses an ophthalmoscope, an instrument that projects light, to examine the back of the eyeball. Fluorescein angiography can also use to diagnose hypertensive retinopathy. The only way to treat hypertensive retinopathy is to diagnose it earlier and treat the hypertension.

Diabetic retinopathy: Diabetic retinopathy (DR), a common complication of diabetes mellitus, affecting the blood vessels in the retina; results from chronically high blood glucose levels in people with poorly controlled DM. If

untreated, it may lead to blindness. If diagnosed and treated promptly, blindness is usually preventable. Diabetic retinopathy begins without any noticeable change in vision. But even then there often are extensive changes in the retina visible to an ophthalmologist. It is therefore important for a diabetic to have an eye examination at least once (ideally twice) a year.

The diagnosis of diabetic retinopathy is made by a dilated retinal examination (eye exam after the eyes are dilated). This may be coupled with a fundus fluorescein angiography, a test done to assess the extent and type of changes in the retina and its blood vessels. In this test a small amount of dye is injected into a vein in the arm and pictures are taken of the eye. Usually this test is done as an outpatient procedure.

1.7 Globally Retinopathy

Retinopathy, the potential sight threatening condition, is a significant public health problem all over the world; however this morbidity is largely preventable and treatable. It is significantly associated with impairment of vision and blindness. The socioeconomic burden resulting from visual impairment or blindness caused by retinopathy, particularly in working age group, is a serious concern. According to the World Health Organization worldwide there are an estimated 45 million people that are blind with an additional 135 million individuals visually impaired (P2: 3). Retinopathy is responsible for about 5% of those 45 million cases of blindness throughout the world. Retinal disease is more frequent cause of blindness in developing countries (P2: 2). Worldwide, the prevalence of retinopathy is increasing at an alarming rate, possibly as it has had a low priority in the prevention of blindness programs in developing countries. There are several reasons for this. Firstly, it was thought that retinal disease was an uncommon cause of blindness in the developing world; secondly, that the results of treating retinal disease did not justify the effort and expense involved; and, thirdly, that the equipment required was too costly and unreliable for use in a developing

country environment. Finally, there is a lack of skilled personnel with sub-speciality training in retinal disease.

About 20 million Asians were estimated as blind by the World Health Organization (WHO), (P2: 4) and this figure is expected to increase as the population ages. The excellent and very detailed Andhra Pradesh Eye Disease Study (APEDS) found that retinal diseases were a much more common cause of adult blindness in India than had previously been thought (P2: 5). As a result of the increasing trend of diabetes mellitus, as well as growing problem of undetected cases of diabetes mellitus in developing countries, the number of people with diabetic complication like diabetic retinopathy will continue to rise. With the epidemic increase in diabetes as reported by the World Health Organization (WHO), DR is fast becoming an important cause of visual disability (29). Global projections suggest that 20% of people with diabetes will develop DR (30). A person with diabetes is 25 times more likely to go blind than a person in the general population (31). WHO has estimated that DR is responsible for 4.8% of the 37 million cases of blindness throughout the world (32).

1.8 Literature Review: Retinopathy

Retinopathy is very much familiar with its risk factors, clinical presentation, and management in patients with diabetes mellitus, commonly termed diabetic retinopathy. As a result, Enormous population based data of retinopathy in patients with diabetes mellitus, commonly termed as diabetic retinopathy (DR) was published. However, other ocular and systemic causes of retinopathy or the clinical significance of retinopathy is fairly common in adults without diabetes (33-36). Worldwide, the prevalence of retinopathy in diabetes population is increasing at an alarming rate due to prolonged survival of diabetic patients. It is a significant cause of visual disability both in type 1 and type 2 diabetes mellitus in earlier epidemiological studies (37-41). The Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) the widest and most prolonged population based ophthalmologic survey of

people with diabetes concluded that retinopathy has been shown to be the cause of visual impairment and blindness in 86 % of type 1 diabetic patients and in 33 % of type 2 diabetic patients (40). It is estimated that retinopathy develops in more than 75% of diabetic patients within 15-20 years of diagnosis of diabetes (38, 42).

There have been many epidemiological studies assessing the prevalence of diabetic retinopathy (41, 43-52). About half of the people with diabetes in the United States have at least some form of retinopathy (41) where 1 of every 12 persons with DM in the age group of 40 yrs and above has advanced or vision-threatening retinopathy. In Western Europe DR has been reported to be the most common cause of blindness among people in working age group and the incidence dose not seem to decline (49). There are few population based studies on the prevalence of diabetic retinopathy (DR) in Asia, with most originating from India (P2: 6-9). In India, DR was the 17th cause of blindness 20 years ago; today it has ascended to the 6th position (31). However, in the Chennai Urban Rural Epidemiology Eye Study (CURES), another population based study found the overall prevalence of DR was 17.6% (43).

Non-diabetic retinopathy has been defined in different studies to include microaneurysms, retinal haemorrhages, hard exudates, cotton wool spots, retinal venular abnormalities, intraretinal microvascular abnormalities, and new vessels (33-35). The ocular and systemic causes of retinopathy in people without diabetes are varied. Only a few population based research has been performed on the prevalence of retinopathy in general population as well as at different levels of hyperglycemia, such as, diabetes mellitus, impaired glucose tolerance, impaired fasting glucose and normal glucose tolerance (P2: 29, 30). So far there is not a single study on the extent of this issue has been carried out in Asian population.

Hypertension is probably the best known systemic condition associated with retinopathy. In people with hypertension, retinopathy is often referred to as

hypertensive retinopathy. Retinopathy has been found to be present in about 11% of hypertensive non-diabetic people over 43 years of age (34). An appreciable proportion (average 6%) of normotensive non-diabetic people may also have retinopathy (33-35). In two population based studies, more than 50% of the participants with non-diabetic retinopathy did not have a history of hypertension (34, 35). Retinopathy may thus represent the cumulative effects of elevated blood pressure throughout life in people not classified as having hypertension.

In the Framingham Eye Study, 2.5% of participants who had a dilated screening ophthalmoscopic examination were observed to have retinopathy (53). After excluding persons with diabetes, the prevalence of retinopathy was only 0.8%. In a series of reports from the Beaver Dam Eye study in Wisconsin, Klein and colleagues described in detail the prevalence (34, 54, 55) and 5-year incidence (56) of retinal microvascular abnormalities, and their relationship with hypertension in nondiabetic population. Based on these data (34, 37, 55, 57), Klein and colleagues have suggested that retinal microvascular abnormalities are common in the general nondiabetic population, although they are more prevalent in persons with hypertension. In the Blue Mountains Eye Study in Australia, using a photographic grading technique similar to that used in Beaver Dam, the prevalence of retinopathy was reported at 10% (35). Although this was slightly higher than in Beaver Dam study, the age-specific rates of retinopathy in men and women were similar between the two studies (34, 35, 55). In summary, available epidemiological data suggest that retinal microvascular abnormalities can be found in 2–14% of the general nondiabetic population, and are fairly common even in persons without hypertension.

Retinopathy lesions are commonly seen in middle aged and elderly people with and without diabetes. Signs of retinopathy are structural markers of microvascular damage which has been strongly linked with hyperglycemia (P2: 11), elevated glycosylated hemoglobin level (P2: 12-14), hypertension (P2:

15-17), lower glomerular filtration rates and microalbuminuria (P2: 18). One study found that retinopathy was associated with increasing fasting blood sugar concentrations in people not classified as having diabetes mellitus (P2: 19), although another study did not find this association (P2: 16). Nevertheless, the distinction between diabetes and pre diabetes is somewhat arbitrary, and the results of some recent studies have shown that some of the subjects with IGT have had retinopathy (P2: 20, 21). However, if these identified risk factors managed with timely diagnosis, the quality of life can be preserved.

1.9 Rationale of the Study

The latest report from World Health Organization (WHO) (P1: 1) illustrates the increasing trend of diabetes mellitus in Bangladeshi population. However, several small-scale population based studies conducted in Bangladesh at different time points have revealed an increasing trend of diabetes prevalence in rural and urban communities. But the pattern of diabetes in Bangladeshi population differs from that in Europeans and Americans in several aspects: The onset is at a younger age, obesity is less common, and changes in lifestyle appear to be stronger. Combination of low BMI and relatively high central obesity with increasing prevalence of DM are general features of diabetes in Bangladeshi population. However, the association of obesity and diabetes in this population is unconventional. These clinical differences and the rising prevalence of diabetes in Bangladesh warrant well-conducted epidemiologic studies on diabetes including lipid profile, serum creatinine and urine albumin creatinine ratio (UACR) as possible confounders for DM in the rural population.

On the other hand, there was only one nationally representative survey concerning the extent of blindness or the main causes of vision impairment in Bangladeshi adults, which has identified low level of diabetic retinopathy as the cause of visual impairment and moreover, no subject was found to be blind due to diabetic retinopathy (P2: 22). As the consequences of increasing

trend of diabetes mellitus, the number of people with diabetic complications like retinopathy will continue to rise in Bangladesh. As blindness caused by diabetes is largely preventable by good control of the risk factors, early detection of retinopathy is an important preventive strategy. Not only the patients with diabetes mellitus, but elderly individuals with pre diabetes (IGT and IFG) and normal glucose metabolism in general, have a substantial risk of developing retinopathy. To the best of our knowledge there is no population based study yet in Bangladeshi population either in diabetic or non diabetic general population to estimate the magnitude of retinopathy. However, the identified risk factors for retinopathy established by others have not been extensively studied in our population. The absence of reliable population based epidemiological data on retinopathy in Bangladesh is a serious impediment to the effective national planning of eye care programmes.

In the above context, we were attempting to carry out an epidemiological study to observe the chronological changes in the prevalence of diabetes mellitus and to identify its associated risk factors, as well as, to make a baseline data focused on retinopathy in a rural Bangladeshi population. This would be the first effort to estimate the prevalence of retinopathy among diabetic and non diabetic population in Bangladesh and to identify the associated risk factors for developing retinopathy in this adult sample.

2 OBJECTIVES

2.1 General Objective

The general objective of the study was to estimate the prevalence and risk factors of diabetes mellitus and retinopathy in a rural population of Bangladesh.

2.2 Specific Objectives

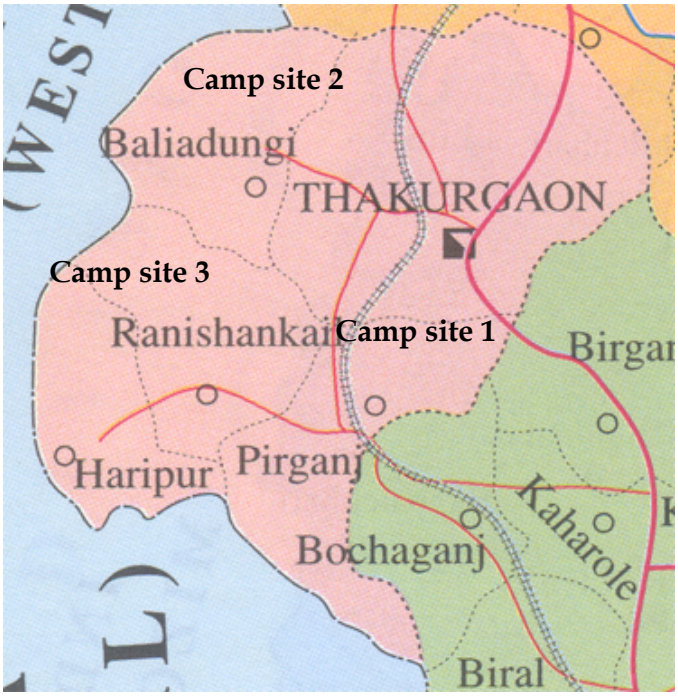
The specific objectives of the study were as follows;

1. To estimate the prevalence of pre diabetes in rural population of Bangladesh.
2. To estimate the prevalence of diabetes in rural population of Bangladesh.
3. To identify the associated risk factors for diabetes in this population.
4. To estimate the prevalence of retinopathy in a rural diabetic population of Bangladesh.
5. To estimate the prevalence of retinopathy in a rural non diabetic general population.
6. To identify the associated risk factors for developing retinopathy in Bangladeshi rural population.

3 SUBJECTS AND METHODS

3.1 Study Area

Bangladesh has 64 districts and the study was conducted in one district of northern Bangladesh called Thakurgaon. Thakurgaon is in the north-west corner of Bangladesh, it is about 467 km from Dhaka, the capital of Bangladesh. The district is a part of the Himalayan plain land and the state of India lies on its west and north side. This district has 5 upazilas (sub-district). Subjects were recruited from all upazilas by following simple random procedure.



3.2 Study Design

The study was a population based general cross-sectional study which was ultimately focused on the prevalence and determinants of diabetes mellitus and retinopathy among the rural population of Bangladesh. This epidemiological survey was conducted through screening in camp settings to

detect diabetes and retinopathy. Three camps were organized in 3 different places of Thakurgaon district.

3.3 Study Population

This study was a part of an ongoing large epidemiologic study of Bangladesh Diabetic Somity, involving a representative population of Thakurgaon district. The study population was both male and female adults aged ≥ 25 years who were the residents of this district.

3.4 Sample Size Calculation

As this study was only a part of a continuing large epidemiologic study, to determine the required sample size for this part of study, the formula: $n = PQ/d^2$ was used. Where P for prevalence (of DM + Pre DM) from the previous study, i.e. 0.14 (14%); Q = 1 – P, i.e. 0.86 and d = allowable error of known prevalence i.e. 0.085 × 0.14. Thus the sample size, n = 850. But a total of 836 subjects participated in the study. The sample size calculation was done for predicting the prevalence of diabetes mellitus in Bangladeshi population. This subset of population was also investigated to estimate the prevalence of retinopathy among diabetes and non diabetes population and explore the associated risk factors for developing retinopathy. Following a simple random procedure 1000 individuals aged ≥25 years were identified to participate in this study. Among them 836 individuals agreed to participate and were investigated in the present study.

3.5 Study Period

The present study took about 6 months for collecting data. Three camps were organized in 3 different places of Thakurgaon district by Thakurgaon Swasthoseba Hospital within this time period. The first camp was held on June 2008, second camp on August 2008 and the last camp on December 2008. Each camp continued for two days.

3.6 Inclusion Criteria

Both men and women ≥25 years of age who are the inhabitants of this district and are willing to participate voluntarily and comply with the instruction of the study e.g. overnight fasting, was considered eligible for the study.

3.7 Exclusion Criteria

People who were not qualified by inclusion criteria were excluded from the study. Pregnant women and physically or mentally disabled persons unable to follow simple questions were excluded.

3.8 Survey Procedures

Sixteen field assistants were recruited from the local community and trained for the field work which included sample selections, organizing the screening camps, collection of data by reviewing the questionnaire and delivering the results to the participants. Seven days of training were provided to the assistants for selection process, interview and data collection prior to the commencement of the study. Each trainee was evaluated before he or she was allowed to participate in the study. The field assistants listed all the adults aged ≥25 years from each area and identified the required number of subjects following simple random procedure.

All the individuals selected for the study were given an identification number. The field assistants approached the potential participants by an information letter and a respond document. Participants were informed of the purpose and the procedure of the study and they were requested to attend the screening camps in the morning on a pre-arranged date after an overnight fast of at least 8-10 hours. Each and every subject was made aware and was explained the necessity of the fasting state of a minimum 8-10 hr prior to the test. On arrival at the pre scheduled time (7.30 am to 8.30 am) on the appointed day, confirmation of the fasting state was verified once again from each participant by asking the fasting state. After receiving the consent general registration of the participant was initiated and the whole investigation procedure was started. Venous blood and urine sample were

collected from each participant at their fasting state and after 2 hours break venous blood sample was again collected from them.

During the 2 hr waiting period the participants were interviewed for some general information through the preseted questionnaire and were measured some biophysical parameters which include anthropometric (height, weight, waist circumference and hip circumference) and blood pressure measurements. Further comprehensive ocular examinations were performed on each subject by trained technical assistants and ophthalmologists.

3.9 Interviewer Administered Questionnaire

The preseted questionnaire was composed of some general information; like the demographic and socioeconomic information, including name, sex, age, education, occupation and economic status. The participants were asked for their 1st degree family history of diabetes, associated complications of diabetes, if any, (nephropathy, neuropathy, hypertension, hyperlipidaemia, coronary artery diseases) and information related to their own medical history of obesity, hypertension, diabetes and associated complications of diabetes. They were also asked for the ocular history which includes details of first and last eye examination, nature of present eye complaint or any ocular surgery.

