ORIGINAL ARTICLE

# Role of Flash Glucose Monitoring System in Diabetic Patients with Chronic Liver Disease

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## ABSTRACT

**Background:** Diabetic patients show serious complications of chronic liver disease. The monitoring of glucose in diabetic patients with chronic liver disease is very challenging. Generally, the glycaemic control monitoring in chronic liver disease patients is the same as in a person who does not have any liver disease. Flash glucose monitoring system is a way to measure glucose levels of body without pricking the body. It is an innovative method of measuring glucose levels. A flash glucose monitor is a small sensor. This sensor is a small sticky chip and is attached on the skin of the arm. One side of the chip has a small needle that goes inside the skin. It records glucose levels throughout day and night continuously. Levels of glucose can be assessed whenever wanted.

**Materials and Methods:** The study was conducted in the Medical Ward 1, Bahawal Victoria Hospital, Bahawalpur and the Department of Pathology, Quaid-e-Azam Medical College, Bahawalpur from 1st January 2018 to June 2020. Freestyle Libre Sensor flash glucose monitoring system (by CoolPlus Medical) was used to measure glucose of subcutaneous interstitial fluid. The disposable sensor was applied to the back of the arm for up to 14 days. Sensor is calibrated by the factory with no automatic alarms.

**Results:** We noticed that the results of the patients who had co-existing disease of chronic hepatitis and diabetes mellitus had same results of glucose readings when measured by flash glucose monitoring system and by finger prick for glucose measurement by glucometer.

**Conclusion:** Flash glucose monitoring system is way better than self monitoring blood glucose method by glucometer in diabetic patients with chronic liver disease.

**Keywords:** Diabetes, glucose, monitoring, chronic liver disease, complications

## INTRODUCTION

A better type of continuous glucose monitoring is flash glucose monitoring system and it is with a recognized effectiveness on glycemic control. Diabetes Mellitus is a known public health problem throughout the world. Diabetes mellitus is a significant cause of mortality and morbidity globally. It is now well established that there is a direct relation between diabetes mellitus / impaired glucose tolerance and chronic liver disease. Liver plays an important role in carbohydrate metabolism so diabetes mellitus is common in patients with chronic liver disease.

The prevalence of diabetes mellitus in chronic liver disease ranges widely in different studies of different countries (1). In fact, diabetic patients show serious complications of chronic liver disease. The monitoring of glucose in diabetic patients with chronic liver disease is very challenging. Generally, the glycaemic control monitoring in chronic liver disease patients is the same as in a person who does not have any liver disease.

Flash glucose monitoring system is a way to measure glucose levels of body without pricking the body. It is a new trending method of measuring glucose levels. A flash glucose monitor is a small sensor. This sensor is a small sticky chip and is attached on the skin of the arm. One side of the chip has a small needle that goes inside the skin (2). It records glucose levels throughout day and night continuously. Levels of glucose can be assessed whenever wanted. This sensor measures the glucose in the interstitial fluid. Each time the sensor is scanned, access to

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the last 8 hours glucose levels and trends can be known. Trends of glucose rise and drop can be easily known without frequent finger pricks. Generally a sensor is used for two weeks and has to be replaced by a new sensor. Sensors are usually worn on arms. As there is more information about the sugar levels going up and down, so target ranges can be achieved more easily. It has the ability of monitoring the levels of glucose when the patient is fast asleep (3). Glycated hemoglobin is done as a routine test in these diabetics to have an idea of long term glucose control.

The dynamics of blood glucose has scarcely been studied in patients with chronic liver disease so we carried out this study. Frequent fluctuations, especially, post prandial hyperglycemia and episodes of hypoglycemia during sleep can be very dangerous (4) .These events cannot be detected by standard tools of glucose measurements in patients with chronic liver disease. So, the option of using flash glucose monitoring system is suitable in the patients of chronic liver disease (5).

## MATERIALS AND METHODS

The study was conducted in the Medical Ward 1, Bahawal Victoria Hospital, Bahawalpur and the Department of Pathology, Quaid-e-Azam Medical College, Bahawalpur from 1st January 2018 to June 2020. Verbal consent was taken from all study subjects. The Ethical committee of the college approved the study and the study expenses were borne by the researchers.

