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"Comparison of Serum Homocysteine Level among Type II Diabetic Patients and IGT Patients with Normal People"

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ABSTRACT: Background: Hyper homo cysteinemia (HHcy) is common in type 2 diabetes mellitus and prediabetes and is associated with an increased risk for cardiovascular events in these patients. But little is known about HHcy status and its cardiovascular relationships in these group of patients in our country. This study was conducted to compare the serum homocysteine level among type 2 Diabetic patients and IGT Patients with normal people. **Objectives**: The objective of the study was to compare the serum homocysteine level among type 2 Diabetic Mellitus and IGT patients with normal people. **Methods:** This was a cross-sectional ovbservational study. Total 120 subjects were selected and allocated into three groups, equal number (n=40) in each group. This study was conducted in Mymensingh Medical College Hospital from June, 2019 to May, 2020. **Results:** The study showed that the mean age of the patients and their BMI were almost similar among the three groups, male female ratio was about 2.5:1, most of the patients were from urban area (61.6%) and most of them were businessman & housewife, major portion of study population belonged to middle class family. Most of the patients were non-smoker and large portion of the group I & group II patients were hypertensive. Among the groups TC, TG & HDL-C shows significant statistical difference. Present study showed that levels of Hcy were significantly higher in the type 2 DM group than those in normoglycemic group (19.86 µmol/L vs. 8.72 µmol/L, $p<0.001$). Similarly levels of Hcy were significantly higher in the IGT group than those in normoglycemic group (17.28 µmol/L vs. 8.72 µmol/l, $p<0.001$). The mean values of the serum Homocysteine level of Group -1 and Group – 2 showed statistical significant difference with group-3. In this study, serum Homocysteine levels shows strongly positive correlation with hyperglycemia. **Conclusions:** The study suggested that homocysteine was higher in patients with type 2 DM and IGT in comparison to normoglycemic people.

Key words: Diabetes mellitus, Serum Homocysteine, Impaired glucose tolerance.

I INTRODUCTION

Diabetes Mellitus (DM) is one of major public health concerns in both developing and developed countries. It is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies beyond glycemic control [1]. The direct and indirect social and economic costs of treating diabetes and its complications have the potential to cripple the countries healthcare budgets. Like many other developing countries, Bangladesh faceces a burden of diabetes with other metabolic syndrome. Changing in life styles, eating habits, sedentary lifestyles, increased use of tobacco and deteriorating environmental conditions are likely to develop non-communicable diseases. At present it is estimated that about 7.1 million cases of diabetes in Bangladesh in 2015 and latest data suggested that prevalence of diabetes in adult (20-59 years) is 7.4% [2]. Type-2 DM is defined as chronic hyperglycemia resulting from either decreased insulin secretion, impaired insulin action or both, in the absence of autoimmune destruction of the pancreatic β-cell [3]. Impaired glucose tolerance (IGT), is a pre-diabetic state of dysglycemia that is associated with insulin resistance and increased risk of cardiovascular pathology. IGT is characterized by high postprandial blood glucose level and it may precede type 2 diabetes mellitus by many years. Both diabetic and IGT individuals are highly prone to cardiovascular diseases (MI, Stroke, PVD) and both are frequently related with more damaging effects on the vasculature, including the activation of abnormal vasomotion, up-regulated inflammatory responses, increased

