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ABNORMAL LIVER FUNCTION TEST ASSOCIATED AMONGST DIABETES PATIENTS IN THE DHAKA CITY OF BANGLADESH.

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ABSTRACT

Objective: In recent era diabetics becomes most pathological condition worldwide. Maximum populations in both develop and developing countries suffering from diabetic. There are several diseases associated with diabetics like as kidney, liver, heart diseases etc. **Methods:** In this study, retrospectively study conducted at BUSB. Then data were entered into computer and results were calculated with the help of Microsoft Excel. **Results:** In the study, it has been found that the percentage of female is found to be 53% with diabetes and the percentage of male is found to be 46%.The level of Serum glutamic pyruvic transaminase (SGPT) also called (Alanin Transaminase) is found to be relatively high amongst the diabetes patient who reflects that the liver problems are prominent amongst diabetes patients. The average value of alanine transaminase which is released from liver is found to be 47.41+2.37 IU/L. Mean level of creatnine is found to be 0.93+0.022 mL/min (Normal range: 0.4to1.2 mL/min). HbA1c is amount of glycated hemoglobin is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. The average HbA1c is found to be 10.81865 + 2.126 mmol/mol. Lipid profiles are other important parameter which is play vital role amongst the health of diabetes patients. The

mean value of cholesterol, TG, LDL, HDL is found to be 193.032353 + 5.962(mg/dl), 176.13+ 10.43 (mg/dl), 127.6262+ 4.8 (mg/dl) and 41.02381 + 1.072 (mg/dl). The most important observation of the study is that the age group of 51.48 years had the highest incidence of diabetes with liver problems. The highest number of patients consumes oral medications which is 53.043%.The average SGPT value amongst the patient is also high which 47.41UI/L. This reflects that the liver problems are prevalent in the diabetic population. **Conclusion:** Further investigation requires identifying other diseases related with abnormal liver function test or diabetic's diseases.

KEYWORDS: Diabetics, Abnormal Liver function, cholesterol, Triglyceride (TG), Low density lipoproteins in blood (LDL), High density lipoproteins in blood (HDL), Serum glutamic pyruvic transaminase (SGPT), Bangladesh.

1. BACKGROUND

The liver is the vital organ to maintain normal blood glucose concentration in postprandial as well as the fasting states. Glycogenolysis and hepatic glucose production enhances due to Loss of insulin effect on the liver. Deformity of triglyceride storage as well as lipolysis in insulin-sensitive tissue such as the liver are an early manifestation of conditions characterized by insulin resistance and are detectable earlier than fasting hyperglycemia. The precise Metabolic factors, environmental, genetic, and sequence of events that lead to the underlying insulin resistance, however, is not fully understood.[1] Previous animal model demonstrated, chronic hyperinsulinaemia to predispose the liver to relative resistance to insulin. This is distinguishing by a failure of insulin to signal an increase in insulin receptor substrate-2. Lipogenesis also enhances due to up regulation of sterol regulatory element-binding protein 1c (SREBP-1c).[2] In spite of up-regulation of SREBP-1c and subsequent simulation of de novo lipogenesis in the liver leads to increased intracellular availability of triglycerides, promoting fatty liver and down regulation of the insulin receptor substrate-2–mediated insulin signaling pathway in insulin-resistant states. This also increases VLDL assembly and secretion.[1] Accordingly, hyperinsulinaemia might directly lead to hepatic insulin resistance with associated fatty changes. The excess in free fatty acids found in the insulin-resistant state is known to be directly toxic to hepatocytes.

Presumed mechanisms comprise toxin formation, mitochondrial dysfunction and cell membrane disruption at high concentration, activation and inhibition of key steps in the regulation of metabolism.[3] Supplementary potential explanation for eminent transaminases

in Insulin-resistant states includes recruited inflammatory cells and oxidant stress from reactive lipid peroxidation, peroxisomal beta-oxidation. An increase in pro-inflammatory cytokines such as tumor necrosis factor- α (TNF- α), which may also contribute to hepatocellular injury by insulin-resistant state. In preliminary studies suggested that, a possible genetic link or predisposition to fatty liver found in insulin-resistant statesan increased frequency of specific TNF-α–promoter polymorphism was found in nonalcoholic steatohepatitis (NASH) patients.[4] The above theories all attribute elevated transaminitis to direct hepatocyte damage. It is also hypothesized that, a gluconeogenic enzyme (elevation in ALT) whose gene transcription is suppressed by insulin, could indicate impairment in insulin signaling rather than merely hepatocyte damage.[5] Chronic liver disease (CLD) is very common in the general U.S. residents and includes 2% of adult Americans (5.3 million) infected with hepatitis B or C1and an predictable 31% or more with non-alcoholic fatty liver ailment (NAFLD).[6,7]