3.10 Clinical Parameters

With proper aseptic precaution, initial 8 ml of venous blood and urine sample were collected from each participant. Fasting blood glucose (FBG), lipid profile (triglyceride, total cholesterol, high density lipoprotein and low density lipoprotein), serum creatinine and glycosylated hemoglobin (HbA_1c) were determined from fasting blood sample and albumin creatinine ratio (ACR) was measured from urine sample. All subjects other than those with known diabetes (n=22) were then given a 75-g oral glucose solution (75-g oral glucose load dissolved in 500 ml of water) to drink. Another 3 ml of venous blood was collected after 2 hours to determine 2 hr post oral glucose tolerance test (OGTT).

After collecting the blood and urine sample it was centrifuged on the site within 3 hours to separate plasma. All samples were then refrigerated and stored at -20^{0}C until laboratory assays was done. Fasting blood glucose (FBG) and oral glucose tolerance test (OGTT) were analyzed by glucose oxidase method (Randox, UK) for the diagnosis of diabetes mellitus. Lipid profile includes total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides (TG), which were measured by enzymatic technique. Glycosylated hemoglobin (HbA1c) was measured by high-performance liquid chromatography (HPLC).

3.11 Anthropometrical Measurement

Anthropometric measurements included height, weight, waist circumference and hip circumference. The measurements were taken with light clothes without shoes. Height was measured by using a portable, locally manufactured, stadiometer, standing upright on a flat surface without shoes to the nearest 0.1 cm. Body weight was measured while wearing light clothes by an adjusted scale and recorded to the nearest 0.1 kg. Body mass index (BMI) was calculated by the formula: weight in kilograms divided by height in meters squared. Waist circumference was measured at 1 cm above the level of navel at minimal respiration and hip circumference was measured at the level of maximum posterior extension of the buttocks by placing a flexible plastic tape horizontally with light clothes. Both circumferences were recorded to the nearest 0.1 cm. Two readings of height, weight, waist circumference and hip circumference were recorded and the mean of the two was taken as the final reading. Asian BMI criteria were used to identify overweight and obese in this population (P1: 16). Five categories of BMI were identified here for presenting the data. Individuals with BMI below 18.49 kg/m2 classified as underweight, healthy weight (BMI 18.5-22.99 kg/m2), overweight (BMI 23.0-24.99 kg/m2), obese I (BMI 25.0-29.99 kg/m2) and obese II (BMI over 30.0 kg/m2)), respectively.Abdominal obesity was evaluated by waist/hip ratio, with android and gynaecoid cut off points taken at 0.8 and 0.9 for females and males respectively (P1: 17).

3.12 Blood Pressure Measurement

Blood pressure was taken after administration of the questionnaire. To reduce the variation, subjects rested for at least 10 minutes before the BP was recorded. The pressure was measured in sitting position on the right arm using normal cuffs for adults fitted with a standard mercury sphygmomanometer, placing the stethoscope bell lightly over the brachial artery. BP was usually recorded to the nearest 2 mm Hg from the top of the mercury meniscus. Two readings were taken 5 minutes apart, and the mean of the two was taken as the final blood pressure reading of the individual. Hypertension was defined as a systolic blood pressure (SBP) of ≥ 140 mm Hg and/or diastolic blood pressure (DBP) of ≥ 90 mm Hg (P1: 18).

3.13 Ophthalmologic Examinations

All the participants were gone through a complete ocular examination on that prearranged day by trained ophthalmologists. Visual acuity was recorded with an illuminated Snellen chart. The presenting and best corrected visual acuity was documented separately for each eye. Intraocular pressure measurement was performed with Schiotz indentation tonometer (Schiotz, John Weiss & Son Ltd, London, UK). Slit lamp was used for anterior segment evaluation including the depth of anterior chamber and rubeosis irids with diluted pupils. Fundus photography was operating with a digital camera (Super 66 equipped with stereo fundus lens). Dilated fundus evaluation was done with binocular indirect opthalmoscope (Keeler Instrument Inc, PA, USA). The photographs were taken in a dark room after a 5 minute adaptation period to allow the pupils to dilate to some extent and were analyzed by two ophthalmologist specialized in retinal diseases. World Health Organization recommended definitions of retinopathy, vision, and visual disability (ICD 10) was used (P2: 25). Among 836 participants 45 were identified with retinopathy and were referred to the Thakurgaon Swasthoseba Hospital, the Health Care Center of the Bangladesh Diabetic Somity for further treatment and follow-up.

3.14 Diagnosis Criteria for Diabetes

After estimation of fasting blood glucose (FBG) and oral glucose tolerance test (OGTT), the participants were classified into non diabetes, diabetes mellitus, IFG (impaired fasting glucose) and IGT (impaired glucose tolerance), according to the recommendation of the World Health Organization Expert Committee (P1: 18). Subjects were defined as having diabetes mellitus (n = 60) based on their fasting blood glucose levels ≥ 7.0 mmol/l or 2 hr post glucose levels ≥11.1 mmol/l or both. IFG was defined when FBG values were between 6.1-7.0 mmol/l and OGTT <7.8 mmol/l. IGT was defined when FBG <7.0 mmol/l and OGTT values were between 7.8-11.1 mmol/l. IFG and IGT subjects were together called pre diabetes (n = 54). Thirteen retinopathy cases were identified from the diabetic subjects and 7 were from pre diabetic subjects. The rest 25 retinopathy cases are non diabetic subjects.

3.15 Criteria for Other Variables

According to the ADA recommendation (P1: 35) the cut of value of other variables like, total cholesterol (<200 mg/dl), triglyceride (<150 mg/dl), LDL (<100 mg/dl), HDL (for male >50 mg/dl and for female >40 mg/dl), serum creatinine (for male <1.4 mg/dl and for female <1.2 mg/dl) and urine albumin creatinine ratio (<30 mg/g) was used for data analysis.

3.16 Ethical Consideration

All necessary ethical and administrative approvals were obtained from the appropriate authorities before commencement of the study. The protocol was approved by the Norwegian Ethical Committee for Medical Research and the National Ethical Committee of Bangladesh. Administrative clearance was obtained from Bangladesh Ministry of Public Health, the District Medical Officer and local official institutes.

Permission to conduct this study was also obtained from the target group. All participants were provided with a detailed information letter about the study objectives, procedures and the risk and benefits involved. This information

was explained sufficiently to the participants who were treated with respect for their dignity. They had an opportunity to discuss with the study team if they required further information and clarification. All subjects selected to participate in the study, signed an informed consent form prior to commencing any study procedure. However, the participants who were illiterate gave verbal consent and the witness signed on the document on behalf of the participant. They were informed of their rights to withdraw from the study at any stage of the study without giving any notification of reasons.

The project was carried out in accordance with the guidelines in the Helsinki Declaration. The participants were reassured about the confidentiality of data. The questionnaires and laboratory documents were kept securely. Folding screens were used to isolate the subjects. Male and female participants were stayed in different separate rooms while conducting anthropometric and clinical examinations. In consideration of safety for both subjects and doctors disposable hypodermic syringes, gloves and other necessities were used while taking blood sample. The blood and urine specimen were frozen and stored well. All of the test on blood and urine were only done for research purpose. Other unrelated persons had no access to data files.

The written results of medical examination were distributed and explained to the participants through Thakurgaon Swasthoseba Hospital, the Health Care Center of the Bangladesh Diabetic Somity. They were free to discuss their test reports with the doctors. They were encouraged to raise health questions and the questions were answered individually. Clinical suggestions were delivered if needed. Anyway, the subjects and the target population were benefited from the research potentially, although our project didn't provide intervention or medication directly. The identified cases for diabetes, trend to diabetes and retinopathy were referred to the Thakurgaon Swasthoseba Hospital for follow up and further treatment.

3.17 Data Analysis

The data was entered in the pre-designed Microsoft office excel format which was imported later into the statistical software SPSS. The prevalence rates of diabetes and retinopathy were determined by simple percentages. Statistical comparisons between categorical variables were made by using χ^2 test and comparisons between continuous variables were made by using independent sample t test. The odds ratio (OR) with 95% confidence interval (CI) for risk factors was calculated assuming the least prevalence of clinically relevant criteria as a reference value. Multiple logistic regression were performed to quantify the individual effect of predictor variables and to adjust for potential confounding factors. All *P*-values presented are two-tailed. The statistical tests were considered significant at a level ≤5% (≤0.05). All the statistical analysis were performed using SPSS 16 software.

4 RESULTS

4.1 Demographic and Socio-economic Characteristics of the study subjects (Table 1)

In this cross sectional study a total of 836 participants were registered to attend all the activities of the camp. The mean (±SD) age (in years) of the participants was 46 (±12) years. All participants were divided into 3 age groups with 15

Table 1: Demographic and Socio-economic Characteristics of the study subjects

Variables		**Frequency**	**Mean±SD/Percentage**
Mean Age	Total Participants	836	46.0(±12)
	Male Participants	468	46.0(±12)
	Female Participants	368	45.0(±11)
Age	25-40yrs	326	39
	41-55yrs	300	36
	> 55 yrs	210	25
Gender	Male	468	56
	Female	368	44
Education	Illiterate	284	34
	Primary	276	33
	SSC	184	22
	HSC	59	7
	BSc	25	3
	MSc	8	1
Occupation	Farmer and day labor	284	34
	Service holder	84	10
	Businessmen	108	13
	Housewives	293	35
	Retirement	67	8
Socio-Economic Status	Poorest of the poor	192	23
	Poor	359	43
	Lower middle class	235	28
	Middle class	50	6

years age interval. Among the participants 326 (39%) participants were between 25 to 40 years, 300 (36%) participants were between 41 to 55 years and 210 (25%) were above 55 years of age. Among the 836 participants 56% (n=468) were male and 44% (n=368) were female participants. Females being younger (mean±SD, 45.0±11) compared to male (mean±SD, 46.0±12) subjects. A major portion of the participants were illiterate (34%) and below primary level (33%). SSC, HSC, Degree, and masters' level participants were 22%, 7%, 3% and 1% accordingly. Major number of participants was housewives (35%). Among the others farmers and day labors were 34%, service holders 10%, small businessmen 13% and retired personnel 8%. Among the participants 23% were poorest of the poor, poor were 43%, Lower middle class 28% and middle class 6%.

4.2 Anthropometric and clinical characteristics of the study subjects (Table 2)

General anthropometric and clinical characteristics of the participants were presented by gender with 15 years age interval. There were no differences in BMI between male and female participants in all age strata. However the mean BMI was 22.2 and 21.9 for the male and female participants, respectively. Mean BMI was increased according to the age group for both males and females. This picture is also reflected in the assessment of other parameters except for LDL. In younger age group there were significant differences in systolic blood pressure, diastolic blood pressure, triglyceride and total cholesterol between male and female participants. But it is not reflected in other age groups. A superior agreement was observed between FBG and OGTT (Kappa value 0.86) among the study participants (data has not shown).

Table 2: Anthropometric and clinical characteristics of the study subjects

Variables	25-40 yrs			41-55 yrs			above 55 yrs		
	Male (n=162)	Female (n=164)	P for difference	Male (n=172)	Female (n=128)	P for difference	Male (n=134)	Female (n=76)	P for difference
BMI (kg/m^2)	21.4±3.2	21.6±3.5	0.650	22.3±3.6	21.8±3.7	0.141	22.9±4.2	22.5±4.6	0.585
WHR*	0.89±0.06	0.87±0.07	0.018	0.92±0.07	0.88±0.07	0.001	0.93±0.07	0.92±0.08	0.122
SBP (mmHg)	117.7±15.4	113.4±15.8	0.014	119.7±16.8	121.3±22.6	0.490	123.7±19.1	125.1±20.1	0.418
DBP (mmHg)	77.5±10.8	74.6±11.6	0.029	78.2±11.4	80.3±15.5	0.253	78.7±12.9	81.2±15.0	0.196
FBG (mmol/l)	5.03±1.7	5.05±1.8	0.913	5.1±1.5	5.3±2.1	0.277	5.2±1.4	5.7±2.3	0.142
AG (mmol/l)	5.9±2.3	6.2±2.6	0.209	6.1±2.7	6.4±3.1	0.325	6.4±3.0	7.3±4.5	0.146
HbA1c (%)	4.9±1.2	5.01±1.1	0.480	5.1±1.3	5.1±1.2	0.996	5.4±1.4	5.8±1.9	0.172
S Creatinine (mg/dl) *	1.12±0.23	1.03±0.21	0.001	1.24±0.33	1.16±0.26	0.050	1.40±0.40	1.31±0.43	0.062
Triglyceride (mg/dl)	156.4±65.3	135.9±54.7	0.002	156.6±62.1	155.7±56.9	0.936	162.2±65.3	163.4±71.9	0.912
Cholesterol (mg/dl)	187.3±32.4	178.0±32.9	0.013	189.5±40.6	192.9±35.2	0.642	190.8±40.3	198.3±40.5	0.068
HDL (mg/dl) *	36.8±8.4	34.1±8.3	0.010	37.8±11.1	34.8±7.4	0.002	38.0±11.2	37.3±8.6	0.615
LDL (mg/dl)	119.7±29.6	116.5±30	0.332	127.1±37.6	126.2±33.6	0.702	118.2±37.1	124.1±39.4	0.310
UACR (mg/g)	13.7±6.2	13.9±5.8	0.996	13.9±6.7	14.7±6.9	0.470	18.3±7.9	18.7±8.4	0.824

Data are presented as mean±SD; independent t- test was done as a test of significance.

Abbreviations: BMI, Body mass index; WHR, Waist hip ratio; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; FBG, Fasting blood glucose; AG, After 2 hr glucose load; $HbA1_c$, Glycosylated hemoglobin; HDL, High density lipoprotein; LDL, Low density lipoprotein; UACR, Urine albumin creatinine ratio

* Data are coded with reference value separately for male and female and then analyzed together.

4.3 Prevalence of diabetes, prediabetes and retinopathy among the study population (Table 3)

The overall prevalence of diabetes was 7.2%, prediabetes (both IGT & IFG) was 6.5% and retinopathy was 5.4%. Prevalence of diabetes, prediabetes and retinopathy increased with increasing age both for males and females. Though non-significant, females had higher prevalence of diabetes, prediabetes and retinopathy compared with males in all age groups. The difference in prevalence of diabetes and retinopathy by sex widened in the older age group (>55 years). But for pre diabetes, the difference in prevalence

by sex was wider in the younger age group (25-40 years), while the difference was very narrow in the older age group (>55 years).

Table 3: Prevalence rate of diabetes and prediabetes and retinopathy by gender distribution

Groups	Total Male	Total Female	Number of cases		Prevalence per 100		Total prevalence (%)	P for difference
			Male	Female	Male	Female		
Diabetes	468	368	32	28	6.8	7.6	7.2	0.668
Prediabetes	468	368	26	28	5.5	7.6	6.5	0.231
Retinopathy	468	368	23	22	4.9	5.9	5.4	0.499

4.4 Prevalence of retinopathy according to glucose metabolism category (Table 4)

In the present study we found that the prevalence of retinopathy was 21.6% among the diabetic subjects (DM), 13% among the prediabetic subjects (Pre DM) and 3.5% among the nondiabetic subjects (NGM), respectively. Males had higher prevalence of retinopathy compared with females in diabetes group. On the contrary, females had higher prevalence of retinopathy compared with males in prediabetes and nondiabetes group.

Table 4: Prevalence rate of retinopathy by glucose metabolism category

Glucose Metabolism Category	Total Male	Total Female	Retinopathy cases		Prevalence per 100		Total prevalence (%)	P for difference
			Male	Female	Male	Female		
DM	32	28	9	4	28.1	14.3	21.6	0.094
Pre DM	26	28	3	4	11.5	14.3	13.0	0.764
NGM	410	312	11	14	2.7	4.5	3.5	0.189

Abbreviations: DM, Diabetes Mellitus; Pre DM, Pre Diabetes Mellitus; NGM, Normal Glucose Metabolism.