oxidative stress, and an extensive procoagulant state [4]. However, the mechanism by which IGT interferes with the cardiovascular system has not been fully defined, hence it is necessary to search for advanced markers to assess the risk of cardiovascular complications of Diabetes Mellitus and IGT. During the past 2 decades, hyperhomocysteinemia has emerged as a risk factor for diabetes mellitus, cardiovascular diseases and stroke [5, 6]. Detrimental effects of homocysteine on endothelial function are well documented. Plasma Homocysteine (Hcy) levels are elevated in type 2 diabetic patients as well as in pre-diabetic individuals with insulin resistance [5]. In such individuals, plasma Hcy concentration is influenced by the insulin concentration and anti-diabetic therapy such as metformin, glitazones or insulin that can alter the plasma Hcy conc [7]. It was evident that folic acid and B-vitamin therapy substantially reduces homocysteine levels. It was evident that hyperhomocysteinemia is associated with hyperinsulinemia and may partially account for increased risk of CVD associated with insulin resistance [7]. Serum homocysteine level is increased in insulin resistant & hyperinsulinemic patients and also in type 2 DM patients with intact pancreatic Beta-cell functions. But when these patients loose pancreatic Beta-cells, they might then show a fall in plasma Hcy concentration. Non diabetic patients who have insulin resistance syndrome also show high plasma Hcy level. Which proves the association between elevated plasma Hcy and increased plasma insulin concentration [7]. The results of the positive link between Hcy levels and insulin values and insulin resistance might partially explain the potential mechanism by which HHcy stimulates the earlier initiation of hyperglycemia. Recent studies have documented that insulin resistance is an independent risk factor for the progression of abnormal glucose metabolism [8]. Oxidative stress might also be involved in the precise mechanism linking HHcy to abnormal glycometabolism. HHcy inhibits the synthesis of glutathione (GSH), the major intracellular antioxidant. The depletion of GSH is related to high oxidative stress [10]. Several studies have suggested that oxidative stress occurs in the context of type 2 diabetes pathology [9,11]. Thus, HHcy might also promote hyperglycemia partially through oxidative stress-mediated parthenogenesis. So it is concluded that, the values of serum Hcy higher in diabetic and prediabetic cases in comparison to non-diabetic cases. It suggests that serum Hcy may serve as an atherogenic and thrombogenic marker and can be used as a predictor of cardiovascular risk in T2DM patients. In addition, high levels of plasma homocysteine are known to exert an adverse effect through a mechanism involving oxidative damage [12]. Serum Hcy evaluation may serve to identify diabetic patients predisposed to vascular complications and more importantly the group of patients that may benefit from intensified screening and treatment strategies. The aim of this study was to compare the serum homocysteine level in type 2 Diabetic & IGT patients with normal people. So that preventive measures can be taken at an early stage.

II OBJECTIVES

1. General objective:

To estimate the serum homocysteine level in patients of type 2 Diabetes mellitus & IGT and to compare it with that of normal people.

2. Specific objectives:

1. To measure serum Hcy level in type 2 Diabetes mellitus patients, IGT patients and normal subjects.
2. To compare serum Hcy level with glycemic status in type 2 Diabetic patients, IGT patients as well as normal people.
3. To observe the relation of serum Hcy with other clinical and biochemical variations in the study subjects.

III REVIEW OF LITERATURE

Diabetes Mellitus (DM): Diabetes is not one disease, but rather is a heterogeneous group of syndromes characterised by an elevation of blood glucose caused by a relative or absolute deficiency in insulin [13]. Diabetes poses an immense global challenge. Individuals, families, communities and economies are all threatened by the seemingly unstoppable rise of this disease. The number of people with diabetes is increasing due to population growth, aging, urbanization and increasing prevalence of obesity and physical inactivity. The prevalence of diabetes is higher in men than women [14]. The prevalence of type 2 diabetes has increased in the early part of the 20th century, particularly in developing countries. There is evidence that the prevalence also continues to increase in developed countries, including the United States. Rapid development has driven a fast- growing epidemic of diabetes in South- East Asia (SEA). Prevalence of diabetes in adults worldwide was estimated to be 4.0% in 1995 and to rise to 5.4% by the year 2025. It is higher in developed than in developing countries. The number of adults with diabetes in the worlds will

rise from 135 million in the year 1995 to 300 million in the year 2025. The major part of this numerical increase will occur in developing countries. There will be a 42% increase, from 51 to 72 million, in the developed countries and a 170% increase, from 84 to 228 million, in the developing countries. In Bangladesh diabetes raw national prevalence is 5.52% [15]. In Bangladesh, which had a population of 149.8 million in 2011 (Bangladesh population and housing census 2011), a recent meta-analysis showed that the prevalence of diabetes among adults had increased substantially, from 4% in 1995 to 2000 and 5% in 2001 to 2005 to 9% in 2006 to 2010 [16, 27]. In the year 2000, Bangladesh was in the 10th position with about 3.2 million people with diabetes but in the year 2030 it is estimated to be in the 7th position with almost 11.1 million people with diabetes. Diabetes is undoubtedly one of the most challenging health problems of the 21st century. According to the International Diabetes Federation, 382 million people worldwide, or 8.3% of adults, are estimated to have diabetes. By 2035 this will rise to 592 Million [6]. At the same time non-communicable diseases and metabolic disorders linked with diabetes (DM), hypertension (HTN) and coronary heart diseases (CHD) are increasing. At present it is estimated that about 7.1 million cases of diabetes in Bangladesh in 2015 and latest data suggested that prevalence of diabetes in adult (20-79 years) is 7.4% (www.idf.org). Diabetes mellitus can lead to diabetes specific complications and end organ damage which can be prevented or delayed by strict glycemic control and thereby reduce morbidity and mortality among these patients. In a major proportion of patients, oral anti-diabetic drugs are used for glycemic control early in disease course and are effective in many cases to reach the therapeutic targets. Summaries of previous studies of oral antidiabetic drugs (OADs) suggest that they reduce A1C levels by 0.5–1.25% [17, 18], demonstrated that type 2 diabetes is a progressive disease and patients are likely require the addition of glucose-lowering medications over time.