The population of Americans with CLD continues to expand because of the epidemics of obesity and diabetes. In some subpopulations such as the morbidly obese, the prevalence of NAFLD is as high as 88%.[8]

The alliance of NAFLD with concurrent diabetes increases general deaths.[9] Chronic liver diseases another important cause by alcohol abuse.[10,11] Genetic conditions such as cystic fibrosis, hemochromatosis (HC), and sclerosing cholangitis are less recurrent causes of CLD. Their pervasiveness is population based; the homozygous state prevalence is 0.6–1% in whites, for HC.[12] Persons with HC have an odds percentage for diabetes as high as 5.4 contrasts to control subjects.[13] CLD has significant limitations like as fructosamine (FA) testing orassessing glucose control using A1C. These confines must be clearly implicit to avoid misinterpretation of the consequences. Sequencing these tests should sometimes be avoided altogether in patients with a high likelihood of falsely low outcome affiliation between CLD and Diabetes. The incidence of CLD is coupled with significant impairment in glucose homeostasis. Patients with CLD and frank diabetes is present in 30–60% and 80% have Glucose intolerance respectively.[14,15]

Based on its etiology, CLD has a significant impact on hepatic glucose metabolismwhich is one of the common causes of CLD is chronic hepatitis C. Multiple mechanisms have been implicated, including fat accumulation in hepatocytes, increased insulin resistance secondary to increased tumor necrosis factor (TNF)-α, and direct or autoimmune damage to β-cells by

the virus. Chronic hepatitis C is accompanied by insulin resistance, which causes by impaired glucose tolerance.[16] In a previous study of 229 Japanese patients with hepatitis C (27.6% of whom had cirrhosis and 8.9% had chronic active hepatitis), 17.5% had diabetes compared to 5.3% in the control inhabitants. Their average BMI was normal at 22.4 kg/m2, and only 10% of the patients had a family narration of diabetes compared to 40% of control patients with diabetes patients.[17] Different hepatitis C virus (HCV) genotypes seem to have different potential for interfering with glucose metabolism. In vitro studies reveal that genotype 1 and 3 HCV interfere with insulin signaling.[18] Clinically, in nonobese, nondiabetic adults infected with genotype 1 or 2 HCV, insulin resistance correlated significantly with the viral load and was independent of patients' visceral adipose tissue area as measured by abdominal computed tomography scan.[19]

In patients with genotype 1 HCV, sustained responders to interferon-ribavirin therapy showed a significant decrease in insulin resistance compared to the baseline insulin resistance index. Also, the incidence of overt diabetes was reported to be lower in cured patients than in nonresponders to antiviral therapy.[20,21]

However, other studies did not find similar beneficial effects of long-term viral clearance.[22] The presence of diabetes is accompanied by poor response to antiviral medications; in a recent study, only 23% of patients with both of hepatitis C and diabetes achieved sustained viral response to pegylated interferon and ribavirin combination therapy compared to 46% of patients with hepatitis C but no diabetes. Patients with concurrent diabetes also reported more side effects to therapy.[23,24,25,26] In contrast, no clear relationship between insulin resistance or diabetes and infection was seen with hepatitis B virus infection.

On the development of diabetes in a prospective study of defined Bangladeshi populations, taking account comprehensive risk factors, including fasting blood sugar, total bilirubin, total protein, albumin, globulin and BMI. The present study was aimed to evaluate the liver function variables in diabetic patients compared to non-diabetic patients.

2. MATERIALS AND METHODS

2.1. Type of study

This was a cross sectional observational study that was attempted to find out for the treatment of diabetes and to determine the impact of different other risk factors on liver disease and associated diabetes.

2.2. Place of study

The study was conducted in National University of Health Sciences (BUHS). BUHS (formally starting academic courses in public health and technology disciplines under Dhaka University since 2007) became the Apex Hospital of the 20 hospitals/health centres under the HCDP Network in around Dhaka and in North-Western Bangladesh and, within few years; it could create substantial reputation in academic and research areas. As a result, BIHS started to attract Grants from Organizations like University of Oslo (Norway), Rockefeller Foundation (USA) and World Diabetes Foundation (Denmark) to sponsor various academic and development Projects. In addition to local students BUHS was able to attract foreign postgraduate students from Nepal, Pakistan and India.