4.5 Baseline characteristics of diabetic, pre diabetic and non diabetic people

The characteristics were compared between subjects with diabetes (n=60) & non diabetes (n=722), pre diabetes (n=54) & non diabetes (n=722) and diabetes (n=60) & pre diabetes (n=54). The subjects with diabetes were significantly older with higher BMI, WHR, blood pressure, serum glucose (fasting and 2 hr after glucose), HbA1c, serum creatinine, triglyceride, total cholesterol, LDL, UACR and significantly lower HDL compared to subjects with non diabetes. Although non significant, the subjects with pre diabetes were older than non diabetes subjects. The comparison of other characteristics between pre diabetes and non diabetes subjects yielded similar results. The subjects with diabetes had significantly higher WHR, serum glucose (fasting and 2 hr after glucose), HbA1c, serum creatinine and triglyceride compared to subjects with pre diabetes. Although non significant, diabetes subjects had higher age, BMI, blood pressure, total cholesterol, HDL, UACR and lower LDL compared to subjects with pre diabetes.

4.6 Baseline characteristics of people with retinopathy and without retinopathy in diabetes and non diabetes group

Forty five individuals were found to have retinopathy among 836 participants which included diabetic, prediabetic and nondiabetic population. The baseline characteristics were compared between subjects with and without retinopathy. The subjects with retinopathy were significantly older with higher BMI, WHR, blood pressure, serum glucose (fasting and 2 hr after glucose), HbA1c, serum creatinine, triglyceride, total cholesterol, LDL, UACR compared to subjects without retinopathy. Although non significant subjects who developed retinopathy had lower HDL compared to subjects without retinopathy.

Diabetic subjects (n=60), with diabetic retinopathy had significantly higher age, BMI, diastolic blood pressure, HbA1c, serum creatinine, total cholesterol, LDL and UACR compared to subjects without retinopathy. However, higher

WHR, systolic blood pressure, serum glucose (fasting and 2 hr after glucose), triglyceride and low level of HDL were not found to be significantly associated with increasing the prevalence of retinopathy among the diabetic subjects. On the contrary, age, WHR, blood pressure, serum fasting glucose, HbA1c, serum creatinine, total cholesterol, LDL and UACR were significantly higher in individuals with retinopathy among the non diabetic individuals (n=776). Subjects with diabetic retinopathy were significantly older with higher BMI, WHR, diastolic blood pressure, serum glucose (fasting and 2 hr after glucose), HbA1c, serum creatinine, triglyceride, total cholesterol and LDL compared to those with retinopathy but without diabetes.

4.7 Associated risk factors for developing Diabetes among the study population

We used logistic regression to quantify the individual effects of age, sex, BMI, WHR, SBP, DBP, S Creatinine, Lipids and UACR with diabetes. Age, BMI, WHR, SBP, DBP, S Creatinine, triglyceride, total cholesterol and UACR were found to be significant risk factors for the occurrence of diabetes mellitus in the univariate model. After adjusting for potential confounders in the multivariate model by using all variables BMI, WHR, S Creatinine, triglyceride, total cholesterol and UACR remained as significant independent risk indicators for the occurrence of diabetes in this population. BMI >23.0 showed to be exceedingly risky state for the occurrence of diabetes. The risk for diabetes was almost 2-fold or sometimes more than 2-fold higher in subjects with BMI >23.0 kg/m^2, high WHR both for male and female, high serum creatinine for both sex, triglyceride >150 mg/dl, cholesterol >200 mg/dl and UACR >30 mg/g.

4.8 Associated risk factors for developing retinopathy among the study population

We used logistic regression to quantify the individual effects of age, sex, glucose metabolism category, BMI, WHR, SBP, DBP, hypertension, HbA1c, S

Creatinine, Lipids and UACR with diabetes. Age, glucose metabolism category, BMI, SBP, DBP, hypertension, HbA1c, S Creatinine, triglyceride, total cholesterol and UACR were found to be significant risk factors for the occurrence of retinopathy in the univariate model. After adjusting for potential confounders in the multivariate model by using all variables in the model age, DM, BMI, SBP, DBP, hypertension, HbA1c, S Creatinine, total cholesterol and UACR remained as significant independent risk indicators for the occurrence of retinopathy in this population. The risk for retinopathy was almost 2-fold in subjects who were above 40 years with fasting glucose of ≥6.1 mmol/l, BMI >25.0 kg/m^2, hypertensive, increased HbA1c level of above 5.3%, high serum creatinine for both sex, cholesterol >200 mg/dl and UACR >30 mg/g.

5 DISCUSSION

5.1 Main Findings

The present study addressed the prevalence and its associated risk factors of diabetes and retinopathy in a rural population in Bangladesh. The prevalence of diabetes was found to be 7.2% which is comparable to the recent rural studies (P1: 6, 7, 9), but significantly higher than the studies conducted in early 2000s (P1: 3, 4, 5). However, moderate but steady rise in the prevalence of pre diabetes (6.5%) was observed compared to a recent published data (P1: 3), but rather a lower prevalence compared to another study (P1: 6). Data on the rising trend of diabetes in Bangladesh were based on the comparison of data collected from different parts of the country at different times and had applied different procedures, other than one (P1: 4). Therefore, it is difficult to make a scientific comprehension of the rising trend of diabetes. To compare secular trends, it would be more accurate to document the prevalence of diabetes within the same region applying the identical procedure.

The prevalence of diabetes documented in this study was comparatively higher than the prevalence found in rural China (5.6%), but more related to that of rural India (6.3%) and was equal to that of rural population in Turkey (7.2%) (P1: 19, 20, 21). However, the observed prevalence rate of diabetes in this report is lower than the prevalence found in rural Pakistan (11.1%) (P1: 22). But the direct comparisons of prevalence rates are challenging owing to differential methodologies applied and diverse characteristics of the population.

Several studies showed that urbanization, economic development and affluent lifestyle are causing high prevalence of DM even in the developing countries (P1: 23, 24, 25). The rural Bangladeshi population is undergoing lifestyle transition due to socio-economic growth, which is associated with this increased rate in the prevalence of diabetes in rural Bangladesh. But BMI

in this population remain low. Therefore, it would be difficult to ascribe the increased prevalence only due to higher calorie intake as a consequence of improved socio-economic condition. Rather higher pre diabetes in a lean population may also indicate genetically susceptible population, who may convert to diabetes with a much lower change in obesity, although the BMI may remain low. Thus there could be a rapid progression from the normal state through pre diabetes to diabetes, which could imply a rapid increase in the diabetes epidemic or a worsening diabetogenic environment. Prospective studies are required to assess the exact changes occurring with regard to the diabetes epidemic in Bangladesh.

As obesity is an established risk factor for diabetes, we have observed an important association of both general obesity and central obesity with diabetes. It is of interest to note that general obesity was found to have more than 2-fold higher risk for developing diabetes in subjects with BMI >23.0 kg/m^2 in the present study. We had previously noted that the risk of diabetes occurred at a lower BMI threshold (<23 kg/m2) in Asian Indians (P1: 28). Data from recent studies in Bangladesh did not show any significant association between BMI and diabetes (P1: 3, 5). However, in other studies higher BMI (>25.0 kg/m^2) was found as an important predictor for occurrence of type 2 diabetes (P1: 4, 7, 9). But the population from previous studies showed lean BMI. A study in India (P1: 29) found the prevalence of diabetes was high even though the rates of obesity were low among the Indian urban and rural population. WHR also appeared to be a significant risk factor for diabetes in the multivariate analysis. The association between WHR and DM was evident in the earlier studies in Bangladesh (P1: 7, 30). We have also noticed that the risk of diabetes occurred by central adiposity along with lower BMI threshold in Asian Indians (P1: 28). We have observed central obesity even among people with normal BMI in our population. Therefore, the transition in lifestyle occurring in the rural population seemed to produce rapid adverse changes favoring diabetogenesis.

Another interesting observation in this present study was that the lipids (triglyceride and total cholesterol) showed as strong risk factor for developing diabetes in rural population of Bangladesh. But this significant association was conflicting with earlier rural study (P1: 6). Surprising fact of this study was that systolic and diastolic hypertension was significantly associated with the occurrence of diabetes mellitus in the univariate model but non significant marginal risky state was observed in the multivariate logistic regression. Only one earlier study among rural subjects showed a significant association with both systolic and diastolic hypertension and higher glycemic status (P1: 31). Other recent studies observed significant association only between systolic hypertension and diabetes (P1: 4, 5). The inconsistent association between diabetes and hypertension has been previously reported in many ethnic groups and the role of hyperglycemia in determining blood pressure for ethnic differences are evident from these studies (P1: 32-34).

Very few data are available on the extent of urine albumin-creatinine ratio (UACR) as a strong predictor for the occurrence of diabetes mellitus. But there has been considerable focus on the concept that, it is an important marker for more pronounced diabetic vascular complications like retinopathy as well as nephropathy. In the present study we tried to observe the association between UACR and diabetes as we don't have any data regarding this. Here UACR was found as a significant risk factor for developing DM in this rural population of Bangladesh. The indices of obesity (increased BMI and WHR), hyperlipidemia (increased triglyceride and cholesterol) and urine ACR may at least in part explain the rising trend of diabetes mellitus in this rural population of Bangladesh.

In this study prevalence of retinopathy was found 21.6% (95% CI 11.2-32.0) among the diabetic subjects, 13% (95% CI 3.4-22.6) among the prediabetic subjects and 3.5% (95% CI 2.2-4.8) among the nondiabetic subjects, respectively. The age standardized prevalence of retinopathy was calculated at 5.4% (95% CI 3.9-6.9) among 836 people aged 25 years and older that were

examined in the course of this study. We have found a higher prevalence of DM in this study population and the prevalence of retinopathy was increased in the subjects with increasing deciles of glycemic level. The prevalence rate of retinopathy in different glucose metabolism categories documented in this study was comparatively similar to other two recent European studies. A population based Hoorn study with cohort design found the incidence of retinopathy as 17.5% in DM, 13.6% in IGT and 7.3% in NGM subjects (P2: 29). Another cross-sectional study done in Finland estimated the prevalence of retinopathy as 25% in DM, 2% in IGT and 3% in normoglycemic or NGM subjects (P2: 30). Early epidemiological evidences showed that the prevalence of retinopathy is increased in the subjects whose glycemic values were in the highest two or three deciles in population with a high prevalence of diabetes (P2: 31, 32). As the consequences of increasing number of diabetic subjects, the number of DM with its associated complications like retinopathy would also rise in Bangladesh. Moreover, a high prevalence of retinopathy was found in this study in normoglycemic subjects, as in the other studies (P2: 31-33). As there is no previous study in Bangladesh, therefore, it is difficult to make a scientific comprehension of the rising trend of retinopathy.

In this study population, retinopathy tended to be associated with several factors such as, increased age, glucose metabolism category, higher BMI, hypertension, HbA1c level, serum creatinine, total cholesterol and UACR. In contrast to other studies (P2: 29, 35), however, the prevalence of retinopathy in our study had a significant tendency to get higher with increasing age. Our study confirmed the well known positive association between hyperglycemic status and retinopathy. This result in accordance with those of previous studies (P2: 12-14, 39), have shown retinopathy to be associated with glucose metabolism status or with high fasting blood glucose levels. There is strong evidence to suggest that the development and progression of retinopathy is influenced by glycosylated hemoglobin (HbA1c) level (P2: 40-44) which was also reflected in our study.

BMI, the indicator for general obesity seemed to indicate a high risk of developing retinopathy in this population. In line with our study, a positive association between BMI and retinopathy was found in few studies (P2: 40, 45, 46, 47) that included diabetic subjects. WHR, the indicator for central obesity was also an independent risk factor for developing retinopathy in diabetic subjects (P2: 42, 44) as well as in nondiabetic subjects (P2: 29). After adjustment for potential confounders in multivariate model WHR did not remain as significant independent risk indicators for the occurrence of retinopathy in this population. The estimated risk for developing retinopathy in individuals with hypertension was almost 2 times as high as in individuals without hypertension, which remained after adjustment for possible confounders. This is in line with previous findings of incident retinopathy in studies (P2: 35, 43, 45, 48) of diabetic subjects and in the 2 other studies (P2: 49, 50) that included nondiabetic individuals. The present study did not find a statistically significant association between serum triglyceride, HDL cholesterol and LDL cholesterol and occurrence of retinopathy. Association between cholesterol and prevalence of retinopathy, although not always statistically significant in multivariate risk models, were described in several studies (P2: 42, 44, 45, 51) that included diabetes subjects. Cross-sectional data (P2: 52, 53) have shown that hard exudates in particular are associated with elevated cholesterol levels. In the present study risk for retinopathy in subjects with high level of cholesterol was more than 2 times as high as in subjects with normal cholesterol level. Cross-sectional (P2: 37) and longitudinal studies (P2: 54, 55) report a relationship between microalbuminuria and retinopathy. Elevated serum creatinine and urine albumin creatinine ratio were found as significant risk indicators for developing retinopathy in this population. The present findings of the combination of these risk indicators for predicting retinopathy may suggest that insulin resistance or associated factors are implicated in the pathogenesis of retinopathy.

5.2 Methodological Considerations

5.2.1 The strength of the study

The main strength of the current study was its study design. A population based study design was applied which ultimately focused on the prevalence and associated risk factors of diabetes mellitus and retinopathy among the rural Bangladeshi population. Population based studies are the most appropriate and useful approach where samples from a representative population are tested. Therefore the data represented the total population. Several hospital based studies have been done focusing on the magnitude of diabetes and retinopathy but the data available from hospital or clinic based studies which have several biases including selection bias and referral bias. Thus, it may not have representativeness and it only provides rough estimates of the disease prevalence with large percentages remaining undetected. Therefore to provide a baseline data on the prevalence of diabetes and retinopathy as well as their associated risk factors in a rural Bangladeshi population, we carried out a population based study. The result of the current study may lay the foundation to develop policies necessary to cope with the challenges of the disease burden.

Other strength of this study lies in the quality control of different measurements for anthropometric, blood pressure, clinical parameters and ocular examinations. Well trained investigators were provided in the field to assure that the standard was up to date. Investigators were asked to take the measurement of biophysical parameters as accurate as possible. Biophysical parameters, which included anthropometric (BMI and WHR) and blood pressure, measured by well trained investigators, which made the result more reliable than self reported results. Two readings of height, weight, waist circumference and hip circumference were recorded and the mean of the two was taken as the final reading of these parameters of the individual and used for analysis.

After collecting the blood and urine samples with proper aseptic precaution by experienced professionals, they were properly centrifuged on the site within the specific time period. All samples were then refrigerated and stored appropriately at -20^0C until laboratory assays were done. The clinical parameters from blood and urine specimen were analysed in the laboratory at BIRDEM, which is known to be one of the best laboratories in Bangladesh. Clinical sensitivity and specificity for the selection of different methods for different variables were considered. Reference serum was used for internal quality control everyday. All ocular examinations were done by trained technical assistants and ophthalmologists.

Cross checking and validate action forms were used as quality measure for data entry helped in the consistency of the results. The sample size calculation was done for predicting the prevalence of diabetes mellitus in Bangladeshi population. This sample (836) was not specifically calculated to estimate the prevalence of retinopathy among diabetes and non diabetes population and to explore the associated risk factors for developing retinopathy; however, the sample size calculation, met the requirement for analysis. We detected a high prevalence of diabetes, pre diabetes, as well as retinopathy in diabetes and non diabetes population in rural Bangladesh. Most potential confounding factors like age, gender, body mass index, hypertension etc were carefully controlled using multivariate analysis (logistic regression).

As no single population based study has yet been done in Bangladeshi general population to estimate the magnitude of the problem of retinopathy, this result will be use as a reference data. The absence of reliable population based epidemiological data on retinopathy in Bangladesh is a serious impediment to the effective national planning of eye care programmes.

Finally, as BIRDEM and its sister organizations all in well known of this population, we recruited local volunteers to serve in the camps by making sure that the participants comply with the dietary and other advices prior to

test for fasting blood glucose, thus increasing the reliability of the data and results.

5.2.2 The validity of the study

Validity refers to whether one is able to measure what he/she intends to measure. It can be divided into internal and external validity. Internal validity is an estimate of how much the measurement is based on clean and safe experimental techniques, which means that it is related to the instruments used. The clinical parameters which included both blood and urine specimen, were analysed in the laboratory at BIRDEM, which is known to be one of the best laboratories in Bangladesh. All the ocular examinations were done by the latest ophthalmic equipment. This increases the internal validity of the study. The strong point of this study was that the diagnosis of retinopathy was based on retinal photograph using fundus camera through dilated pupils, instead of nonmydriatic photograph. It has been argued that the use of nonmydriatic camera results in a moderately high frequency of ungradable photograph, especially in the presence of media opacities. Accuracy of the anthropometric measurements by the quality staffs and blood pressure measurements by trained nurses and repeatability of these measurements were likely to have increased the reliability of the data and results.