Insulin resistance: This is caused by the decreased ability of insulin to act effectively on peripheral target tissues (especially muscle and liver) and is a prominent feature of type 2 diabetes.

Impaired insulin secretion: Insulin secretion and sensitivity are interrelated. In type 2 diabetes, insulin secretion initially increases in response to insulin resistance in order to maintain normal glucose tolerance. Initially, the insulin secretory defect is mild and selectively involves glucose - stimulated insulin secretion. Eventually, the insulin secretory defect progresses to a state of grossly inadequate insulin secretion.

Impaired hepatic glucose production: The liver maintains plasma glucose during periods of fasting through glycogenolysis and gluconeogenesis using substrate derived from skeletal muscle and fat (alanine, lactate, glycerol and fatty acid). Insulin promotes the storage of glucose as hepatic glycogen and suppresses gluconeogenesis. In type 2 diabetes, insulin resistance in the live arises from the failure of hyperinsulinaemia to suppress gluconeogenesis, which results in fasting hyperglycemia and decreased glucose storage by the liver in the postprandial state. Increased hepatic glucose production occurs early in the course of diabetes, though likely after the onset of insulin secretory abnormalities and insulin resistance in skeletal muscle.

Impaired Glucose Tolerance: Impaired glucose tolerance (IGT), an intermediate stage between normal glucose tolerance (NGT) and overt type 2 diabetes, may be induced by insulin resistance and can lead to the development of type 2 diabetes and cardiovascular diseases [26]. Vascular complication is a long term and specific complication of diabetes mellitus. It includes nephropathy, retinopathy and neuropathy. Also cerebrovascular disease, coronary artery disease and peripheral vascular disease. Long standing hyperglycemia plays the key role for the development of characteristics clinical syndrome of vascular complication, which is thought to result from the local response to the generalized vascular injury. Hyperglycemia is considered a primary cause of diabetic vascular complications and in associated with oxidative stress, impaired trace element and lipid metabolism as well as pancreatic enzyme abnormalities [24]. Beside this another glycemic condition is impaired glucose tolerance (IGT), an intermediate stage between normal glucose tolerance (NGT) and overt type 2 diabetes, may be induced by insulin resistance and can lead to the development of type 2 diabetes and cardiovascular diseases [19, 25]. It was found that HHcy was related to hyperinsulinemia and insulin resistance Bansal et al. [5], linked HHcy to DM and IGT. Serum Hcy evaluation may serve to identify diabetic patients predisposed to vascular complications and more importantly the group of pts. that may benefit from intensified screening and

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treatment strategies. The aim of this study was to compare the serum homocysteine level in IGT and type 2 diabetic pts. with normal people. So that preventive measures can be taken at an early stage.

IV MATERIAL AND METHODS

Study design: Cross sectional descriptive comparative study.

Place of study: Study was conducted in Departments of Medicine & Endocrinology, Mymensingh Medical College Hospital, Mymensingh, Bangladesh.

Study periods: Study was conducted from June, 2019 to May, 2020.

Study Population: Patients with type 2 Diabetes mellitus & IGT attended in the inpatient Departments of Endocrinology & Medicine of Mymensingh Medical College Hospital were included after fulfillment of selection criteria. Similar number of nornal subjects were recruited as control.

Sample size: = 120. So, 120 cases included among them 40 type 2 diabetic pts, 40 IGT pts. and 40 normal people (control group).

Inclusion criteria:

Patients diagnosed with DM & IGT after admission were included in the sample & peoples with normal blood glucose level as comparison group.