It was a prospective, case-control and single-center study.

Eighty patients (Males: 65 and Females: 15) aged thirty years to seventy two years (mean ± 40) having chronic liver disease along with diabetes mellitus were enrolled in the study. Patients having hepatitis for more than six months were considered to have chronic liver disease. Abnormal liver function tests (LFT) were defined as following: bilirubin > 1mgdl, alanine trasaminase (ALT) > 40 U/l; Albumin < 3mgdl. Patients with glycated haemoglobin more than 6.5% were considered to be diabetics. All patients having a history of cognitive state abnormalities, chronic pancreatitis, malignant tumor, congestive cardiac failure, chronic kidney failure, Mycobacterium tuberculosis, Human Immunodeficiency Virus infection or on steroid intervention were excluded from the study. Ten diabetic patients without chronic liver disease were also studied as controls. Chronic liver disease was excluded using biochemical tests and sonology. All study subjects underwent laboratory tests which were done on blood. These tests included: ALT, AST, bilirubin, gamma GT, Alpha feto proteins, albumin, globulins, glycated hemoglobin and blood complete examination. Radiographic imaging was done to evaluate the degree of chronic liver disease

Freestyle Libre Sensor flash glucose monitoring system (by CoolPlus Medical) was used to measure glucose of subcutaneous interstitial fluid. The disposable sensor was applied to the back of the arm for up to 14 days.

Sensor is calibrated by the factory with no automatic alarms. According to manufacturer's guide, when reader is brought near the sensor, all the information is transferred and the glucose level is indicated. The sensor has got an application to store all the data and the glucose levels are automatically shows all the previous dates glucose via the device.

Patients were asked to use glucometers to check capillary blood glucose. They were advised to take fasting blood glucose sample, then take sample two hours after breakfast, two hours after lunch and two hours after dinner. They were asked to note down the glucose values on a register. Then the readings of the flash glucose monitoring system by the scanner were matched with the readings of glucometer. This was repeated daily for 14 days. The chip was examined daily, so that if it is misplaced or moved, it can be fixed. For the next 14 days, a new sticking chip was applied. After one month the readings of glucometer and that of flash glucose monitoring system were matched.

Biochemical investigations advised to various patients were performed on AU680 Beckman Coulter which is a fully automated Chemistry analyser. Tumor markers as Alpha feto proteins and CEA were done on ABBOTT Architect 1000 I which is chemiluminiscence based fully automated hormone analyzer.

Screening tests, ELISA and PCR were performed for Hepatitis B and C. For the confirmation of Hepatitis B and C antigen ELISA was performed on fully automated ELISA Reader, ADC ELISA 200. Further confirmation of hepatitis B and C were done by PCR on Gene Xpert. Those patients who had detectable copies of hepatitis C vius were further tested for genotype on GeneXpert PCR.

Complete urine examination was done using dry strips. Proteinuria was confirmed on 24 hour urinary collection by quantitative estimation on AU680 Beckman Coulter by pyrogylol method.

Statistical analysis was performed using SPSS software.

## RESULTS

In our study we found out that the majority of the study subjects were male. The demographic distribution of study subjects is shown in Table.1.

Table 1: Epidemiological parameters of study subjects (n=90)

| Gender | Mean Age ( years) |
|---|---|
| Male Patients ( n=65) | 51 |
| Female Patients (n=15) | 39 |
| Male Controls (n=7) | 41 |
| Females Controls (n=3) | 32 |

Table 2: Results of Liver Function Tests (LFTs) of study subjects

| Liver Diseases | ALT (U\L) Mean (± SD) | Bilirubin (mg\dl) Mean (± SD) | Albumin (G\dl) Mean (± SD) |
|---|---|---|---|
| Hepatitis B | 930 ± 25.1 | 6 ± 1.2 | 4.6 ± 2.1 |
| Hepatitis C | 820 ± 11.4 | 8 ± 2.2 | 3.5 ± 2.1 |
| Steatohepatitis | 84 ± 7.1 | 7 ± 3.4 | 4.5 ± 2.1 |
| Cirrhosis | 70 ± 8.2 | 5 ± 1.2 | 3.3 ± 2.1 |
| Hepatoma | 60 ± 23.1 | 4 ± 1.3 | 2.1 ± 2.1 |
| Non-alcoholic fatty liver disease | 30 ± 2.1 | 11 ± 1.1 | 4 ± 2.1 |
| Hemochromatosis | 90 ± 1.7 | 4 ± 2.1 | 4.5 ± 2.1 |