The issue of external validity is the question to what extent one may generalize and apply the conclusion derived from this study to the general population of Bangladesh. Since the current study was a population based study where samples were from a representative general population provided a baseline data regarding the prevalence and risk factors of diabetes and retinopathy. Therefore this study would contribute to prevention approaches and suggestions to address these problems.

5.2.3 The limitation of the study

Some limitations should however be pointed out in the present study. The cross-sectional nature of this study was the major limitation. In the cross-sectional method we have measured the disease outcome and exposure at the

same point in time. The cross-sectional nature limits the causal interference between disease outcome and exposure. Therefore, we cannot draw any firm conclusion regarding the risk factors since the data on temporal sequence is lacking. It is just a description of diseases or exposure at one time point. It is important to be aware that multiple factors may have influenced the dependent factors- diabetes or retinopathy. To control for the confounding factors, multivariate logistic regression analysis was done with diabetes or retinopathy as the dependent variables. However, it cannot exclude the possibility of some uncontrolled variables which were not included in the study and in the analysis.

Nevertheless, we would have needed a much larger sample size in order to generalize our results in whole Bangladeshi population. As we had limited time frame and resources to conduct the study, we used the most convenient formula to calculate the sample size for estimating diabetes prevalence. Therefore, the sample size became smaller which may decrease the statistical power. The small sample size is a possible cause for only being able to identify the established risk factors like age and hypertension for developing diabetes, as statistically non significant but marginal risk factors. With a bigger sample size, it may be assumed that age and hypertension would have become statistically highly significant risk factors for developing diabetes in this population. Furthermore, it can be argued that the sample size calculation was not properly done for estimating the prevalence of retinopathy in this population. So far, no study has been conducted either in Bangladesh or in the Asian subcontinent on the extent of retinopathy and its association with glucose metabolism including non diabetic general people as well; it was difficult to get any data, which we could have used to estimate our desired sample size.

5.3 Implications

In view of the fact that the present study was a population based one which provided a baseline data regarding the prevalence and risk factors of diabetes

and retinopathy. Therefore this study would contribute to appropriate prevention approaches and suggestions to address these problems. The result of the current study may lay the foundation to develop policies necessary to cope with the challenges of the disease burden. It would contribute to all phase of prevention strategies in this population. Primary prevention aims at modification of the risk factors such as sedentary lifestyle, obesity, and hypertension and so on, in high risk population to reduce the occurrence of IGT and IFG. Secondary prevention aims to prevent the development from pre diabetes to overt diabetes. Tertiary prevention involves standardized treatment and management of diseases, for example, control of blood glucose to prevent the complications of diabetes and improve the life quality.

Some participants of the study were diagnosed as newly detected diabetic and retinopathy subjects and could also be treated in early stage. Subjects with positive results would attach more importance to the treatment and management of diseases, so would their family. And also a large number of people were found with or at risk of diabetes and retinopathy which require more attention than that given at present. Several associated risk factors for developing diabetes and retinopathy were identified in the present study which will serve as basis of prevention. In conjunction with data from other, active prevention campaign can be done in the whole population aiming at altering modifiable risk factors and with emphasis on population with nonmodifiable risk factors. It can also enhance people's concern of prevention, control and decrease the possibility of disease occurrence. Moreover, associated factors identified in our study are expected to be similar with other Bangladeshi population in other parts of the country or Bangladeshi overseas immigrants. Therefore, similar intervention and prevention suggestions can be made for Bangladesh in general.

As explained in the beginning, prevention is the most cost-effective method to deal with these problems. Extensive prevention and control of diseases in the society is, in fact, not a research issue any more, but it needs the cooperation

and effort of many stake holder including government, NGOs, media and general people. It is only the feasible approach to help reverse the negative trends in the incidence of diseases.

5.4 Recommendation

In addition to useful experiences and observations made during the field work, the data presented in this study generated several issues that warrant further evaluation. In a society like Bangladesh, where the resources are already diminutive relative to its population size, the increasing life expectancy and elevated prevalence of diabetes, retinopathy and diabetic retinopathy may dramatically raise the burden and expenses of the health care system. The important recommendation is related to the knowledge regarding diabetes and its associated microvascular complications and retinopathy. In order to prevent this disease burden the community needs to be mobilized. It is strongly suggested to involve the local community in awareness building activities to encourage people to seek health care facilities. It was noticeable that a significant number of participants never visited any ophthalmologist before the eye camp because of unawareness. Ultimately, the patient is responsible for his/her own health. So everybody needs to be aware of the risk factors. The attention regarding these issues should be increased to reduce the total burden of those diseases, suffering of the patients, their families and the community. Maintenance of optimal glycemic status, healthy weight, blood pressure, lipid level and proteinuria deserve closer consideration. Feasible diagnostic tests may be applied in health care services in a developing country like Bangladesh to identify patients at high risk of developing these complications. These risk factors should be identified in time and the person should receive improved health care immediately. Necessary follow-up activities may be designed to increase awareness, to diminish the risk and further, to reduce the burden and cost for both to the individual and the society at large.

In order to address this issue, large-scale cohort studies are required with control population. Furthermore, this work gives new information on the prevalence and associated risk indicators of retinopathy in one region of Bangladesh. While there were imperfection in the design and execution of the study, it does highlight several problems that must be addressed and overcome if definitive data are to be produced from subsequent studies. Further research should be executed regarding both issues.

5.5 Conclusions

Since literacy rate is comparatively lower in northern part of Bangladesh and most of the people are poor and hardly perceiving the need of early health care services, this kind of study, which was held in the peripheral areas of Thakurgaon district, is a strategic approach to identify diabetes and eye diseases. The higher prevalence of diabetes (7.2%), diabetic retinopathy (21.6%) and nondiabetic retinopathy (3.5%) found in the present study, indicated the changing environmental factors which may have increased occurrence of these diseases. Even though the sample size of this study is relatively small, the findings should be interpreted with caution. Adequate treatment of the risk indicators might prevent and reduce the burden of these diseases and improve the quality of health care services.

Prevalence of Diabetes Mellitus and its Associated Risk Factors in Rural Bangladeshi Population

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ABSTRACT

Objective: The purposes of the study are to estimate the prevalence of diabetes and to identify its associated risk factors in a rural Bangladeshi population.

Methods: This population based cross-sectional study was conducted through screening in camp settings, which included a total of 836 participants (aged ≥25 years) by following simple random procedure. Fasting blood glucose (FBG) and oral glucose tolerance test (OGTT) were performed for all participants to diagnosis diabetes according to the diagnostic criteria of World Health Organization. Anthropometric measurements (BMI and WHR), blood pressure, lipid profile and urine albumin creatinine ratio were also estimated.

Results: An increased prevalence of diabetes was found with 7.2% (95% CI 5.4-9.0) in the present study. A superior agreement was observed between FBG and OGTT (Kappa value 0.86) among the study participants. Non significant female predominance was observed compared with male for developing diabetes in rural Bangladesh. After adjusting for potential confounders BMI, WHR, serum creatinine, triglyceride, total cholesterol and UACR were found as significant independent risk indicators for the occurrence of diabetes in this population.

Conclusion: The indices of obesity (increased BMI and WHR), hyperlipidemia (increased triglyceride and cholesterol) and urine ACR may at least in part explain the rising trend of diabetes mellitus in this rural population of Bangladesh. Considering rapid urbanization influencing individual's lifestyle leading to increase occurrence of diabetes, prospective studies are required in order to address this issue.

INTRODUCTION

Diabetes mellitus (DM) is becoming a pandemic worldwide. According to the World Health Organization (WHO) Report there were 171 million people worldwide with diabetes in 2000 and predicted that the prevalence of this disease will increase to 366 million by 2030 (1). The highest percentages of increases in disease prevalence are likely to be in developing nations. It is estimated that the developing countries will bear the brunt of this epidemic in the 21st century, with 80% of all new cases of diabetes expected to appear in the developing countries by 2025 (2), with major increases in the Middle-East, Sub-Saharan Africa, South Asia, and Latin America (1).

WHO listed 10 countries to have the highest numbers of people with diabetes in 2000 and 2030 (1). Bangladesh appears in the list for both 2000 and 2030 with India, Pakistan, China, Japan and USA etc. According to the report, Bangladesh has 3.2 million of diabetic subjects, and the number is expected to increase to a staggering 11.1 million by 2030. Several small-scale population based studies conducted in Bangladesh at different time points have revealed an increasing trend of diabetes prevalence in rural and urban communities (3-10). A recent population based study (4) showed a significant increase in the prevalence of DM in rural Bangladesh from 2.3% to 6.8% over 5 years. This prevalence was higher than found in the previous rural studies of Bangladesh (6, 8).

Abdominal obesity as measured by waist/hip ratio (WHR), general obesity as measured by body mass index (BMI), hypertension and dislipidemia are common indicator for diabetes mellitus. There are several epidemiologic and physiologic evidence linking insulin resistance and hyperglycemia to the presence of these predictors (11-15). The pattern of diabetes in Bangladeshi population differs from that in Europeans and Americans in several aspects: The onset is at a younger age, obesity is less common, and changes in lifestyle appear to be stronger. However, the association of obesity and diabetes in this population is unconventional. Some studies showed that BMI and WHR were

important predictors of diabetes in rural Bangladeshi population, although the population was considered as lean (4, 6), while the others did not (3, 5).

Combination of low BMI and relatively high central obesity with increasing prevalence of DM are general features of diabetes in Bangladeshi population. These clinical differences and the rising prevalence of diabetes in Bangladesh warrant well-conducted epidemiologic studies on diabetes including lipid profile, serum creatinine and urine albumin creatinine ratio (UACR) as possible confounders for DM in this population. The study was conducted to observe the sequential changes in the prevalence of diabetes and to identify its associated risk factors in a rural Bangladeshi population.

MATERIALS AND METHODS

Study area and population

Bangladesh has 64 districts and the study was conducted in one district of northern Bangladesh called Thakurgaon. Thakurgaon is in the north-west corner of Bangladesh, it is about 467 km from Dhaka, the capital of Bangladesh. The district is a part of the Himalayan plain land and the state of India lies on its west and north side. This district has 5 upazilas (sub-district). Subjects were recruited from all upazilas by following simple random procedure.

This study was only a part of an ongoing large epidemiologic study of Bangladesh Diabetic Somity, involving a representative population of Thakurgaon district. To determine the required sample size for this part of study, the formula: $n = PQ/d^2$ was used. Where P for prevalence (of DM + Pre DM) from the previous study, i.e. 0.14 (14%); Q = 1 – P, i.e. 0.86 and d = allowable error of known prevalence i.e. 0.085 × 0.14. Thus the sample size, n = 850. Following a simple random procedure 1000 individuals aged ≥25 years were identified to participate in this study. Among them 836 individuals agreed to participate and were investigated in the present study.

Ethical consideration

The protocol was approved by the Norwegian Ethical Committee for Medical Research and the National Ethical Committee of Bangladesh. Administrative clearance was obtained from Bangladesh Ministry of Public Health, the District Medical Officer and local official institutes. All participants signed an informed consent form prior to commencing any study procedure. However, the participants who were illiterate gave verbal consent and the witness signed on the document on behalf of the participant. They were informed of their rights to withdraw from the study at any stage of the study without giving any notification of reasons. The written results of medical examination were distributed and explained to the participants through Thakurgaon Swasthoseba Hospital, the Health Care Center of the Bangladesh Diabetic Somity. The identified cases for diabetes were referred to this hospital for follow up and further treatment.

Survey procedures

The study was a population based cross-sectional study. This epidemiological survey was conducted through screening in camp settings. Three camps were organized in 3 different places by Thakurgaon Swasthoseba Hospital within 6 months. The first camp was held on June 2008, second camp on August 2008 and the last camp on December 2008. Each camp continued for two days.

Sixteen field assistants were recruited from the local community and trained for the field work which included sample selections, organizing the screening camps, collection of data by reviewing the questionnaire and delivering the results to the participants. Seven days of training were provided to the assistants for selection process, interview and data collection prior to the commencement of the study. Each trainee was evaluated before he or she was allowed to participate in the study. The field assistants listed all the adults aged ≥25 years from each area and identified the required number of subjects following simple random procedure. Pregnant women and physically or mentally disabled persons unable to follow simple questions were excluded from the study.

All the individuals selected for the study were given an identification number. The field assistants approached the potential participants by an information letter and a respond document. Participants were informed of the purpose and the procedure of the study and they were requested to attend the screening camps in the morning on a pre-arranged date after an overnight fast of at least 8-10 hours. Each and every subject was made aware and was explained the necessity of the fasting state of a minimum 8-10 hr prior to the test. On arrival at the pre scheduled time (7.30 am to 8.30 am) on the appointed day, confirmation of the fasting state was taken/verified once again from each participant. After receiving the consent general registration of the participant was initiated. With proper aseptic precaution, initial 8 ml of venous blood and urine sample were collected from each participant. Fasting blood glucose (FBG), lipid profile, serum creatinine and glycosylated hemoglobin (HbA_1c) were determined from fasting blood sample and albumin creatinine ratio (ACR) was measured from urine sample. All subjects other than those with known diabetes (n=22) were then given a 75-g oral glucose solution (75-g oral glucose load dissolved in 500 ml of water) to drink. Another 3 ml of venous blood was collected after 2 hours to determine 2 hr post oral glucose tolerance test (OGTT).

During the 2 hr waiting period the participants were interviewed for some general information through the preseted questionnaire and were measured some biophysical parameters which include anthropometric measures (height, weight, waist circumference and hip circumference). Further blood pressure measurement was recorded.

After collecting the blood and urine sample it was centrifuged on the site within 3 hours to separate plasma. All samples were then refrigerated and stored at -20^0C until laboratory assays was done. Fasting blood glucose (FBG) and oral glucose tolerance test (OGTT) were analyzed by glucose oxidase method (Randox, UK) for the diagnosis of diabetes mellitus. Lipid profile includes total cholesterol (TC), high-density lipoprotein (HDL), low-density

lipoprotein (LDL) and triglycerides (TG), which were measured by enzymatic technique. Glycosylated hemoglobin (HbA1c) was measured by high-performance liquid chromatography (HPLC).

Interviewer administered questionnaire:

The preseted questionnaire was composed of some general information; like the demographic and socioeconomic information, including name, sex, age, education, occupation and economic status. The participants were asked for their 1st degree family history of diabetes and associated complications of diabetes, if any, (nephropathy, neuropathy, hypertension, hyperlipidaemia, coronary artery diseases). They were also asked for some information related to their own medical history of obesity, hypertension, diabetes and associated complications of diabetes.

Anthropometrical measurement

Anthropometric measurements included height, weight, waist circumference and hip circumference. The measurements were taken with light clothes without shoes. Height was measured by using a portable, locally manufactured, stadiometer, standing upright on a flat surface without shoes to the nearest 0.1 cm. Body weight was measured while wearing light clothes by an adjusted scale and recorded to the nearest 0.1 kg. Body mass index (BMI) was calculated by the formula: weight in kilograms divided by height in meters squared [weight (kg)/height (m^2)]. Waist circumference was measured at 1 cm above the level of navel at minimal respiration and hip circumference was measured at the level of maximum posterior extension of the buttocks by placing a flexible plastic tape horizontally with light clothes. Both circumferences were recorded to the nearest 0.1 cm. Two readings of height, weight, waist circumference and hip circumference were recorded and the mean of the two was taken as the final reading. Asian BMI criteria were used to identify overweight and obese in this population (16). Five categories of BMI were identified here for presenting the data. Individuals with BMI below 18.49 kg/m2 classified as underweight, healthy weight (BMI 18.5-

22.99 kg/m2), overweight (BMI 23.0-24.99 kg/m2), obese I (BMI 25.0-29.99 kg/m2) and obese II (BMI over 30.0 kg/m2)), respectively. Abdominal obesity was evaluated by waist/hip ratio, with android and gynaecoid cut off points taken at 0.8 and 0.9 for females and males respectively (17).