1. Age: 30-60 years
2. Gender: Male & Female
3. Case:

- Diagnosed type 2 diabetes mellitus by performing fasting blood glucose > 7.0 mmol/l & 2 hours ABF >11.1 mmol/l. Group-1)
- IGT patients diagnosed by performing fasting blood glucose <5.6mmol/l &after 75g of OGTT blood glucose 7.8-11.0 mmol/l. (Group-2)
- Normoglycemic people. (Group-3)

Exclusion criteria:

1. Any gross macrovascular or microvascular disease
2. Pregnancy.
3. Renal disease eg. ARF, CRF.
4. Hepatic disorder eg. CLD, NAFLD, ALD, NASH.
5. Chronic debilitating disease eg. TB, Malignancy.
6. Other hormonal disorder e.g. Hypothyroidism, Hyperthyroidism and Hypercalcemia.
7. Current medication that may influence serum homocysteine level including antifolates (methotrexate, anticonvulsants, trimethoprim), L-Dopa, fibrates, cyclosporine.
8. Cobalamin (vitamin B12), folate or pyridoxine (vitamin B6) supplementation.

Study procedure: This study was conducted in the Departments of Medicine & Endocrinology, Mymensingh Medical College Hospital, Mymensingh, Bangladesh after approved by the institutional review board. Patients with IGT & type 2 Diabetes mellitus were approached and were selected in according to the inclusion and exclusion criteria. Subjects were briefed about the objectives of the study, risk and benefits, freedom for participating in the study and confidentiality. Informed consent was obtained accordingly. Subjects were grouped into three groups, group 1 (patients with DM), group-2 (patients with IGT) & group-3 (normoglycemic people). Compare of homocysteine was investigated among the groups. The data collection sheet filled up by the study physician herself. The data regarding sociodemographic, clinical and biochemical were recorded. Initial evaluation of the subjects were done by history taking and demographic profile and pulse, BP, Height, Weight, BMI etc. measured and recorded in the preformed data collection sheet.

Laboratory investigation procedure: With all aseptic precaution 5 mL venous blood was drawn from anticubital vein after in a disposable plastic syringe and delivered immediately into a clean dry heparinized tube. Then plasma was separated after centrifuging at 3000 rpm for 5 minutes & collected in ependrop tube, label properly and store in ultra-freezer at -35^0C and all the biochemical tests were done at the department of Biochemistry, MMCH. Blood samples was collected from study subjects to estimate the fasting blood glucose, serum homocysteine, Fasting lipid profile and then 2 hours after postprandial glucose status was observed. Collected data were recorded in a separate case record form. Hcy concentrations were determined by the clinical chemistry method. Blood glucose levels were detected using the glucose oxidase method. Blood lipids were detected as follows: TC was measured by an enzymatic cholesterol oxidase reaction, HDL-C and LDL- C were measured by the direct assay and TG was measured by a glycerol lipase oxidase reaction. Serum glucose, lipid, and Hcy levels were analyzed using a Dade Behring Dimension RXL Max Chemistry Analyzer (Siemen, German). All collected questionnaire checked very carefully to identify the error in the data. Collected data were

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checked and edited and then processed with the help of the software Statistical Package for Social Sciences (SPSS) version 22 and analyzed. The results were expressed using mean ± SD, frequency, t test and pearsons correlation test.

Data analysis: All statistical analysis were performed using the Statistical Package for Social Science (SPSS) program, version 22 and Windows. All data were presented in suitable table, box plot, pie chart and graph according to their affinity. A description of each table and graph was given to understand them clearly. . Continuous parameters were expressed as mean ±SD and categorical parameters as frequency and percentage. Comparisons between groups (continuous parameters) were done by Students t- test. Categorical parameters compared by Chi-square test. The significance of the results as determined in 95.0% confidence interval and value of P<0.05 was consider to be statistically significant.

V RESULTS

This cross sectional descriptive comparative study was conducted in the department of Medicine & Endocrinology, Mymensingh Medical College Hospital. Total 120 patients were divided into three groups; patients with Type 2 diabetes (group-1), IGT (group 2) and normal subject (group-3). This study was conducted to compare serum Homocysteine level among Type 2 DM & IGT patients with normal people.

Table- I: Age distribution of the patients (n=120)

Age (years)	Frequency & Percentage			p-value
	Group-1 (n=40)	Group-2 (n=40)	Group-3 (n=40)	
< 40	5 (12.5)	8 (20.0)	7 (17.5)	
40 - 49	11 (27.5)	9 (22.5)	8 (20.0)	
50 - 59	12 (30.0)	13 (32.5)	10 (25.0)	0.566
≥ 60	12 (30.0)	10 (25.0)	15 (37.5)	
Total	40 (100.0)	40 (100.0)	40 (100.0)	
Mean ± SD	48.31 ± 10.6	47.29 ± 11.0	48.28 ± 12.3	0.614

P -value is obtained by Chi- square test.
One way ANOVA was done to find out the level of significance.