2.3. Study Population

All patients of diabetes are diagnosed by the hospital physicians.

· Patients of diagnosed diabetes ages 18- 80 years.

· Both sexes irrespective of occupation and social class.

· Patients of diabetes including patients with liver problems

· Post and pre- operative patients

2.4. Sample size

Sample size was 115.

2.5. Sampling Technique

In this retrospective study, pre–tested questionnaire sampling technique was followed.

2.6. Research Approach

After getting the approval of the research proposal from the honorable faculty members, formal permission was obtained from the competent authorities of BUHS. The data were collected from the wards and **outpatient department** of BUHS hospital.

2.7. Research Equipments

The following equipments were used in this study

· Interview schedule checked in diabetes books

· Prescription

· Diagnosis report

2.8. Data collection method

After explaining the purpose of the study to the respondents and obtaining their verbal consent, the researcher interviewed all the respondents by asking questions in Bengali and using a thoroughly pre–tested questionnaire. The questionnaire consisted of three parts. Part - 1 consisted of the respondent's general information, Part-2 consisted of behavioral characteristics and Part-3 consisted of information on diabetes and liver function tests parameters.

2.9. Blood sugar Recording

Recording of blood sugar was done on the requirement of the patients by the physicians in the hospital. From the book of diabetes, blood sugar of individual patient was collected.

2.10. Diagnosis of diabetes patients

This study was performed on 115 patients of diabetes in the outpatient department of BUHS for treatment and irrespective of age and sex. All patients of diabetes including liver problems were included in the study. Patients were diagnosed on the basis of following criteria: one of the Biochemical tests of the patients, another one is Physical characteristics of the patients.

2.11. Study period

Study period was four months commencing from September 2014 to December 2014. To complete the study in time, a work schedule was prepared depending on different tasks of the study. Four months were spent on board meeting for literature review, selection of topic, development of the protocol. Subsequent months were spent on official correspondence, data collection, data analysis, report writing and submission of report.

2.12. Data analysis: All the data were checked after collection. Then data were entered into computer and results were calculated with the help of Microsoft Excel. The results were shown in column, cylinder, bar and pie chart.

To find out the impact of risk factors of diabetes and the liver function tests that are commonly used for the treatment of diabetes and liver problems, this study was performed in National University of health sciences (BUHS) & the data were collected from the outpatient department patients with diabetes. A total of 115 patients were included in the study. Among them 52 were male and 48 were female.

3. RESULTS AND DISCUSSIONS

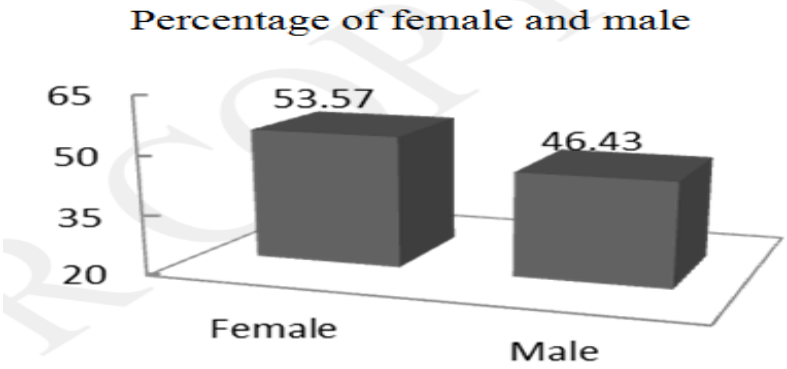

Fig-1. Distribution of diabetes according to patients Sex where as female 53.57% and male 46.43% suffering liver and diabetics diseases. X axis demonstrated percentages of patients.