We noticed that the results of the patients who had co-existing disease of chronic hepatitis and diabetes mellitus had same results of glucose readings when measured by flash glucose monitoring system and by finger prick for glucose measurement by glucometer . There was no statistical difference (p < 0.001). Almost all of the patients including the controls said that they found the flash glucose monitoring system more easy. They unanimously stated that it was difficult and cumbersome for them to prick four times a day. This diagnostic method for monitoring glucose by glucometer was found unpleasant due to the fear of hyperglycemia or episodes of hypoglycemia during sleep. Especially, the females were more satisfied with the novel method of flash glucose monitoring system for managing the treatment modalities. All the patients were checked daily to see the scanner in place (on the back side of the arm) and compared the four readings of the day. One of the patients was found to have a displaced needle of the sticky chip, which was fixed immediately. After 14 days the chip was changed. Sixty five percent of the cases were suffering from anxiety due to uncontrolled diabetes which could lead to complications of chronic hepatitis. Almost all (99%) females including the controls were phobic of needle prick four times a day to monitor glucose control. These women seemed relaxed when they were informed about the fact that they will need not to be pricked

frequently. The study revealed that there is no statistical difference between the blood glucose levels of capillaries by glucometer and the glucose of interstitial fluid by flash glucose monitoring system (p<0.001). It was also found out in our study that there was no difference in results of patients with varying degrees of chronic liver disease Table 2. We found out that that the patients were sick and wanted an easy and less painful way of controlling diabetes mellitus. This study led to the possible control of diabetes mellitus because the patients were out of anxiety and phobias during the study and were keenly observed and advised. All co-operated well. Their meticulous control of glucose was further confirmed by glycated hemoglobin after 120 days. All of our patients and controls had a meticulous control of diabetes mellitus.

## DISCUSSION

Chronic liver disease and Diabetes mellitus are two common diseases which can have drastic effects on the quality of life. Studies have shown that combination of these two diseases can lead to complications and lesser survival of patient. Picardi in his research work found out and stated that it has been evident that many diabetic patients with co-existence of both diseases have psychological problems that usually are not noticed and, finally, are either not treated or poorly treated (6). These poor management strategies can possibly save patients from upgrading their individual care in terms of getting many self care jobs and reaching good plasma glucose level. This clinical importance of finding out and managing hepatogenous diabetes-linked psychological depression and its outcomes has an accomplished health hazard is emphasized by only knowing that hepatogenous diabetes lies among the important factors that are the cause towards both depression and distress in a high prevalence of patients who suffer from this disease (7). Diabetes has been debated in different ways, and many steps to deal with it are being practiced these days. Clear view in its management is an important tool from both the diagnostic and clinical perspectives (1).

Prevalence of diabetes mellitus in chronic liver disease has been estimated to be approximately 12-57% (8). However, the prevalence of impaired glucose tolerance in patients of chronic liver disease has been estimated to be 30-80% (8,9).

This is because of the fact that liver plays an important role in the metabolism of carbohydrates.

Patients who have cirrhosis and develop diabetes are called hepatogenous diabetes. Hepatogenous diabetes can be easily diagnosed because it does have a family history (10). There is insulin resistance in liver, adipose tissue and muscles in patients with chronic liver disease so the patient gets diabetes mellitus. Peripherally there is hyperinsulinemia because of insulin resistance. The etiology of chronic liver disease plays an important role in the development of diabetes mellitus. There is also affect of genetic and environmental factors. Diabetes mellitus is also associated with raised alanine transaminase enzyme. The pathophysiology of diabetes mellitus in chronic liver disease largely revolves around insulin resistance in liver. Hepatitis C viral hepatitis and hemochromatosis, more commonly, have been proved to result in hematogenous