Table I shows, the age distribution among the groups. Mean ± SD of age was (48.31 ± 10.62) for Group–1, (47.29 ± 11.0) for Group–2 and (48.28 ± 12.3) for Group–3. P-value = 0.614 (one-way ANOVA); which explains that there was no significant statistical difference among the groups in respect of age.

Table- II: Gender distribution of the patients (n=120)

Gender	Frequency & Percentage			Total	p-value
	Group-1 (n=40)	Group-2 (n=40)	Group-3 (n=40)		
Male	28 (70.0)	31 (77.5)	27 (67.5)	86	
Female	12 (30.0)	9 (22.5)	13 (32.5)	34	0.925

International Journal Dental and Medical Sciences Research
Volume 3, Issue 2, Mar-Apr. 2021 pp 644-656 www.ijdmsrjournal.com ISSN: 2582-6018

Total	40 (100.0)	40 (100.0)	40 (100.0)		

Chi square test was done to find out the level of significance

Table II illustrates that, most of the participants in all Group-1 [28 (70.0%)], Group-2 [31 (77.5%)] and Group-3 [27 (67.5%)] were males. Male: Female ratio was about 2.5:1. There was no statistically significant difference in male-female distribution between the groups.

Table- III: Distribution of patients in urban and rural area (n=120)

Residence	**Frequency & Percentage**			**Total**	**p-value**
	Group-1 (n=40)	**Group-2 (n=40)**	**Group-3 (n=40)**		
Urban	25 (62.5)	22 (55.0)	27 (67.5)	74 (61.6)	
Rural	15 (37.5)	18 (45.0)	13 (32.5)	46 (38.4)	0.086
Total	40 (100.0)	40 (100.0)	40 (100.0)		

Chi square test was done to find out the level of significance

Table III illustrates that, most of the participants hailing from urban area (61.6%).

Table- IV: Distribution of the patients according to occupation category (n=120)

Occupation	**Frequency & Percentage**			**Total**	**p-value**
	Group-1 (n=40)	**Group-2 (n=40)**	**Group-3 (n=40)**		
Service holder	3 (7.5)	6 (15.0)	6 (15.0)	15	
Businessman	11 (27.5)	12 (30.0)	7 (17.5)	30	
Day Laborer	6 (15.0)	6 (15.0)	10 (25.0)	22	
Retired	8 (20.0)	7 (17.5)	2 (5)	17	0.308
House wife	9 (22.5)	8 (22.5)	10 (32.5)	27	
Unemployed,	3 (7.5)	1 (2.5)	5 (12.5)	8	

Chi square test was done to find out the level of significance

Table IV shows occupation status of the patients. Large number of respondents were businessman, house wife.

Table- V: Socioeconomic status of the study population (n=120)

Socio Economic Status	**Frequency & Percentage**			**Total**	**p-value**
	Group-1 (n=40)	**Group-2 (n=40)**	**Group-3 (n=40)**		
Poor class	15 (37.5)	18 (45.0)	13 (32.5)	46 (38.4)	

International Journal Dental and Medical Sciences Research
Volume 3, Issue 2, Mar-Apr. 2021 pp 644-656 www.ijdmsrjournal.com ISSN: 2582-6018

Middle class	18 (45.0)	24 (60.0)	19 (47.5)	61 (50.8)	0.086
Upper class	7 (17.5)	6 (15.0)	8 (20.0)	21 (17.5)	
Total	40 (100.0)	40 (100.0)	40 (100.0)		

Chi square test was done to find out the level of significance

Table V shows the socioeconomic status of the study population. Subjects monthly income <5000 taka refereed as poor class, income 5000-50000 taka is middle class and monthly income >50000 taka denotes upper class. Among the patients the middle class 50.8% comprising the major percentage of the patients, which is followed by poor class 38.4% and remaining are upper class 17.5%.