Blood pressure measurement

Blood pressure was taken after completion of the questionnaire. To reduce the variation, subjects rested for at least 10 minutes before the BP was recorded. The pressure was measured in sitting position on the right arm using normal cuffs for adults fitted with a standard mercury sphygmomanometer, placing the stethoscope bell lightly over the brachial artery. BP was usually recorded to the nearest 2 mm Hg from the top of the mercury meniscus. Two readings were taken 5 minutes apart, and the mean of the two was taken as the final blood pressure reading of the individual. Hypertension was defined as a systolic blood pressure (SBP) of ≥ 140 mm Hg and/or diastolic blood pressure (DBP) of ≥ 90 mm Hg (18).

Diagnosis criteria for diabetes

After estimation of fasting blood glucose (FBG) and oral glucose tolerance test (OGTT), the participants were classified into non diabetes, diabetes mellitus, IFG (impaired fasting glucose) and IGT (impaired glucose tolerance), according to the recommendation of the World Health Organization Expert Committee (18). Subjects were defined as having diabetes mellitus (n = 60) based on their fasting blood glucose levels ≥ 7.0 mmol/l or 2 hr post glucose levels ≥11.1 mmol/l or both. IFG was defined when FBG values were between 6.1-7.0 mmol/l and OGTT <7.8 mmol/l. IGT was defined when FBG <7.0 mmol/l and OGTT values were between 7.8-11.1 mmol/l. IFG and IGT subjects were together called pre diabetes (n = 54).

Criteria for other variables

According to the ADA recommendation (35) the cut of value of other variables like, total cholesterol (<200 mg/dl), triglyceride (<150 mg/dl), LDL

(<100 mg/dl), HDL (for male >50 mg/dl and for female >40 mg/dl), serum creatinine (for male <1.4 mg/dl and for female <1.2 mg/dl) and urine albumin creatinine ratio (<30 mg/g) was used for data analysis.

Data analysis

The data was entered in the pre-designed Microsoft office excel format which was imported later into the statistical software SPSS. The prevalence rates of diabetes were determined by simple percentages. Statistical comparisons between categorical variables were made by using χ^2 test and comparisons between continuous variables were made by using independent sample t test. The odds ratio (OR) with 95% confidence interval (CI) for risk factors was calculated assuming the least prevalence of clinically relevant criteria as a reference value. Multiple logistic regression were performed to quantify the individual effect of predictor variables and to adjust for potential confounding factors. All *P*-values presented are two-tailed. The statistical tests were considered significant at a level ≤5% (≤0.05). All the statistical analysis were performed using SPSS 16 software.

RESULTS

Table P1.1: Prevalence rate of diabetes and pre diabetes (IGT & IFG) by age and gender distribution

Age group in years	Male	Female	Diabetic cases		Prevalence per 100		Total prevalence	P for difference
			Male	Female	Male	Female		
25-40 yrs	162	164	10	8	6.2	4.9	5.5	0.609
41-55 yrs	172	128	12	9	6.9	7.0	6.9	0.985
above 55 yrs	134	76	10	11	7.5	14.5	11.0	0.068
Total	468	368	32	28	6.8	7.6	7.2	0.668

Age group in years	Male	Female	Pre diabetic cases		Prevalence per 100		Total prevalence	P for difference
			Male	Female	Male	Female		
25-40 yrs	162	164	6	12	3.7	7.3	5.5	0.104
41-55 yrs	172	128	10	10	5.8	7.8	6.8	0.492

above 55 yrs	134	76	10	6	7.5	7.9	7.7	0.811
Total	468	368	26	28	5.5	7.6	6.5	0.231

The overall prevalence of diabetes was 7.2% (95% CI 5.4-9.0) and pre diabetes (both IGT & IFG) was 6.5% (95% CI 4.8-8.2). Prevalence of diabetes and pre diabetes increased with increasing age both for males and females (Table 1). Though non-significant, females had higher prevalence of both diabetes and pre diabetes compared with males in all age group. The difference in prevalence of diabetes by sex widened in the older age group (>55 years). But for pre diabetes, the difference in prevalence by sex was wider in the younger age group (25-40 years), while the difference was very narrow in the older age group (>55 years).

Table P1.2: Distribution of participants for different variables by age and gender

Variables	**25-40 yrs**			**41-55 yrs**			**above 55 yrs**		
	Male (n=162)	**Female (n=164)**	**P for difference**	**Male (n=172)**	**Female (n=128)**	**P for difference**	**Male (n=134)**	**Female (n=76)**	**P for difference**
BMI (kg/m^2)	21.4±3.2	21.6±3.5	0.650	22.3±3.6	21.8±3.7	0.141	22.9±4.2	22.5±4.6	0.585
WHR*	0.89±0.06	0.87±0.07	0.018	0.92±0.07	0.88±0.07	0.001	0.93±0.07	0.92±0.08	0.122
SBP (mmHg)	117.7±15.4	113.4±15.8	0.014	119.7±16.8	121.3±22.6	0.490	123.7±19.1	125.1±20.1	0.418
DBP (mmHg)	77.5±10.8	74.6±11.6	0.029	78.2±11.4	80.3±15.5	0.253	78.7±12.9	81.2±15.0	0.196
FBG (mmol/l)	5.03±1.7	5.05±1.8	0.913	5.1±1.5	5.3±2.1	0.277	5.2±1.4	5.7±2.3	0.142
AG (mmol/l)	5.9±2.3	6.2±2.6	0.209	6.1±2.7	6.4±3.1	0.325	6.4±3.0	7.3±4.5	0.146
HbA1c (%)	4.9±1.2	5.01±1.1	0.480	5.1±1.3	5.1±1.2	0.996	5.4±1.4	5.8±1.9	0.172
S Creatinine (mg/dl)*	1.12±0.23	1.03±0.21	0.001	1.24±0.33	1.16±0.26	0.050	1.40±0.40	1.31±0.43	0.062
Triglyceride (mg/dl)	156.4±65.3	135.9±54.7	0.002	156.6±62.1	155.7±56.9	0.936	162.2±65.3	163.4±71.9	0.912
Cholesterol (mg/dl)	187.3±32.4	178.0±32.9	0.013	189.5±40.6	192.9±35.2	0.642	190.8±40.3	198.3±40.5	0.068
HDL (mg/dl)*	36.8±8.4	34.1±8.3	0.010	37.8±11.1	34.8±7.4	0.002	38.0±11.2	37.3±8.6	0.615
LDL (mg/dl)	119.7±29.6	116.5±30	0.332	127.1±37.6	126.2±33.6	0.702	118.2±37.1	124.1±39.4	0.310
UACR (mg/g)	13.7±6.2	13.9±5.8	0.996	13.9±6.7	14.7±6.9	0.470	18.3±7.9	18.7±8.4	0.824

Data are presented as mean±SD; independent t- test was done as a test of significance.

Abbreviations: BMI, Body mass index; WHR, Waist hip ratio; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; FBG, Fasting blood glucose; AG, After 2 hr glucose load; $HbA1_c$,

Glycosylated hemoglobin; HDL, High density lipoprotein; LDL, Low density lipoprotein; UACR, Urine albumin creatinine ratio

* Data were coded with reference value separately for male and female and then analyzed together.

General characteristics of the participants were presented by gender in table 2 with 15 years age interval. Among the 836 participants 56% (n=468) were male and 44% (n=368) were female participants. The mean age of the participants was 46 years. Male subjects were older compared to the female participants. There were no differences in BMI between male and female participants in all age strata. However the mean BMI was 22.2 and 21.9 for the male and female participants, respectively. Mean BMI was increased according to the age group for both males and females. This picture is also reflected in the assessment of other parameters except for LDL. In younger age group there were significant differences in systolic blood pressure, diastolic blood pressure, triglyceride and total cholesterol between male and female participants. But it is not reflected in other age groups. A superior agreement was observed between FBG and OGTT (Kappa value 0.86) among the study participants (data has not shown).

Table P1.3: Baseline characteristics of diabetic, pre diabetic and non diabetic people

Variables	Diabetic (n=60)	Non Diabetic (n=722)	P for difference	Pre Diabetic (n=54)	Non Diabetic (n=722)	P for difference	Diabetic (n=60)	Pre Diabetic (n=54)	P for difference
Age (yrs)	48.8±10.7	45.3±11.8	0.019	47.0±11.4	45.3±11.8	0.285	48.8±10.7	47.0±11.4	0.408
BMI (kg/m^2)	23.9±4.7	21.7±3.6	0.002	23.1±4.4	21.7±3.6	0.006	23.9±4.7	23.1±4.4	0.235
WHR *	0.97±0.09	0.89±0.07	0.001	0.92±0.06	0.89±0.07	0.005	0.97±0.09	0.92±0.06	0.004
SBP (mmHg)	129.4±18.7	118.0±17.9	0.001	126.4±19.2	118.0±17.9	0.003	129.4±18.7	126.4±19.2	0.402
DBP (mmHg)	85.8±15.6	77.2±12.4	0.001	81.5±12.5	77.2±12.4	0.018	85.8±15.6	81.5±12.5	0.066
FBG (mmol/l)	10.5±3.1	4.7±0.60	0.001	6.3±0.40	4.7±0.60	0.001	10.5±3.1	6.3±0.40	0.001
AG (mmol/l)	14.9±4.1	5.3±1.0	0.001	9.2±1.5	5.3±1.01	0.001	14.9±4.1	9.2±1.5	0.001
HbA1c (%)	8.6±1.9	4.8±0.68	0.001	6.8±0.91	4.8±0.68	0.001	8.6±1.9	6.8±0.91	0.001
S Creatinine (mg/dl)*	1.66±0.60	1.16±0.28	0.001	1.27±0.30	1.16±0.28	0.019	1.66±0.60	1.27±0.30	0.001
Triglyceride (mg/dl)	250.1±75.5	143.5±53.1	0.001	186.5±70.7	143.5±53.1	0.001	250.1±75.5	186.5±70.7	0.001
Cholesterol (mg/dl)	220.2±46.4	184.7±35.0	0.001	209.1±40.4	184.7±35.0	0.001	220.2±46.4	209.1±40.4	0.221

HDL (mg/dl)*	33.9±9.3	37.2±10.1	0.024	33.2±6.9	37.2±10.1	0.001	33.9±9.3	33.2±6.9	0.480
LDL (mg/dl)	136.2±46.1	119.5±32.8	0.008	138.1±38.3	119.5±32.8	0.001	136.2±46.1	138.1±38.3	0.804
UACR (mg/g)	18.4±8.2	14.1±7.2	0.001	16.8±7.8	14.1±7.2	0.016	18.4±8.2	16.8±7.8	0.135

Data are presented as mean±SD; independent t- test was done as a test of significance.

Abbreviations: BMI, Body mass index; WHR, Waist hip ratio; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; FBG, Fasting blood glucose; AG, After 2 hr glucose load; $HbA1_c$, Glycosylated hemoglobin; HDL, High density lipoprotein; LDL, Low density lipoprotein; UACR, Urine albumin creatinine ratio

* Data were coded with reference value separately for male and female and then analyzed together.

The characteristics were compared between subjects with diabetes (n=60) & non diabetes (n=722), pre diabetes (n=54) & non diabetes (n=722) and diabetes (n=60) & pre diabetes (n=54) (Table 3). The subjects with diabetes were significantly older with higher BMI, WHR, blood pressure, serum glucose (fasting and 2 hr after glucose), HbA1c, serum creatinine, triglyceride, total cholesterol, LDL, UACR and significantly lower HDL compared to subjects with non diabetes. Although non significant, the subjects with pre diabetes were older than non diabetes subjects. The comparison of other characteristics between pre diabetes and non diabetes subjects yielded similar results. The subjects with diabetes had significantly higher WHR, serum glucose (fasting and 2 hr after glucose), HbA1c, serum creatinine and triglyceride compared to subjects with pre diabetes. Although non significant, diabetes subjects had higher age, BMI, blood pressure, total cholesterol, HDL, UACR and lower LDL compared to subjects with pre diabetes.

Table P1.4: Prevalence, odds ratio (OR) and 95% CI of diabetes by the following risk factors

Variables	**Diabetic cases**	**n**	**Prevalence per 100**	**OR [1] (95% CI)**	**OR [2] (95% CI)**
Age (yrs)					
25-40 *	18	326	5.52	1.0	1.0
41-55	21	300	7.00	1.90 (1.18-3.66)	0.78 (0.34-1.74)
Above 55	21	210	10.00	1.48 (0.98-2.78)	0.92 (0.46-2.03)
Sex					
Male *	32	468	6.84	1.0	1.0
Female	28	368	7.60	1.12 (0.66-1.90)	1.13 (0.60-2.14)
BMI (kg/m^2)					

18.5-22.99 normal *	17	377	4.51	1.0	1.0
Below 18.49 underweight	15	173	8.67	0.94 (0.62-6.32)	0.85 (0.56-3.50)
23.0-24.99 overweight	8	60	13.3	2.92 (1.62-7.04)	2.50 (1.49-6.32)
25.0-29.99 obese I	10	180	5.55	4.72 (1.83-12.17)	3.94 (1.39-11.21)
Above 30.0 obese II	10	46	21.74	5.88 (2.51-13.8)	4.65 (2.12-12.65)
WHR					
Normal *	8	226	3.54	1.0	1.0
High	52	610	8.52	2.54 (1.59-5.43)	1.81 (1.16-4.34)
SBP (mmHg)					
Below 140 *	36	663	5.43	1.0	1.0
Above 140 high	24	173	13.87	2.81 (1.62-4.85)	1.38 (0.89-3.92)
DBP (mmHg)					
Below 90 *	35	657	5.33	1.0	1.0
Above 90 high	25	179	13.96	2.89 (1.68-4.96)	1.62 (0.98-4.52)
S Creatinine (mg/dl)					
Normal *	33	671	4.92	1.0	1.0
High	27	165	16.36	3.78 (2.20-6.50)	3.40 (1.77-6.55)
Triglyceride (mg/dl)					
Below 150 *	17	475	3.58	1.0	1.0
Above 150	43	361	11.91	3.64 (2.04-6.50)	2.37 (1.55-5.37)
Cholesterol (mg/dl)					
Below 200 *	25	584	4.28	1.0	1.0
Above 200	35	252	13.88	3.61 (2.11-6.17)	2.03 (1.15-3.92)
HDL (mg/dl)					
Normal *	11	217	5.07	1.0	1.0
Low	49	619	7.91	1.61 (0.82-3.16)	1.24 (0.55-2.71)
LDL (mg/dl)					
Below 100 *	14	251	5.58	1.0	1.0
Above 100	46	585	7.86	1.45 (0.78-2.68)	0.79 (.34-1.64)
UACR (mg/g)					
Below 30 *	47	312	15.06	1.0	1.0
Above 30	13	45	28.88	2.29 (1.42-4.68)	1.89 (1.14-3.26)

Abbreviations: OR, Odds ratio; CI, Confidence interval; BMI, Body mass index; WHR, Waist hip ratio; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; $HbA1_c$, Glycosylated hemoglobin; LDL, Low density lipoprotein; UACR, Urine albumin creatinine ratio

OR [1], Crude odds ratio after univariate logistic regression; OR [2], Adjusted odds ratio for age, sex, glucose metabolism category, BMI, WHR, SBP, DBP, hypertension, HbA1c, S Creatinine, Lipids and UACR

* Referent

We used logistic regression to quantify the individual effects of age, sex, BMI, WHR, SBP, DBP, S Creatinine, Lipids and UACR with diabetes (Table 4). Age, BMI, WHR, SBP, DBP, S Creatinine, triglyceride, total cholesterol and UACR were found to be significant risk factors for the occurrence of diabetes mellitus in the univariate model. After adjusting for potential confounders in the multivariate model by using all variables BMI, WHR, S Creatinine, triglyceride, total cholesterol and UACR remained as significant independent risk indicators for the occurrence of diabetes in this population. BMI >23.0 showed to be exceedingly risky state for the occurrence of diabetes. The risk for diabetes was almost 2-fold or sometimes more than 2-fold higher in subjects with BMI >23.0 kg/m^2, high WHR both for male and female, high serum creatinine for both sex, triglyceride >150 mg/dl, cholesterol >200 mg/dl and UACR >30 mg/g.