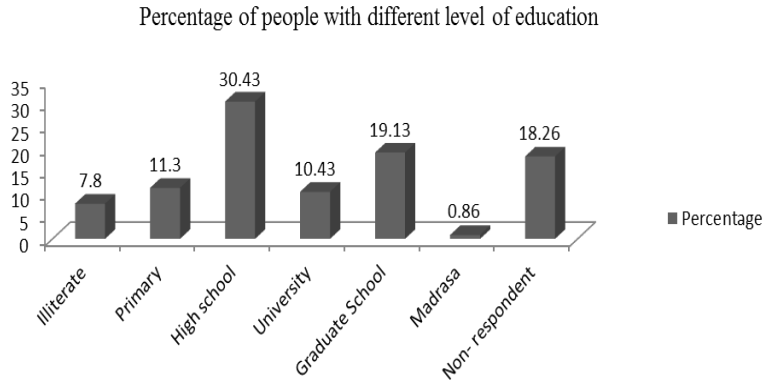

Fig-2. Distribution of diabetes and liver function tests according to level of education. High school level patients are prominent to diabetics and liver diseases 30.43 %, graduate school patients 19.13% are moderately prominent.

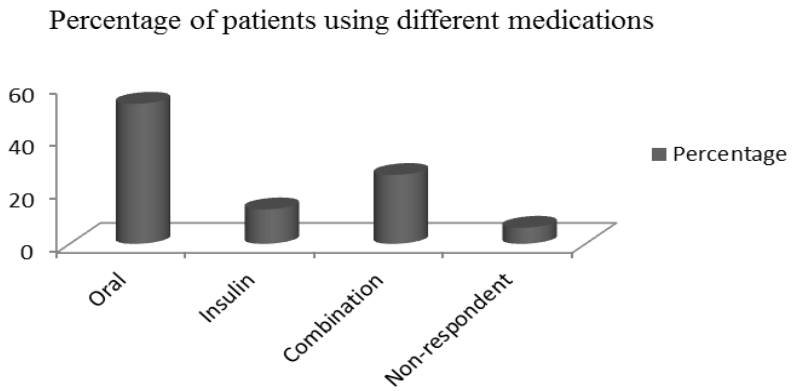

Fig-3. Distribution of diabetes and liver function tests according to type of medication intake for the treatment of diabetics and liver diseases. X axis demonstrated percentages of patients. Y axis demonstrated types of medication uses of patients.

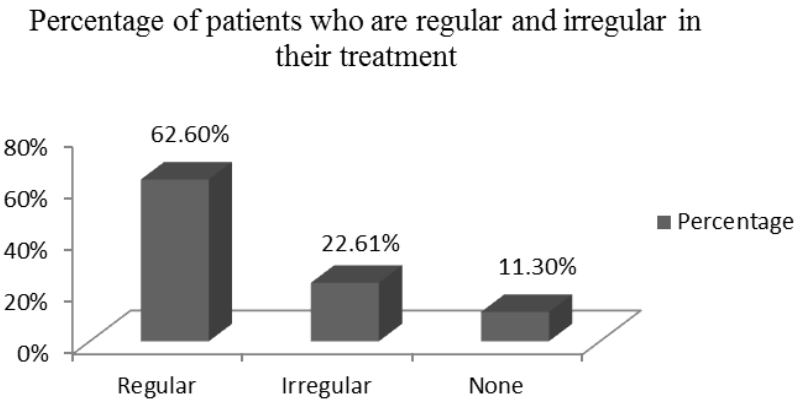

Fig-4. Distribution of diabetes and liver function tests according to regularity of patients in their treatment. Most of the patients take regular treatment 62.60% where as 22.61% patients do not take regular treatments. X axis demonstrated percentages of patients. Y axis demonstrated types of treatment types of patients.

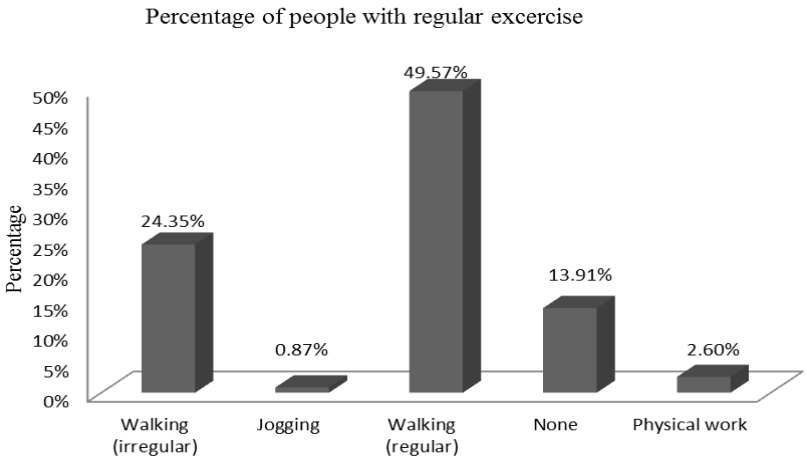

Fig-5. Distribution of diabetes and liver function tests according to habit of regular exercise. Moderate irregular working 24.35%, highest regular working 49.57%, jogging 0.87%, none 13.91% and physical work 2.60%. X axis demonstrated percentages of patients. Y axis demonstrated types of exercise uses of patients.