Table- VI: Distribution of the participants by their smoking habits (n=120)

Smoking	**Frequency & Percentage**			**p-value**
	Group-1 (n=40)	**Group-2 (n=40)**	**Group-3 (n=40)**	
No	25 (62.5)	23 (57.4)	31 (77.5)	
Yes	15 (37.5)	17 (42.5)	9 (22.5)	0.268
Total	40 (100.0)	40 (100.0)	40 (100.0)	

Chi-square test was done to find out the level of significance

Table VI explains that, in all groups most of the participants were non-smokers. P-value was calculated to be, 0.268 (Chi-square); which explains that there was no significant statistical difference in the groups.

Table- VII: Distribution of the participants by their hypertensive status (n=120)

Hypertension	**Frequency & Percentage**			**p-value**
	Group-1 (n=40)	**Group-2 (n=40)**	**Group-3 (n=40)**	
No	4 (10.0)	11 (27.5)	27 (67.5)	
Yes	36 (90.0)	29 (72.5)	13 (32.5)	0.085
Total	40 (100.0)	40 (100.0)	40 (100.0)	

Chi-square test was done to find out the level of significance

Table VII shows that, for groups 1 & 2 history of hypertension showed similar pattern of distribution both arithmetically and statistically, as 72.5% of Group 2 and 90.0% of Group 1 were found to have positive history of hypertension. Statistical calculation by Chi-square was done resulting, which explains that there was no significant statistical difference in the groups.

International Journal Dental and Medical Sciences Research
Volume 3, Issue 2, Mar-Apr. 2021 pp 644-656 www.ijdmsrjournal.com ISSN: 2582-6018

Table- VIII: Baseline clinical profile of the participants (n=120)

Variables	Frequency & Percentage			p-value
	Group-1 (n=40)	Group-2 (n=40)	Group-3 (n=40)	
Height (m)	62.96 ± 5.26	61.58 ± 4.06	63.29 ± 4.63	0.17
Weight (Kg)	66.58 ± 9.72	62.61 ± 9.91	64.51 ± 8.75	0.61
BMI	21.04 ± 2.92	20.42 ± 3.24	20.66 ± 2.67	0.15
Systolic BP (mm of Hg)	124.68 ± 12.24	119.76 ± 12.74	121.40 ± 16.84	0.15
Diastolic BP (mm of Hg)	78.47 ± 10.11	78.66 ± 8.44	80.12 ± 11.10	0.83

One way ANOVA was done to find out the level of significance

Table VIII shows, the clinical and anthropometric measurements of the participants among the groups and there was no significant statistical difference among the groups.

Table- IX: Evaluation of serum lipid status among study population (n=120)

Variables	Frequency & Percentage			p-value
	Group-1 (n=40)	Group-2 (n=40)	Group-3 (n=40)	
TC (mg/dl)	215.0 ± 40.38	205.1 ± 35.08	196.0 ± 30.59	<0.001
TG (mg/dl)	253.0 ± 71.7	250.2 ± 48.5	226.50 ± 62.5	<0.05
LDL-C (mg/dl)	127.8 ± 33.3	125.2 ± 32.0	124.5± 35.9	>0.05
HDL-C (mg/dl)	36.8 ± 10.4	35.85 ± 9.8	39.8 ± 9.8	<0.05

One way ANOVA was done to find out the level of significance

Table IX shows, the serum lipid status among study population. Among the groups, TC, TG & HDL-C were significant statistical difference among the groups.

Table- X: Distribution of cases according to serum Homocysteine level (n=120)

S. Homocysteine status	Frequency & Percentage			p-value
	Group-1 (n=40)	Group-2 (n=40)	Group-3 (n=40)	
Hyperhomocysteinaemia	19 (47.5)	14 (35.0)	0	
Normal Homocysteine	21 (52.5)	26 (65.0)	40 (100.0)	0.001
Total	40 (100.0)	40 (100.0)	40 (100.0)	

Chi-square test was done to find out the level of significance

International Journal Dental and Medical Sciences Research
Volume 3, Issue 2, Mar-Apr. 2021 pp 644-656 www.ijdmsrjournal.com ISSN: 2582-6018

Table- X shows the distribution of cases according to serum Homocysteine level. All patients in group-3 had normal level of S. Homocysteine. But in group-1 & 2 had raised level of homocysteine, which shows statistical significant difference.

Table- XI: Mean Serum Homocysteine level among study people (n=120)

S. Homocysteine status	**Mean Serum Hcy level**			**p-value**
	Group-1 (n=40)	**Group-2 (n=40)**	**Group-3 (n=40)**	
Mean Serum Hcy level				
Mean ± SD	19.86 ± 5.20	17.28 ± 5.38	8.72 ± 2.96	0.0001

One way ANOVA was done to find out the level of significance

Table- XI shows mean serum Homocysteine level. All patients in group-3 had normal level of S. Homocysteine. But in group-1 & 2 had raised level of homocysteine, which shows statistical significant difference.