DISCUSSION

This study addressed the prevalence of diabetes and pre diabetes in a rural population in Bangladesh. The prevalence of diabetes was found to be 7.2% which is comparable to the recent rural studies (6, 7, 9), but significantly higher than the studies conducted in early 2000s (3, 4, 5). However, moderate but steady rise in the prevalence of pre diabetes (6.5%) was observed compared to a recent published data (3), but rather a lower prevalence compared to another study (6). Data on the rising trend of diabetes in Bangladesh were based on the comparison of data collected from different parts of the country at different times and had applied different procedures, other than one (4). Therefore, it is difficult to make a scientific comprehension of the rising trend of diabetes. To compare secular trends, it would be more accurate to document the prevalence of diabetes within the same region applying the identical procedure.

The prevalence of diabetes documented in this study was comparatively higher than the prevalence found in rural China (5.6%), but more related to that of rural India (6.3%) and was equal to that of rural population in Turkey

(7.2%) (19, 20, 21). However, the observed prevalence rate of diabetes in this report is lower than the prevalence found in rural Pakistan (11.1%) (22). But the direct comparisons of prevalence rates are challenging owing to differential methodologies applied and diverse characteristics of the population.

Several studies showed that urbanization, economic development and affluent lifestyle are causing high prevalence of DM even in the developing countries (23, 24, 25). The rural Bangladeshi population is undergoing lifestyle transition due to socio-economic growth; road communication, electrification, and mechanized cultivation in recent years and have changed the rural lifestyle. This demographic transition due to improved living conditions in rural area was associated with this increased rate in the prevalence of diabetes in rural Bangladesh. But BMI in this population remain low. Therefore, it would be difficult to ascribe the increased prevalence only due to higher calorie intake as a consequence of improved socio-economic condition. Rather higher pre diabetes in a lean population may also indicate genetically susceptible population, who may convert to diabetes with a much lower change in obesity, although the BMI may remain low. Thus there could be a rapid progression from the normal state through pre diabetes to diabetes, which could imply a rapid increase in the diabetes epidemic or a worsening diabetogenic environment. Prospective studies are required to assess the exact changes occurring with regard to the diabetes epidemic in Bangladesh.

We have observed a higher, though non significant, occurrence of diabetes and pre diabetes among females in almost all age categories compared with males especially in the highest age strata. The finding of female predominance is consistent with the most previous studies in Bangladesh (4, 5, 7, 8). We have observed higher mean values of FBG and AG among females in all age group compared to males. Gender difference was not significant in India (26), though non significant higher prevalence of type 2 diabetes was found among

women in another investigation in India (27). Higher prevalence of diabetes in women was found in Pakistan (22) and Turkey (21).

As obesity is an established risk factor for diabetes, we have observed an important association of both general obesity and central obesity with diabetes. It is of interest to note that general obesity was found to have more than 2-fold higher risk for developing diabetes in subjects with BMI >23.0 kg/m^2 in the present study. We had previously noted that the risk of diabetes occurred at a lower BMI threshold (<23 kg/m2) in Asian Indians (28). Data from recent studies in Bangladesh did not show any significant association between BMI and diabetes (3, 5). However, in other studies higher BMI (>25.0 kg/m^2) was found as an important predictor for occurrence of type 2 diabetes (4, 7, 9). But the population from previous studies showed lean BMI. A study in India (29) found the prevalence of diabetes was high even though the rates of obesity were low among the Indian urban and rural population. WHR also appeared to be a significant risk factor for diabetes in the multivariate analysis. The association between WHR and DM was evident in the earlier studies in Bangladesh (7, 30). We have also noticed that the risk of diabetes occurred by central adiposity along with lower BMI threshold in Asian Indians (28). We have observed central obesity even among people with normal BMI in our population (data has not shown). Therefore, the transition in lifestyle occurring in the rural population seemed to produce rapid adverse changes favoring diabetogenesis.

Another interesting observation in this present study was that the lipids (triglyceride and total cholesterol) showed as strong risk factor for developing diabetes in rural population of Bangladesh. But this significant association was conflicting with earlier rural study (6). Surprising fact of this study was that systolic and diastolic hypertension was significantly associated with the occurrence of diabetes mellitus in the univariate model but non significant marginal risky state was observed in the multivariate logistic regression. Only one earlier study among rural subjects showed a significant association with

both systolic and diastolic hypertension and higher glycemic status (31). Other recent studies observed significant association only between systolic hypertension and diabetes (4, 5). The inconsistent association between diabetes and hypertension has been previously reported in many ethnic groups and the role of hyperglycemia in determining blood pressure for ethnic differences are evident from these studies (32-34).

Very few data are available on the extent of urine albumin-creatinine ratio (UACR) as a strong predictor for the occurrence of diabetes mellitus. But there has been considerable focus on the concept that, it is an important marker for more pronounced diabetic vascular complications like retinopathy as well as nephropathy. In the present study we tried to observe the association between UACR and diabetes as we don't have any data regarding this. Here UACR was found as a significant risk factor for developing DM in this rural population of Bangladesh.

Population based study design was the main strength of the study. It was the most appropriate and useful approach where samples from a representative population were tested. Therefore this study would contribute to prevention approaches and suggestions to address these problems. But we would have needed a much larger sample size in order to generalize our results in Bangladeshi population. As we had limited time frame and resources to conduct the study, we used the most convenient formula for calculate the sample size. Therefore, the sample size became smaller which may decrease the statistical power. Moreover, clinical sensitivity and specificity for the selection of different methods for different variables were considered here, which have increased the reliability of the data and results.

The indices of obesity (increased BMI and WHR), hyperlipidemia (increased triglyceride and cholesterol) and urine ACR may at least in part explain the rising trend of diabetes mellitus in this rural population of Bangladesh. The higher prevalence of diabetes in the present study may also be indicated the changing environmental factors where rapid urbanization may have

influenced individual's lifestyle leading to increased occurrence of diabetes. In order to address this issue, large-scale cohort studies are required with control population.

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Prevalence and Risk Factors of Retinopathy in a Rural Bangladeshi Population in With and Without Diabetes

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ABSTRACT

Objective: This study aimed to make a baseline data focused on retinopathy regarding the prevalence in people with normal and abnormal glucose metabolism in rural Bangladesh and to identify the associated risk factors for developing retinopathy in this population.

Methods: This population based cross-sectional study was conducted through screening in camp settings, which included a total of 836 participants (aged ≥25 years) by following simple random procedure. Retinopathy was determined by ophthalmoscopy and fundus photography. Anthropometric measurements (BMI and WHR), serum glucose (fasting and 2 hr after glucose), glycosylated hemoglobin, blood pressure, lipid profile and urine albumin creatinine ratio were also observed. Logistic regression analysis was used, without and with adjustment for potential confounders.

Results: The overall prevalence rate of retinopathy was 5.4% (95% CI 3.9-6.9). Moreover, the prevalence of retinopathy among the diabetic, pre diabetic and non diabetic subjects were 21.6% (95% CI 11.2-32.0), 13% (95% CI 3.4-22.6) and 3.5% (95% CI 2.2-4.8), respectively. Adjusted odds ratios for retinopathy were 2.53 (95% CI, 1.52-5.41) for diabetic glucose metabolism and 1.98 (95% CI, 1.17-5.63), 1.74 (95% CI, 1.09-3.02) and 1.63 (95% CI, 1.08-3.12) for hypertension, 2nd highest tertiles of glycosylated hemoglobin level and urine albumin creatinine ratio, respectively. Additionally, age, BMI, SBP, DBP, serum creatinine and total cholesterol were also found as significant independent risk indicators for the occurrence of retinopathy in this population.

Conclusion: Finally, the study results suggest that, in addition to serum glucose control in diabetic patients, screening for hypertension, general obesity, hypercholesterolemia and proteinuria and adequate treatment of these risk factors might prevent retinopathy in rural Bangladeshi population.

INTRODUCTION

Retinopathy, the potential sight threatening condition, is a significant public health problem; however this morbidity is largely preventable and treatable. It is significantly associated with impairment of vision and blindness (1). Retinal disease is frequent cause of blindness in developing countries (2). The socioeconomic burden resulting from visual impairment or blindness caused by retinopathy, particularly in working age group, is a serious concern. According to the World Health Organization worldwide there are an estimated 45 million people that are blind with an additional 135 million individuals visually impaired (3). Retinopathy is responsible for about 5% of those 45 million cases of blindness throughout the world. Worldwide, the prevalence of retinopathy is increasing at an alarming rate, possibly due to undetected cases of diabetes and as it has had a low priority in the prevention of blindness programs in developing countries.

About 20 million Asians were estimated as blind by the World Health Organization (WHO), (4) and this figure is expected to increase as the population ages. The excellent and very detailed Andhra Pradesh Eye Disease Study (APEDS) found that retinal diseases were a much more common cause of adult blindness in India than had previously been thought (5). Enormous population based data of retinopathy in patients with diabetes mellitus, commonly termed as diabetic retinopathy (DR), has been published. But very few facts are available about other ocular and systemic causes of retinopathy or the clinical significance of retinopathy in patients without diabetes. There are few population based studies on the prevalence of diabetic retinopathy (DR) in Asia, with most originating from India (6-9).

Apart from diabetes, other conditions associated with retinal ischemia, may lead to retinopathy (10). Retinopathy lesions are commonly seen in middle aged and elderly people with and without diabetes. Signs of retinopathy are structural markers of microvascular damage which has been strongly linked with hyperglycemia (11), elevated glycosylated hemoglobin level (12-14),

hypertension (15-17), lower glomerular filtration rates and microalbuminuria (18). One study found that retinopathy was associated with increasing fasting blood sugar concentrations in people not classified as having diabetes mellitus (19), although another study did not find this association (16). Nevertheless, the distinction between diabetes and prediabetes is somewhat arbitrary, and the results of some recent studies have shown that some of the subjects with IGT have had retinopathy (20, 21).

There was only one nationally representative survey concerning the extent of blindness or the main causes of vision impairment in Bangladeshi adults, which has identified low level of diabetic retinopathy as the cause of visual impairment and moreover, no subject was found to be blind due to diabetic retinopathy (22). As the consequences of increasing trend of diabetes mellitus, the number of people with diabetic complications like retinopathy will continue to rise in Bangladesh. To the best of our knowledge there is no population based study yet in Bangladeshi general population to estimate the magnitude of retinopathy. However, the identified risk factors for retinopathy established by others have not been extensively studied in our population.

The absence of reliable population based epidemiological data on retinopathy in Bangladesh is a serious impediment to the effective national planning of eye care programmes. In the above context, we planned to carry out an epidemiological study to create a baseline data focused on retinopathy. This would be the first effort to estimate the prevalence of retinopathy among diabetic and non diabetic population in Bangladesh and to identify the associated risk factors for developing retinopathy among adults.

MATERIALS AND METHODS

Study area and population

Bangladesh has 64 districts and the study was conducted in one district of northern Bangladesh called Thakurgaon. Thakurgaon is in the north-west

corner of Bangladesh, it is about 467 km from Dhaka, the capital of Bangladesh. The district is a part of the Himalayan plain land and the state of India lies on its west and north side. This district has 5 upazilas (sub-district). Subjects were recruited from all upazilas by following simple random procedure. A total of 836 subjects participated in the study. This study was only a part of an ongoing large epidemiologic study of Bangladesh Diabetic Somity, involving a representative population of Thakurgaon district. For this subset of population for DM and retinopathy a sample size calculation was performed for diabetes prevalence (paper 1). Following a simple random procedure 1000 individuals aged ≥25 years were identified to participate in this study. Among them 836 individuals agreed to participate and were investigated in the present study.

Ethical consideration

The protocol was approved by the Norwegian Ethical Committee for Medical Research and the National Ethical Committee of Bangladesh. Administrative clearance was obtained from Bangladesh Ministry of Public Health, the District Medical Officer and local official institutes. All participants signed an informed consent form prior to commencing any study procedure. However, the participants who were illiterate gave verbal consent and the witness signed on the document on behalf of the participant. They were informed of their rights to withdraw from the study at any stage of the study without giving any notification of reasons. The written results of medical examination were distributed and explained to the participants through Thakurgaon Swasthoseba Hospital, the Health Care Center of the Bangladesh Diabetic Somity. The identified cases for diabetes and retinopathy were referred to this hospital for follow up and further treatment.

Survey procedures

The study was a population based cross-sectional study. This epidemiological survey was conducted through screening in camp settings. Three camps were organized in 3 different places by Thakurgaon Swasthoseba Hospital within 6

months. The first camp was held on June 2008, second camp on August 2008 and the last camp on December 2008. Each camp continued for two days.

Sixteen field assistants were recruited from the local community and trained for the field work which included sample selections, organizing the screening camps, collection of data by reviewing the questionnaire and delivering the results to the participants. Seven days of training were provided to the assistants for selection process, interview and data collection prior to the commencement of the study. Each trainee was evaluated before he or she was allowed to participate in the study. The field assistants listed all the adults aged ≥25 years from each area and identified the required number of subjects following simple random procedure. Pregnant women and physically or mentally disabled persons unable to follow simple questions were excluded from the study.

All the individuals selected for the study were given an identification number. The field assistants approached the potential participants by an information letter and a respond document. Participants were informed of the purpose and the procedure of the study and they were requested to attend the screening camps in the morning on a pre-arranged date after an overnight fast of at least 8-10 hours. Each and every subject was made aware and was explained the necessity of the fasting state of a minimum 8-10 hr prior to the test. On arrival at the pre scheduled time (7.30 am to 8.30 am) on the appointed day, confirmation of the fasting state was verified once again from each participant by asking the fasting state. After receiving the consent general registration of the participant was initiated. With proper aseptic precaution, initial 8 ml of venous blood and urine sample were collected from each participant. Fasting blood glucose (FBG), lipid profile, serum creatinine and glycosylated hemoglobin (HbA_1c) were determined from fasting blood sample and albumin creatinine ratio (ACR) was measured from urine sample. All subjects other than those with known diabetes (n=22) were then given a 75-g oral glucose solution (75-g oral glucose load dissolved in 500 ml of water)

to drink. Another 3 ml of venous blood was collected after 2 hours to determine 2 hr post oral glucose tolerance test (OGTT).

During the 2 hr waiting period the participants were interviewed for some general information through the preseted questionnaire and were measured some biophysical parameters which include anthropometric (height, weight, waist circumference and hip circumference) and blood pressure measurements. Further comprehensive ocular examinations were performed on each subject by trained technical assistants and ophthalmologists.

After collecting the blood and urine sample it was centrifuged on the site within 3 hours to separate plasma. All samples were then refrigerated and stored at -20^0C until laboratory assays was done. Fasting blood glucose (FBG) and oral glucose tolerance test (OGTT) were analyzed by glucose oxidase method (Randox, UK) for the diagnosis of diabetes mellitus. Lipid profile includes total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides (TG), which were measured by enzymatic technique. Glycosylated hemoglobin (HbA1c) was measured by high-performance liquid chromatography (HPLC).

Interviewer administered questionnaire:

The preseted questionnaire was composed of some general information; like the demographic and socioeconomic information, including name, sex, age, education, occupation and economic status. The participants were asked for their 1st degree family history of diabetes, associated complications of diabetes, if any, (nephropathy, neuropathy, hypertension, hyperlipidaemia, coronary artery diseases) and information related to their own medical history of obesity, hypertension, diabetes and associated complications of diabetes. They were also asked for the ocular history which includes details of first and last eye examination, nature of present eye complaint or any ocular surgery.

Anthropometrical measurement

Anthropometric measurements included height, weight, waist circumference and hip circumference. The measurements were taken with light clothes without shoes. Height was measured by using a portable, locally manufactured, stadiometer, standing upright on a flat surface without shoes to the nearest 0.1 cm. Body weight was measured while wearing light clothes by an adjusted scale and recorded to the nearest 0.1 kg. Body mass index (BMI) was calculated by the formula: weight in kilograms divided by height in meters squared. Waist circumference was measured at 1 cm above the level of navel at minimal respiration and hip circumference was measured at the level of maximum posterior extension of the buttocks by placing a flexible plastic tape horizontally with light clothes. Both circumferences were recorded to the nearest 0.1 cm. Two readings of height, weight, waist circumference and hip circumference were recorded and the mean of the two was taken as the final reading. Asian BMI criteria were used to identify overweight and obese in this population (23). Five categories of BMI were identified here for presenting the data. Individuals with BMI below 18.49 kg/m2 classified as underweight, healthy weight (BMI 18.5-22.9 kg/m2), overweight (BMI 23.0-24.99 kg/m2), obese I (BMI 25.0-29.99 kg/m2) and

obese II (BMI over 30.0 kg/m2)), respectively. Abdominal obesity was evaluated by waist/hip ratio, with android and gynaecoid cut off points taken at 0.8 and 0.9 for females and males respectively (24).