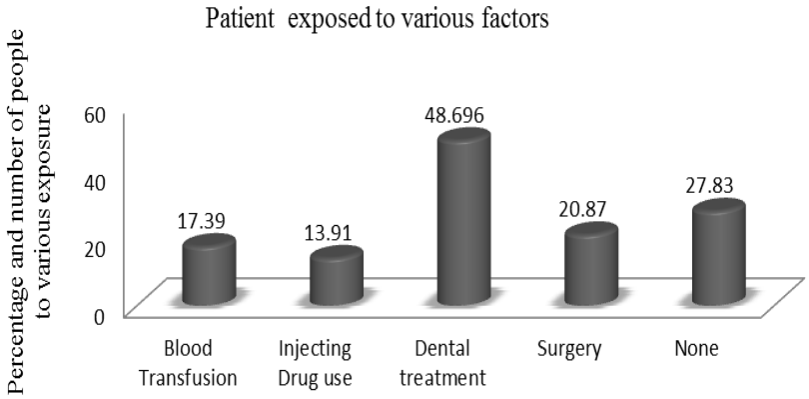

Fig-6. Distribution of diabetes and liver function tests according to patient exposure like as blood transfusion, injecting drug use, dental treatment, surgery, and none (do not take such kind treatment). X axis demonstrated percentages of patients. Y axis demonstrated exposure factor of patients like as blood transfusion, injecting drug use, dental treatment, surgery.

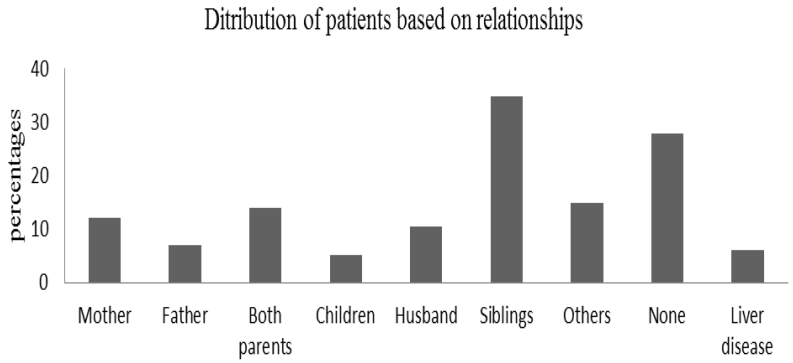

Fig-7. Distribution of diabetes and liver function tests according to relatives with diabetes. Most of the patient's siblings 34.74% suffering both diabetics and liver diseases among related with other relationship.

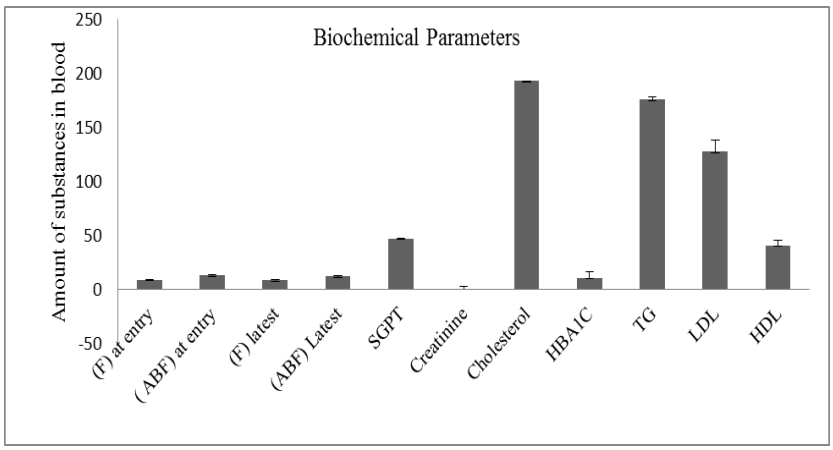

Fig-8. All biochemistry parameters obtained from the biochemical report of the patients

(F) At entry- fasting sugar at the beginning of treatment/ 2 years before (mmol/L); (ABF) at entry- sugar after 2 hours of intake of food at the beginning/ 2 years before (mmol/L); (F) latest- The latest value of fasting sugar (mmol/L); (ABF) latest- The latest value of sugar level after 2 hours of food intake (mmol/L); SGPT also called alanine aminotransferase (ALT). (UI/L); Creatinine- Level of creatinine in blood; Cholesterol-(mg/dl); HBA1C- Glycated Heamoglobin; TG- (mg/dl); LDL- (mg/dl); HDL- (mg/dl).