Table- XII: Blood glucose level of the participants among groups (n=120)

Variables	**Frequency & Percentage**			**p-value**
	Group-1 (n=40)	**Group-2 (n=40)**	**Group-3 (n=40)**	
FBG (mmol/L)	9.4 ± 3.6	6.8 ± 2.7	5.09 ± 1.5	0.048
2hrPPG (mmol/L)	13.5 ± 4.7	9.7 ± 3.1	6.5 ± 1.8	0.025

One way ANOVA was done to find out the level of significance

Table XII represents, the blood glucose level of participants among groups and mean values of Fasting blood glucose (FBG), 2-hour plasma postprandial glucose in patients with Type 2 DM & IGT have higher blood glucose levels, which shows statistical significant difference.

Table- XIII: Correlation analysis of different clinical & demographic profile with serum Homocysteine (n=120)

Parameters	**r**	**p value**
Age	-0.092	0.614
Sex	1.772	0.925
BMI	-0.259	0.152
SBP	-6.391	0.153
DBP	0.427	0.831
FBG	0.296	<0.001

2 HABF	0.078	0.004
TC	7.655	<0.001
TG	13.52	<0.05
LDL-C	0.295	>0.05
HDL-C	1.165	<0.05

Table XIII shows the ccorrelation analysis of different clinical & demographic profile with serum Homocysteine. The correlation between glycemic status and Serum Homocysteine levels of participants, which differ considerably, so that, Pearson correlation & Spearman correlation showed statistically significant difference. Hcy was positively associated with FBG (r=0.296, p<0.001), 2hPG (r=0.078, p=0.004). Similarly positive significant correlation was found with TC (r=7.655, p<0.001), TG (r=13.52, p=<0.05) and HDL-C (r=1.165, p<0.05).

VI DISCUSSION

This study was a cross sectional descriptive comparative study conducted in Mymensingh Medical College & Hospital to compare serum homocysteine level among type 2 Diabetes mellitus & IGT patients with normal people. Total 120 patients were enrolled and were allocated into three groups: Group I - type 2 diabetic patients, Group II - patients with IGT and Group III – normoglycemic people. The age distribution revealed, mean ± SD of age was 48.31 ± 10.62 year for Group- 1, 47.29 ± 11.0 year for Group-2 and 48.28 ± 12.3 year for Group-3. There was no statistically significant difference in respect to age, gender distribution and other demographic characteristics. Findings are consistent with the results of similar studies at home and abroad, e.g. a cross-sectional study reported that mean age was 62.35 ± 8.88 years [20]. A study in Bangladesh reported that among 1555 study subjects, 731 were male, 824 were female, most of the population were young with a mean age 33 years, and about 78 percent were in age category between 20-40 years [21]. Sex distribution showed that, in group 1, 70% were male, 30% were female. In group 2 , 77.5% male & 22.5% female and in group 3, around 67.5% male & 32.5% female. Male - Female ratio was about 2.5:1 and no significant difference was observed between sex distributions. In the study of Ceriello et al., [22] female proportion was higher. Another study done by Andayani et al.,[23] in which among 115 patients, 58 were men and 57 were women. In this study 38.4% patients came from rural, 61.6% from urban areas. So it was revealed that most of the participants hailing from urban area. Another study by Rahim M.A. et al., [3] reported that prevalence of diabetes was found to be higher among the urban subjects 8.1% compared to rural 2.3%. Almost three to five-fold higher prevalence was found with increasing age in urban subjects compared to rural. In this study about 30% patients were businessman, 25% housewife, 20% Day Laborer and service holder, retired, unemployed were around 25%. It was evident that large number of respondents was businessman, house wife and Day Laborer. In study done by Rahim M.A. et al., [3] among the female subjects, 76 percent were housewives and 19 percent were engaged in job. In the study patients, the middle class were 50.8%, comprising the major percentage, which is followed by poor class - 38% and the remaining were upper class -18%. All findings are consistent with result of other study. Rahim MA, et al., [3] showed that 81 percent had a monthly income below 3000/ taka, 47 percent were literates who could read or write their own name and 25 percent were employed in service in Bangladesh. In this study, 37.5% were smoker in group 1, 42.5% in group 2 & 22.5% in group 3. In all group, most of the participants were nonsmoker and there was no significant statistical difference in the groups. This was probably due to small sample size. In another study conducted by Johan, et al., [28] reported that 85% were smoker and 15% non-smoker. It was estimated that an overwhelming number 29(72.5%) of group-1, 36(90.0%) of group- 2 were found to have positive history of hypertension. This finding were not in line with the study findings conducted by Amin, et al., [20] where 6(20.0%) of patients had no history of hypertension. It might be due to most of the patients were from urban slum, housewife who were not aware about hypertension and due to small sample size. In study anthropometric measurements of the participants among the groups showed no significant statistical difference. Among them BMI in group- 1(21.09), group -2 (20.42%)