Blood pressure measurement

Blood pressure was taken after completion of the questionnaire. To reduce the variation, subjects rested for at least 10 minutes before the BP was recorded. The pressure was measured in sitting position on the right arm using normal cuffs for adults fitted with a standard mercury sphygmomanometer, placing the stethoscope bell lightly over the brachial artery. BP was usually recorded to the nearest 2 mm Hg from the top of the mercury meniscus. Two readings were taken 5 minutes apart, and the mean of the two was taken as the final blood pressure reading of the individual. Hypertension was defined as a systolic blood pressure (SBP) of ≥ 140 mm Hg and/or diastolic blood pressure (DBP) of ≥ 90 mm Hg (25).

Ophthalmologic examinations

All the participants were gone through a complete ocular examination on that prearranged day by trained ophthalmologists. Visual acuity was recorded with an illuminated Snellen chart. The presenting and best corrected visual acuity was documented separately for each eye. Intraocular pressure measurement was performed with Schiotz indentation tonometer (Schiotz, John Weiss & Son Ltd, London, UK). Slit lamp was used for anterior segment evaluation including the depth of anterior chamber and rubeosis irids with diluted pupils. Fundus photography was operating with a digital camera (Super 66 equipped with stereo fundus lens). Dilated fundus evaluation was done with binocular indirect opthalmoscope (Keeler Instrument Inc, PA, USA). The photographs were taken in a dark room after a 5 minute adaptation period to allow the pupils to dilate to some extent and were analyzed by two ophthalmologist specialized in retinal diseases. World Health Organization recommended definitions of retinopathy, vision, and visual disability (ICD 10) was used (25). Among 836 participants 45 were

identified with retinopathy and were referred to the Thakurgaon Swasthoseba Hospital, the Health Care Center of the Bangladesh Diabetic Somity for further treatment and follow-up.

Diagnosis criteria for diabetes

After estimation of fasting blood glucose (FBG) and oral glucose tolerance test (OGTT), the participants were classified into non diabetes, diabetes mellitus, IFG (impaired fasting glucose) and IGT (impaired glucose tolerance), according to the recommendations of the World Health Organization Expert Committee (25). Subjects were defined as having diabetes mellitus (n = 60) based on their fasting blood glucose levels ≥ 7.0 mmol/l or 2 hr post glucose levels ≥11.1 mmol/l or both. IFG was defined when FBG values were between 6.1-7.0 mmol/l and OGTT <7.8 mmol/l. IGT was defined when FBG <7.0 mmol/l and OGTT values were between 7.8-11.1 mmol/l. IFG and IGT subjects were together called pre diabetes (n = 54). Thirteen retinopathy cases were identified from the diabetic subjects and 7 were from pre diabetic subjects. The rest 25 retinopathy cases are non diabetic subjects.

Criteria for other variables

According to the ADA recommendation (26) the cut of value of other variables like, total cholesterol (<200 mg/dl), triglyceride (<150 mg/dl), LDL (<100 mg/dl), HDL (for male >50 mg/dl and for female >40 mg/dl), serum creatinine (for male <1.4 mg/dl and for female <1.2 mg/dl) and urine albumin creatinine ratio (<30 mg/g) was used for data analysis.

Data analysis

The data was entered in the pre-designed Microsoft office excel format which was imported later into the statistical software SPSS. The prevalence rates of retinopathy were determined by simple percentages. Statistical comparisons between categorical variables were made by using χ^2 test and comparisons between continuous variables were made by using independent sample t test.

The odds ratio (OR) with 95% confidence interval (CI) for risk factors was calculated assuming the least prevalence of clinically relevant criteria as a reference value. Multiple logistic regression were performed to quantify the individual effect of predictor variables and to adjust for potential confounding factors. All *P*-values presented are two-tailed. The statistical tests were considered significant at a level ≤5% (≤0.05). All the statistical analysis were performed using SPSS 16 software.

RESULTS

Table P2.1: Distribution of participants for different variables by age and gender

Variables	25-40 yrs			41-55 yrs			above 55 yrs		
	Male (n=162)	Female (n=164)	P for difference	Male (n=172)	Female (n=128)	P for difference	Male (n=134)	Female (n=76)	P for difference
BMI (kg/m^2)	21.4±3.2	21.6±3.5	0.650	22.3±3.6	21.8±3.7	0.141	22.9±4.2	22.5±4.6	0.585
WHR*	0.89±0.06	0.87±0.07	0.018	0.92±0.07	0.88±0.07	0.001	0.93±0.07	0.92±0.08	0.122
SBP (mmHg)	117.7±15.4	113.4±15.8	0.014	119.7±16.8	121.3±22.6	0.490	123.7±19.1	125.1±20.1	0.418
DBP (mmHg)	77.5±10.8	74.6±11.6	0.029	78.2±11.4	80.3±15.5	0.253	78.7±12.9	81.2±15.0	0.196
FBG (mmol/l)	5.03±1.7	5.05±1.8	0.913	5.1±1.5	5.3±2.1	0.277	5.2±1.4	5.7±2.3	0.142
AG (mmol/l)	5.9±2.3	6.2±2.6	0.209	6.1±2.7	6.4±3.1	0.325	6.4±3.0	7.3±4.5	0.146
HbA1c (%)	4.9±1.2	5.01±1.1	0.480	5.1±1.3	5.1±1.2	0.996	5.4±1.4	5.8±1.9	0.172
SCreatinine (mg/dl) *	1.12±0.23	1.03±0.21	0.001	1.24±0.33	1.16±0.26	0.050	1.40±0.40	1.31±0.43	0.062
Trygliceride (mg/dl)	156.4±65.3	135.9±54.7	0.002	156.6±62.1	155.7±56.9	0.936	162.2±65.3	163.4±71.9	0.912
Cholesterol (mg/dl)	187.3±32.4	178.0±32.9	0.013	189.5±40.6	192.9±35.2	0.642	190.8±40.3	198.3±40.5	0.068
HDL (mg/dl)*	36.8±8.4	34.1±8.3	0.010	37.8±11.1	34.8±7.4	0.002	38.0±11.2	37.3±8.6	0.615
LDL (mg/dl)	119.7±29.6	116.5±30	0.332	127.1±37.6	126.2±33.6	0.702	118.2±37.1	124.1±39.4	0.310
UACR (mg/g)	13.7±6.2	13.9±5.8	0.996	13.9±6.7	14.7±6.9	0.470	18.3±7.9	18.7±8.4	0.824

Abbreviations: BMI, Body mass index; WHR, Waist hip ratio; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; FBG, Fasting blood glucose; AG, After 2 hr glucose load; $HbA1_c$, Glycosylated hemoglobin; HDL, High density lipoprotein; LDL, Low density lipoprotein; UACR, Urine albumin creatinine ratio.

* Data were coded with reference value separately for male and female and then analyzed together.

General characteristics of the participants are presented by gender in table 1 with 15 years age interval. Among the 836 participants 56% (n=468) were male and 44% (n=368) were female participants. The mean age of the participants was 46 years. Male subjects were older compared to the female participants. There were no differences in BMI between male and female participants in all age strata. The mean BMI was 22.2 and 21.9 for the male and female participants, respectively and showed some what increased mean BMI with increasing age. This picture is also reflected in the assessment of other parameters except for LDL. In younger age group there were significant differences in systolic blood pressure, diastolic blood pressure, triglyceride and total cholesterol between male and female participants. But it was not depicted in other age groups.

Table P2.2: Baseline characteristics of people with retinopathy and without retinopathy in diabetes and non diabetes group

Variables	Retinopathy		P for difference	Diabetes		P for difference	Non Diabetes		P for difference
	Yes (n=45)	No (n=791)		With Retinopathy (n=13)	Without Retinopathy (n=47)		With Retinopathy (n=32)	Without Retinopathy (n=744)	
NGM/ IGM/ DM ratio	25:7:13	697:47:47							
Age (yrs)	52.6±8.4	45.3±11.7	<0.001	56.7±6.8	46.5±9.7	<0.001	50.8±8.5	45.2±11.8	<0.001
BMI (kg/m^2)	24.1±4.3	21.9±3.7	0.002	26.9±3.8	22.9±4.5	0.004	22.9±3.9	21.8±3.6	0.140
WHR *	0.94±0.09	0.90 ±0.07	0.002	1.03±0.11	0.96±0.09	0.249	0.92 ±0.07	0.89±0.07	0.039
SBP (mmHg)	130.8±19.5	118.8±18.1	<0.001	136.5±15.9	127.5±19.1	0.079	128.4±20.5	118.2±17.9	0.009
DBP (mmHg)	85.8±15.9	77.7±12.5	0.002	93.1±13.1	83.8±15.8	0.043	82.6±16.1	74.3±12.2	0.049
FBG (mmol/l)	6.8±3.01	5.1±1.67	0.001	10.9±2.3	10.3±3.3	0.438	5.1±0.9	4.7±0.7	0.040
AG (mmol/l)	9.1±4.1	6.1±3.0	0.001	16.7±4.9	14.5±3.7	0.151	6.1±1.8	5.6±1.4	0.131
HbA1c (%)	6.96±2.7	5.09±1.16	<0.001	11.0±1.2	8.6±1.3	<0.001	5.3±0.81	4.9±0.87	0.011
SCreatinine (mg/dl) *	1.67±0.57	1.18±0.30	<0.001	2.31±0.49	1.48±0.50	<0.001	1.41±0.37	1.16±0.27	<0.001
Trygliceride (mg/dl)	189.7±75.5	151.9±61.3	0.003	260.5±63.4	247.1±77.3	0.533	160.9±68.5	145.9±54.8	0.230
Cholesterol (mg/dl)	216.3±46.4	187.2±35.6	<0.001	250.7±42.2	210.3±44.0	0.007	202.3±40.8	185.7±35.5	0.031
HDL (mg/dl) *	34.7±8.9	36.9±10.1	0.119	33.7±8.6	34.5±9.6	0.798	35.1±9.1	37.0±10.0	0.246
LDL (mg/dl)	143.6±39.1	120.7±34.2	<0.001	167.3±37.0	127.6±44.8	0.003	133.9±36.7	120.2±33.3	0.046

UACR (mg/g)	21.5±8.1	14.3±7.2	<0.001	23.9±8.4	16.9±7.6	0.014	20.5±7.8	12.4±6.4	0.018

Data are presented as mean±SD; independent t- test was done as a test of significance.

Abbreviations: BMI, Body mass index; WHR, Waist hip ratio; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; FBG, Fasting blood glucose; AG, After 2 hr glucose load; $HbA1_c$, Glycosylated hemoglobin; HDL, High density lipoprotein; LDL, Low density lipoprotein; UACR, Urine albumin creatinine ratio

* Data were coded with reference value separately for male and female and then analyzed together.

Forty five individuals were found to have retinopathy among 836 participants which included diabetic, prediabetic and nondiabetic population. The baseline characteristics were compared between subjects with and without retinopathy (Table 2). The subjects with retinopathy were significantly older with higher BMI, WHR, blood pressure, serum glucose (fasting and 2 hr after glucose), HbA1c, serum creatinine, triglyceride, total cholesterol, LDL, UACR compared to subjects without retinopathy. Although non significant subjects who developed retinopathy had lower HDL compared to subjects without retinopathy.

Diabetic subjects (n=60), with diabetic retinopathy had significantly higher age, BMI, diastolic blood pressure, HbA1c, serum creatinine, total cholesterol, LDL and UACR compared to subjects without retinopathy (Table 2). However, higher WHR, systolic blood pressure, serum glucose (fasting and 2 hr after glucose), triglyceride and low level of HDL were not found to be significantly associated with increasing the prevalence of retinopathy among the diabetic subjects. On the contrary, age, WHR, blood pressure, serum fasting glucose, HbA1c, serum creatinine, total cholesterol, LDL and UACR were significantly higher in individuals with retinopathy among the non diabetic individuals (n=776). Subjects with diabetic retinopathy were significantly older with higher BMI, WHR, diastolic blood pressure, serum glucose (fasting and 2 hr after glucose), HbA1c, serum creatinine, triglyceride, total cholesterol and LDL compared to those with retinopathy but without diabetes (data has not shown).

Table P2.3: Prevalence rate of retinopathy by age and glucose metabolism category

Age group in years	Male	Female	Retinopathy cases		Prevalence per 100		Total prevalence (%)	P for difference
			Male	Female	Male	Female		
25-40 yrs	162	164	4	6	2.5	3.7	3.1	0.533
41-55 yrs	172	128	8	6	4.7	4.7	4.7	0.988
above 55 yrs	134	76	11	10	8.2	13.1	10.7	0.151
Total	468	368	23	22	4.9	5.9	5.4	0.499

Glucose Metabolism Category	Male	Female	Retinopathy cases		Prevalence per 100		Total prevalence (%)	P for difference
			Male	Female	Male	Female		
DM	32	28	9	4	28.1	14.3	21.6	0.094
Pre DM	26	28	3	4	11.5	14.3	13.0	0.764
NGM	410	312	11	14	2.7	4.5	3.5	0.189

Abbreviations: DM, Diabetes Mellitus; Pre DM, Pre Diabetes Mellitus; NGM, Normal Glucose Metabolism;

The overall prevalence rate of retinopathy was 5.4% and the prevalence increased with increasing age both for males and females (Table 3). Though non-significant, females had higher prevalence of retinopathy compared with males in all age groups. The difference in prevalence of retinopathy by sex widened in the older age group (>55 years). Moreover, we found that the prevalence of retinopathy was 21.6% among the diabetic subjects (DM), 13% among the prediabetic subjects (Pre DM) and 3.5% among the nondiabetic subjects (NGM), respectively. Males had higher prevalence of retinopathy compared with females in diabetes group. On the contrary, females had higher prevalence of retinopathy compared with males in prediabetes and nondiabetes group.