Type 2 diabetes patients have been reported to be associated with higher incidence of abnormal liver function tests (LFT) compared to the individuals without diabetes, elevated ALT being the most common abnormality.[27]

To find out the impact of risk factors amongst diabetes and the problems in liver, this study was performed in BUHS and the data were collected from the outpatients department with diabetes irrespective of sex, occupation and economic class. Patient's personal information and diagnostic report for example, blood sugar and SGPT level and other diagnosis profile were also collected. They were interviewed by asking question in Bengali, using a thoroughly preplanned questionnaire.

The male and female ratio amongst the diabetes patients demonstrates important information regarding the susceptibility of certain gender over another. In the study, it has been found that the percentage of female is found to be approximately 54% with diabetes and the percentage of male is found to be 46% mentioned in figure-1. This shows that the females are more susceptible to diabetes and liver problems rather than males in overall population. Then again, the number of female patients interviewed may be more then the males and therefore, the data may not represent the real picture of the whole population. Diabetes is a chronic condition and diabetes-related complications like diabetic neuropathy, nephropathy, retinopathy and diabetic foot ulcer are now alarming public health issues.[28]

The level of education amongst patients shows a fascinating pattern with liver and diabetes problems. The prevalence of patients with diabetes and liver problems are most frequently seen amongst the patients who has been educated till high school which is approximately 30%. There is a decrease in the percentage of patients who has been educated up to university, which is only approximately 10% shown in figure-2. This is probably because university students are more health conscious and therefore, their health conditions are more improved. The number of patients with graduation education level is seen to be

approximately 19 % which is again relatively high in amount. The least number of patients is seen with education level of Madrasa, illiterate and primary level which are approximately 0.86%, 7.8% and 11.3%. The number of non respondents is found to be 18 %. The most important observation of the study is that the age group of approximately 51 years had the highest incidence of diabetes with liver problems. The age at which the diabetes is diagnosed most frequently is approximately 46 years. Considering Bangladesh perspective, middle aged group people mostly suffered from diabetes. But elderly people are also affected in a significant percentage. It is seen that the metabolic dysfunction increases around this age and therefore, diabetes is seen prevalent.

The type of medication used by the patients reflects a lot more about the types of diabetes which is more prevalent in the population mentioned in figure-3. The highest number of patients consumes oral medications which is approximately 53%. Whereas, the combination drugs were consumed by diabetic populations were approximately 26%. The numbers of patients who are taking insulin only are approximately 13 %. In the study, the number of non respondents is found to be approximately 6% which is the group from whom the data were not possible to collect for various reasons.

In the study, it has been noticed that the diabetic patients are more concern regarding the health. The percentages of patients who are regular in their treatment are approximately 63%. The percentage of population with irregular and non- complaint is approximately 23 %. There is population of approximately 11% only who is not at all concerned about their health and has shown irregularity in their treatment mentioned in figure-4.

Diabetes patients are more concerned about physical exercises with habit of regular walking amongst approximately 49.57% where as habit of irregular walking is seen amongst approximately 24 %. But in the population of Bangladesh, habit of other exercise is very rare for example, jogging comprise only 0.87% of overall population. There is also approximately 14% of population who has no habit of physical exercise. There is only 2.60% of population who is involved in regular physical activity but has diabetes mentioned in figure-5.