and group – 3 (20.66%). Nevin, et al., [29] demonstrated that frequency of overweight in men & women was found to be 13.3% & 6.6% respectively. In the current study total cholesterol was 205±35.08 mg/dl in group 1 & 215±40.98 mg/dl in group 2 and 196±30.59mg/dl in controls. Numerous studies have shown an association of serum cholesterol with diabetic complications. Rema, et al., [31] reported mean serum cholesterol level in diabetic group was 262±11.39 mg/dl and in control group was 174±7.87mg/dl. That is serum cholesterol level was higher in IGT & DM group than that of normal people. The concentration of TG in the current study was 253±71.76 mg/dl in group 1, 250 ± 65.1mg/dl in group 2and 226 ± 62.59mg/dl in controls. Which is supported by the studies done by Kareem, et al.,[32] and Reema, et al., [31] found significantly higher TG concentration in cases (174 ± 7.87 mg/dl) than in controls group (151 ± 10.86 mg/dl). In the current study LDL- C level was 127 ± 33.03 mg/dl and 125 ± 32.03mg/dl in group 1 & 2 and 124.58 ± 35.97mg/dl in control. Here, there was no significant difference in LDL- C concentration between cases and controls. This findings of no significant difference in LDL- C concentration between the groups is similar with that of [30]. Regarding the concentration of HDL - C this study found significantly lower level in cases (36.86±10.42mg/dl & 35.85±9.86 mg/dl than controls (39.85±9.80mg/dl). This finding differs with that of Nayak, et al., [32] and Rema, et al., [31]. This conflicting findings regarding different components of lipid profile may be due to different dietary habit, life style and ethnicity of our study subjects than of the studies done abroad. In the present study, patients with DM and IGT presented significantly higher levels of Hcy than subjects with normoglycemic people. Serum Hcy level in group 1 -19.86 ± 5.20 µmol/L & group 2 - 17.28 ± 5.38 µmol/L and in comparison group 3 - 8.72 ± 2.96 µmol/L. Present study showed that mean values of the Serum Homocysteine levels were considerably lower in normoglycemic group. Patients with type II DM & IGT, have higher homocysteine levels, which differ considerably to show statistically significant difference. Numerous studies have shown altered serum Hcy concentrations in T2DM & IGT patients. The outcome of earlier studies are variable but many of them have shown increased serum Hcy levels in T2DM & IGT patients [33, 34].

VII CONCLUSION

Present study concluded that serum homocysteine levels are elevated in type 2 diabetic and prediabetic individuals. A significant positive correlation between serum Hcy with Fasting plasma glucose & Two-hour plasma glucose were observed in our study. We know that the association between hyperhomocysteinemia and increased rate of coronary heart disease, stroke events is significant in the diabetic patients. Therefore, it can be concluded that serum homocysteine can be used as a predictor for cardiovascular risk events in T2DM patients and prediabetic patients.

VIII LIMITATIONS OF THE STUDY

1) Sample size was small.
2)This research was a single-center study. So, this will not reflect the overall picture of the country.
3) The cross-sectional design of the present study does not allow us to determine the existence of a causal relationship.
4) This study did not estimate insulin resistance.
5) Sample were taken by purposive method in which question of personal biasness might arise.

IX RECOMMENDATIONS

- Further larger study may be done to get the conclusive result of the study findings.
- As homocyteine level may be detected in IGT group, awareness and preventive measures should be taken as early as possible for reduction of fatal outcome.
- Awareness about clinical manifestation, complications, risk factors, dietary habits and preventive measures is needed.
- In resource poor settings, prevention program should be commenced on the basis of common risk factors.
- Interventional study should be conducted to determine the supplemental effect of vit 6, vit 12 and folic acid

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