Table P2.4: Prevalence, odds ratio (OR) and 95% CI of Retinopathy by the following risk factors in the study population

Variables	Retinopathy cases	n	Prevalence per 100	OR [1] (95% CI)	OR [2] (95% CI)
Age (yrs)					
25-40 yrs *	10	326	3.1	1.0	1.0
41-55 yrs	14	300	4.7	3.51 (1.82-7.61)	1.97 (1.55-4.66)

Above 55 yrs	21	210	10.0	2.32 (1.43-4.60)	1.86 (1.24-4.17)
Sex					
Male *	23	468	4.9	1.0	1.0
Female	22	368	6.0	1.23 (0.67-2.24)	1.63 (0.78-3.12)
Glucose metabolism category					
Normal Glucose Metabolism (NGM) *	25	722	3.5	1.0	1.0
Prediabetes Mellitus (Pre DM)	7	54	13.0	1.98 (1.21-5.07)	1.75 (0.99-4.34)
Diabetes Mellitus (DM)	13	60	21.6	3.61 (1.82-6.40)	2.53 (1.52-5.41)
BMI (kg/m^2)					
18.5-22.99 normal *	12	377	3.18	1.0	1.0
Below 18.49 underweight	11	173	6.35	0.87 (0.46-2.53)	0.69 (0.40-2.37)
23.0-24.99 overweight	8	60	13.3	0.59 (0.38-1.32)	0.49 (0.18-1.23)
25.0-29.99 obese I	7	180	3.89	2.64 (1.68-9.37)	2.44 (1.51-7.02)
Above 30.0 obese II	7	46	15.21	4.43 (1.87-13.37)	3.83 (1.74-12.85)
WHR					
Normal *	10	226	4.4	1.0	1.0
High	35	610	5.7	1.32 (0.64-2.70)	0.87 (0.29-1.71)
SBP (mmHg)					
Below 140 *	24	663	3.6	1.0	1.0
Above 140 high	21	173	12.1	3.68 (1.80-6.78)	1.81 (1.25-5.90)
DBP (mmHg)					
Below 90 *	23	657	3.5	1.0	1.0
Above 90 high	22	179	12.3	3.86 (2.14-7.11)	1.76 (1.16-5.67)
Hypertension					
No *	24	664	3.6	1.0	1.0
Yes	21	172	12.2	3.56 (1.87-6.06)	1.98 (1.17-5.63)
HbA1c (%)					
Below 5.2 *	19	492	3.9	1.0	1.0
5.3 – 5.7	8	208	3.9	3.60 (1.85-7.02)	1.74 (1.09-3.02)
Above 5.8	18	136	13.2	4.38 (1.98-10.80)	3.10 (1.24-8.31)
S Creatinine (mg/dl)					
Normal *	23	671	3.4	1.0	1.0
High	22	165	13.3	4.33 (2.35-7.99)	3.22 (1.53-6.76)
Triglyceride (mg/dl)					
Below 150 *	16	475	3.4	1.0	1.0
Above 150	29	361	8.03	2.51 (1.34-4.69)	1.27 (0.61-2.66)
Cholesterol (mg/dl)					
Below 200 *	19	584	3.2	1.0	1.0

Above 200	26	224	11.6	3.42 (1.86-6.31)	2.46 (1.44-5.29)
LDL (mg/dl)					
Below 100 *	9	251	3.6	1.0	1.0
Above 100	36	585	6.1	1.76 (0.84-3.72)	0.95 (0.34-2.16)
UACR (mg/g)					
Below 30 *	34	312	10.8	1.0	1.0
Above 30	11	45	24.4	2.65 (1.53-5.69)	1.63 (1.08-3.12)

Abbreviations: OR, Odds ratio; CI, Confidence interval; BMI, Body mass index; WHR, Waist hip ratio; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; $HbA1_c$, Glycosylated hemoglobin; LDL, Low density lipoprotein; UACR, Urine albumin creatinine ratio

OR [1], Crude odds ratio after univariate logistic regression; OR [2], Adjusted odds ratio for age, sex, glucose metabolism category, BMI, WHR, SBP, DBP, hypertension, HbA1c, S Creatinine, Lipids and UACR

* Referent

We used logistic regression to quantify the individual effects of age, sex, glucose metabolism category, BMI, WHR, SBP, DBP, hypertension, HbA1c, S Creatinine, Lipids and UACR with diabetes (Table 4). Age, glucose metabolism category, BMI, SBP, DBP, hypertension, HbA1c, S Creatinine, triglyceride, total cholesterol and UACR were found to be significant risk factors for the occurrence of retinopathy in the univariate model. After adjusting for potential confounders in the multivariate model by using all variables in the model age, DM, BMI, SBP, DBP, hypertension, HbA1c, S Creatinine, total cholesterol and UACR remained as significant independent risk indicators for the occurrence of retinopathy in this population. The risk for retinopathy was almost 2-fold in subjects who were above 40 years with fasting glucose of ≥6.1 mmol/l, BMI >25.0 kg/m^2, hypertensive, increased HbA1c level of above 5.3%, high serum creatinine for both sex, cholesterol >200 mg/dl and UACR >30 mg/g.

DISCUSSION

Only a few population based research has been performed on the prevalence of retinopathy in general population as well as at different levels of hyperglycemia, such as, diabetes mellitus, impaired glucose tolerance, impaired fasting glucose and normal glucose tolerance. So far there is no study in Indian subcontinent on such diseases group of populations. Few

studies have been done on Indian population which highlighted the prevalence of diabetic retinopathy, the microvascular complication of diabetes mellitus among known diabetic and newly diagnosed diabetic individuals (6, 8, 9, 36, 37). Not only the patients with diabetes mellitus, but elderly individuals with prediabetes (IGT and IFG) and normal glucose metabolism have a substantial risk of developing retinopathy. Our survey is the first representative study concerning the prevalence and associated risk indicators of retinopathy in rural Bangladeshi adults. This research provides vital epidemiological data regarding retinopathy among diabetes and nondiabetes population in the country that will be useful for the rational planning and implementation of organized eye care service delivery. Our findings indicate a high prevalence rate of retinopathy among general population and higher age, glucose metabolism, BMI, hypertension, HbA1c, serum creatinine, total cholesterol and UACR are significant independent risk indicators for the occurrence of retinopathy in this population.

Prevalence of retinopathy was found 21.6% (95% CI 11.2-32.0) among the diabetic subjects, 13% (95% CI 3.4-22.6) among the prediabetic subjects and 3.5% (95% CI 2.2-4.8) among the nondiabetic subjects, respectively. The age standardized prevalence of retinopathy was calculated at 5.4% (95% CI 3.9-6.9) among 836 people aged 25 years and older that were examined in the course of this study. We have found a higher prevalence of DM in this study population and the prevalence of retinopathy was increased in the subjects with increasing deciles of glycemic level. The prevalence rate of retinopathy in different glucose metabolism categories documented in this study was comparatively similar to other two recent European studies. A population based Hoorn study with cohort design found the incidence of retinopathy as 17.5% in DM, 13.6% in IGT and 7.3% in NGM subjects (29). Another cross-sectional study done in Finland estimated the prevalence of retinopathy as 25% in DM, 2% in IGT and 3% in normoglycemic or NGM subjects (30). Early epidemiological evidences showed that the prevalence of retinopathy is increased in the subjects whose glycemic values were in the highest two or

three deciles in population with a high prevalence of diabetes (31, 32). As the consequences of increasing number of diabetic subjects, the number of DM with its associated complications like retinopathy would also rise in Bangladesh. Moreover, a high prevalence of retinopathy was found in this study in normoglycemic subjects, as in the other studies (31-33). As there is no previous study in Bangladesh, therefore, it is difficult to make a scientific comprehension of the rising trend of retinopathy.

In this study population, retinopathy tended to be associated with several factors such as, increased age, glucose metabolism category, higher BMI, hypertension, HbA1c level, serum creatinine, total cholesterol and UACR. In the present study females had higher prevalence of retinopathy compared with males in all age groups but it did not show any significant difference in accordance with findings in other DM population (34, 35). Though non-significant, the current data showed that males had higher prevalence of retinopathy compared with females in diabetes group. Retinopathy in diabetes population appeared to be prevalent more in males compared to females has been reported from CURES Eye study, UKPDS study, and Hyderabad study (6, 9, 36, 38). In contrast to other studies (29, 35), however, the prevalence of retinopathy in our study had a significant tendency to get higher with increasing age. Our study confirmed the well known positive association between hyperglycemic status and retinopathy. This result in accordance with those of previous studies (12-14, 39), have shown retinopathy to be associated with glucose metabolism status or with high fasting blood glucose levels. There is strong evidence to suggest that the development and progression of retinopathy is influenced by glycosylated hemoglobin (HbA1c) level (40-44) which was also reflected in our study. The cumulative prevalence increased from 3.9% for those in the lowest to 13.2% for those in the highest tertile of HbA1c level. Risk for developing retinopathy increased with HbA1c level.

BMI, the indicator for general obesity seemed to indicate a high risk of developing retinopathy in this population. In line with our study, a positive association between BMI and retinopathy was found in few studies (40, 45, 46, 47) that included diabetic subjects. On the other hand, BMI did not manifest as a risk factor for retinopathy among diabetic subjects in CURES Eye study. WHR, the indicator for central obesity was also an independent risk factor for developing retinopathy in diabetic subjects (42, 44) as well as in nondiabetic subjects (29). After adjustment for potential confounders in multivariate model WHR did not remain as significant independent risk indicators for the occurrence of retinopathy in this population. The estimated risk for developing retinopathy in individuals with hypertension was almost 2 times as high as in individuals without hypertension, which remained after adjustment for possible confounders. This is in line with previous findings of incident retinopathy in studies (35, 43, 45, 48) of diabetic subjects and in the 2 other studies (49, 50) that included nondiabetic individuals. The present study did not find a statistically significant association between serum triglyceride, HDL cholesterol and LDL cholesterol and occurrence of retinopathy. Association between cholesterol and prevalence of retinopathy, although not always statistically significant in multivariate risk models, were described in several studies (42, 44, 45, 51) that included diabetes subjects. Cross-sectional data (52, 53) have shown that hard exudates in particular are associated with elevated cholesterol levels. In the present study risk for retinopathy in subjects with high level of cholesterol was more than 2 times as high as in subjects with normal cholesterol level. Cross-sectional (37) and longitudinal studies (54, 55) report a relationship between microalbuminuria and retinopathy. Elevated serum creatinine and urine albumin creatinine ratio were found as significant risk indicators for developing retinopathy in this population. The present findings of the combination of these risk indicators for predicting retinopathy may suggest that insulin resistance or associated factors are implicated in the pathogenesis of retinopathy.

The current study had some limitations. First, the evaluation was presented by cross-sectional design. Second, it can be argued that the sample size calculation was not properly done for estimating the prevalence of retinopathy in this population. So far, no data has been generated either in Bangladesh or in the Asian subcontinent on the extent of retinopathy and its association with glucose metabolism including nondiabetic general people as well, which could we use to estimate our desired sample size. The strong point of this study was that the diagnosis of retinopathy was based on retinal photograph using fundus camera through dilated pupils, instead of nonmydriatic photograph. It has been argued that the use of nonmydriatic camera results in a moderately high frequency of ungradable photograph, especially in the presence of media opacities (27, 28).

In conclusion, the present data suggest that, in addition to serum glucose control in diabetic patients, screening for hypertension, general obesity, hypercholesterolemia and proteinuria (urine albumin creatine ratio) and adequate treatment of these risk factors help to prevent retinopathy in diabetic and nondiabetic individuals. This work gives new information on the prevalence and associated risk indicators of retinopathy in one region of Bangladesh. While there were imperfection in the design and execution of the study, it does highlight several problems that must be addressed and overcome if definitive data are to be produced from subsequent studies.

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9.1 Appendix 1

QUESTIONNAIRE

Questionnaire
Diabetes & Eye Camp

Date: Place:

ID No:

Name:

Age:

Sex:

Marital status:

Address:

Contact No:

Education:

Occupation:

Family Member:

Monthly Income:

Monthly expenditure:

Anthropometry:	
a) Height (cm):	1st reading -
	2nd reading -
b) Weight (Kg):	1st reading -
	2nd reading -
c) BMI (kg/m^2):	
d) Waist (cm):	1st reading -
	2nd reading -
e) Hip (cm):	1st reading -
	2nd reading -
f) Waist/Hip ratio:	
Blood Pressure:	1st reading -
	2nd reading -

History of Diabetes: Yes / No Duration:

Family History of DM: Yes / No Relation: Duration:

Complication:

a) Problem in eye (Retinopathy)

b) Nephropathy

i. Swelling of leg or face

c) Neuropathy

i. Lingbing ii. Numbness iii. Abnormal sensation in hand or foot

d) Cardio vascular diseases

e) Hypertension

Others related complication if any

History of smoking: a) Type

b) Stick/ Day

c) Duration

Exercise:

a) Type

b) Duration/ Day

Investigation Performed:

Urine Sugar	Negative	Trace	250 +	500 ++	1000 +++	2000 ++++
Urine Protein	Negative	10 ±	30 +	100 ++	300 +++	

S Fasting Blood Glucose

S Oral Glucose Tolerance Test

S Triglyceride

S Total Cholesterol

S Low Density Lipoprotein

S High Density Lipoprotein

HbA_1c

S Creatinine

Urine Albumin Creatinine Ratio

Ocular Examination

ID No:

Name:

Visual Acuity:	**Right Eye**	**Left Eye**
i.Un aided		
ii. With glass		
iii. With Pinhole		
iv. PH+ glass		
Lids		
Conjunctiva		
Cornea		
Iris		
Pupil		
Lens		
Vitreous		

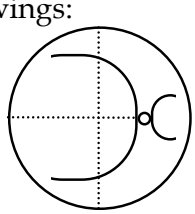
Fundus

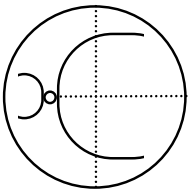
Diabetic Retinopathy		**Right Eye**	**Left Eye**
NPDR:	i. Mild		
	ii. Moderate		
	iii. Severe		
	iv. Very severe		

PDR:	i. Early		

	ii. High Risk		
	iii. ADED		
Maculopathy	i. Focal		
	ii. Diffuse		
	iii. Ishchemic		
	iv. CSMO		
Hypertensive Retinopathy			
Mics:	i. CRVO		
	ii. BRVO		
	iii. Vascullar		
	iv. Others		

Fundus Drawings:





Notes:

Optic Disc Change	**Right Eye**	**Left Eye**
Colour		
CD Ratio		
Margin		
Others		
Ocular investigation and findings:		
Investigation	**Right Eye**	**Left Eye**
i. CFP		

ii.FFA		
iii. Perimetry		
iv. B scan		
v. Boimetry		
vi. Others		

Provisional Diagnosis:

Other Investigation:

Treatment:

a. Medication

b. Plan for procedure	Right Eye	Left Eye
i. LASER		
ii. Operation		
iii. Others		

c. Follow up:

Report and Remarks:

9.2 Appendix 2

INFORMED CONSENT FORM

Information and agreement paper between the subject and the researcher

Letter of Information

Dear Sir/Madam,

I am a student of International Community Health at the University of Oslo, Norway. This letter of information is to invite you to participate in a health research. This project is carried out with the permission from the Norwegian Research ethical Committee and the National Ethical Committee of Bangladesh. You are selected randomly as a possible participant in this study because our study subjects are adults both male and females. The objective of the project is to estimate the prevalence and to investigate the determinants of diabetes and retinopathy in rural population of Bangladesh. The result of the study will serve as the base line data for further research regarding the development and management of diabetes and eye care in an attempt to prevent visual loss in Bangladeshi population. To do this, we have to collect some information from you and also need to conduct some physical and clinical examinations which will help to fulfill the objectives of the project with your kind permission. Therefore, if you agree to participate you have to come to the screening camp between 8.00 am to 9.00 am on the appointed day after fasting for at least 8-10 hours and will answer to some questions and have to provide blood sample twice to do some examinations. The blood will be drawn by a well-trained technician maintaining all aseptic measures and by using a small syringe. We will use a new syringe for each participant and once his/her blood is drawn, it will be disposed safely. It may make the participants' feel only a little discomfort during the whole process. In the

phase of blood examination possible side effects may include local swelling after drawing blood, slight congestion, dizziness etc. However, we have been well prepared to protect the study subjects and to minimize potential harm to the lowest degree. All the participants will go through some modernized ocular examination during this visit to check whether they have developed retinopathy or not. Test results will be informed you in time. All the subjects with diabetes, retinopathy and diabetic retinopathy will refer you to the Health Care Center of the Diabetic Association of Bangladesh for further treatment and follow up. Choosing to participate will be advantageous to you for some reasons: You will know whether or not you have diabetes.

- You will know whether or not you are about to have diabetes.
- Knowing your diabetic status will help you to take appropriate decisions regarding diabetic complications.
- You will know whether or not you have retinopathy.

You are free to choose either to participate or not to participate in this project. You can trust that any information you will give us, including the results of your examinations, will all be treated very confidentially and will only be used for research purpose. For that reason, it is important that the information you give be as correct and truthful as possible. You also have the right to withdraw from the project at any time during the study without the prior reasons. This will have no negative consequences on you.

May be you cannot receive too much direct benefit from taking part in this research, but it will have a favorable impact on public health in future. Your participation will contribute greatly to our research. We thank you in advance for agreeing to help us out. If you have any question on concern about the study please contact local diabetic center.

Respond Document

I …….. hereby give my well informed and coercion free consent to participate in the study. I fully understand that my participation in the study will bring fruitful medical information which will be used for many other researches in future.

I am convinced that during participation in the study, I shall not be exposed to any physical, psychological, social or legal risks. My privacy and confidentiality will be safeguarded and any anonymity will be protected. I also consent to use my blood and urine for the study.

Date: …….. **Date: ……..**

Signature of the participant **Signature of the interviewer**

……

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9.3 Appendix 3

PICTURES FROM THE FIELD WORK

Picture 1: Participants were waiting to start the survey procedure

Picture 2: participants were interviewed the questionnaire

Picture 3: Field worker was calculating the anthropometric measurement

Picture 4: Visual acuity test

Picture 5: Ocular examination by slit lamp

Picture 6: Ocular examination by ophthalmoscope

Picture 9: Ophthalmologists were prescribing the participants

Picture 10: Team of the laboratory technicians

Picture 11: Team of the volunteers