The study aimed to determine that whether external factors such as surgery, dental treatment, injecting drug use and blood transfusion as any effect over the population. It was seen that the external factor such as dental treatment is most prominent amongst patients with highest percentage of approximately 48.7%.The other external exposures such as blood transfusions,

injecting drug use and surgery has shown 17.39%, 13.91%, 20.87 % amongst the patients mentioned in figure-6. Only approximately 28% showed no such exposure In order to assess the prevalence of diabetes and liver problems amongst the patients, they were asked regarding their family members and their previous history of diabetes mentioned in the figure-7. It is visible that the generation of middle aged people is more effected by diabetes rather than previous generations. In approximately 7%% of population, father had diabetes, where as in 12% population, mother had diabetes in their family. Approximately 14% of population had diabetes in both of their parents. But diabetes amongst siblings is highest with percentage of 34.78%. Liver disease is seen amongst approximately 6% of the family members of diabetic patients. Oral therapy is indicated in any patients in whom diet and exercise fail to achieve acceptable glycemic control. Although initial response may be good, oral hypoglycemic drugs may lose their effectiveness in a significant percentage of patients. The drug category includes sulfonylurea, biguanide, alpha-glucosidase inhibitor, thiazolidinedione, and meglitinide. These drugs have various side effects such as sulfonylurea causes weight gain due to hyperinsulenemia[29,30] biguanide cause weakness, fatigue, lactic acidosis, alpha glucosidase inhibitor may cause diarrhea while thiazolidinediones may increase LDL-cholesterol level.[31]

Insulin is usually added to an oral agent when glycemic control is suboptimal at maximal dose of oral medication. Weight gain and hypoglycemia are common side effect of insulin.[32-34] Vigorous insulin treatment may also carry an increase in atherogenesis.[33]

The average fasting sugar amongst patients is seen to be 8.978 +0.54 mmol/L (Normal range value: 3.9 to 7.2 mmol/L) at the beginning of their treatment and during the treatment the fasting sugar is 8.4623 + 0.258mmol/L which is relatively low. The sugar level after 2 hours of intake of food at entry is 13.146 +0.847 mmol/L where as the average blood sugar after 2 hours is 12.276 + 0.391 mmol/L which is also relatively less than previous values mentioned in figure-8. The level of SGPT (Alanine Transaminase) is found to be relatively high amongst the diabetes patient who reflects that the liver problems are prominent amongst diabetes patients. The average value of alanine transaminase which is released from liver is found to be 47.41+2.37 IU/L where as reference ranges; female: ≤ 34 IU/L and male; ≤ 52 IU/L. Mean level of creatnine is found to be 0.9283+0.022 mL/min (Normal range: 0.4 - 1.2 mL/min). Diabetes is continuously given blood tests for checking of creatinine level. HbA1c is amount of glycated hemoglobin is a form of hemoglobin that is measured primarily to identify the

average plasma glucose concentration over prolonged periods of time. The average HbA1c is found to be 10.81865 + 2.126 mmol/mol. Lipid profiles are other important parameters which are play very role amongst the health of diabetes patients. The mean value with SEM of cholesterol, TG, LDL, HDL is found to be 193.032353 + 5.962(mg/dl), 176.13+ 10.43 (mg/dl), 127.6262+ 4.8 (mg/dl), and 41.02381 + 1.072 (mg/dl).The mean value of HbA1c is comparatively high amongst the patients which reflect that there is high level of sugar in blood. As the glycated hemoglobin is high, the sugar is uncontrolled amongst the patients. Moreover, the level of TG is also relative high over the normal value (50-150 mg/dl). The average SGPT value amongst the patient is also high which 47.41UI/L shown in the figure-8. Diabetes is associated with both microvascular and macrovascular diseases affecting numerous organs, including skeletal muscle, skin, heart, brain and kidneys. Common pathogenic mechanisms link the different types of diabetes-associated vascular disease (such as CVD and PAD). Common risk factors for vascular disease in diabetes include hyperglycemia, insulin resistance, dyslipidemia, hypertension, tobacco use, and obesity. Mechanisms for microvascular disease in diabetes include the pathologic effects of AGE accumulation, overproduction of endothelial growth factors, and abnormal stimulation of the PKC and polyol pathways and the RAS. Mechanisms for macrovascular disease in diabetes include the pathologic effects of AGE accumulation, impaired vasodilatory response attributable to NO inhibition, smooth muscle cell dysfunction, overproduction of endothelial growth factors, chronic inflammation, hemodynamic dysregulation, impaired fibrinolytic ability, and enhanced platelet aggregation (clotting).[35]

CONCLUSION

This reflects that the liver problems are prevalent in the diabetic population. Female's diabetic's patients are more venerable to abnormal liver function then male patients. Further investigation requires identifying other diseases related with abnormal liver function test or diabetic's diseases.

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