diabetes. There is very little data available in Pakistan on the subject of diabetes mellitus and chronic liver disease. In various studies there is mounting evidence of increased risk of hepatocellular carcinoma in patients with type 2 diabetes. It has been studied that by a meticulous control of glucose the incidence of complications in cirrhotic patients is lessened. Kishimoto's study revealed that no doubt, the results of scientific research on hepatogenous diabetes in patients with type 2 diabetes have not any comparison with those from latest researches in which the patients have type 1 diabetes, who exhibit very different disease-related problems and issues (11). Adult patients with type 1 diabetes show symptoms of only fears and hypertension with anxiety and distress. Along with this depression related diabetes has double the incidence found in the general population. Especially, phobias and depression in patients with type 1 diabetes have also been related to poor plasma glucose control, which in turn has very detrimental effects on daily routine and quality of patient's life (2).

In our study it was found out that patients were more comfortable by flash glucose monitoring rather than pricking their fingers frequently. The same has been proved by another study that says that the flash glucose monitoring system is a novel method to measure blood glucose levels and prevents the pain of needle prick so is an easy and comfortable method. The novel method actually measures the glucose level of interstitium which is almost the same as the capillary blood glucose by the glucometer (4). Similar to our study another author reports that this novel method of monitoring glucose in critically ill patients is accurate and correct intervention is possible and is also simple to perform (3,5,6).

The findings of our study are the same as of the outcomes of several earlier studies which reported that many diabetics suffer from mental stress due to the disability and difficulty in management of the treatment and fear of complications (7). The results of many studies have revealed that in order to control normal plasma glucose daily, children and adolescents with type 1 diabetes has to do a complicated self-monitoring behavior each and every day that has the completion of many day to day binding behaviors, such as routine checks for plasma glucose levels and insulin dosage, that may be meticulous and result in a variety of treatment of depression-related problems. Self-control along with mental problems is inversely related, with the main psychological problems being stress and distress. In comparison with the adults, adolescents are twice in incidence of having such psychosocial problems (8). We noticed that treatment depression among the hepatogenous diabetic patients was high at the beginning and that a noticeable decrease in this anxiety had occurred after 2 weeks of the intervention with flash glucose monitoring system (11, 12). This confirms that the flash glucose monitoring system intervention apparently decreased the treatment and diagnostic distress among the diabetic patients with chronic hepatic disease (13).

## CONCLUSION

Flash glucose monitoring system is way better than self monitoring blood glucose method by glucometer in diabetic patients with chronic liver disease.

## REFERENCES

1. Picardi A, D'Avola D, Gentilucci UV, Galati G, Fiori E, Spataro S, et al. Diabetes in chronic liver disease: from old concepts to new evidence. Diabetes Metab Res Rev. 2006; 22:274–83.
2. Kishimoto M, Noda, M. Verification of glycemic profiles using continuous glucose monitoring: cases with steroid use, liver cirrhosis, enteral nutrition, or late dumping syndrome. J Med Invest. 2015; 62:1–10.
3. Kawaguchi T, Taniguchi E, Itou M, Sakata M, Sumie S, Sata M. Insulin resistance and chronic liver disease. World J Hepatol. 2011;3:99–107.
4. Elkrief L, Rautou PE, Sarin S, Valla D, Paradis V, Moreau R. Diabetes mellitus in patients with cirrhosis: clinical implications and management. Liver Int. 2016;36:936–48.
5. Silva T, Ronsoni M, Schiavon L. Challenges in diagnosing and monitoring diabetes in patients with chronic liver diseases. Diabetes Metab Syndr.2018;12:431–40..
6. Blendea M, Thompson M, Malkani S. Diabetes and Chronic Liver Disease: Etiology and Pitfalls in Monitoring. Clin Diabetes. 2010;28:139–44.
7. Garcia-Compean D, Jáquez-Quintana J, González-González J, Lavalle-González FJ, Villarreal-Pérez JZ, Maldonado-Garza HJ. Diabetes in liver cirrhosis. Gastroenterol Hepatol. 2013;36:473–42.
8. Gundling F, Seidl H, Strassen I, Haller B, Siegmund T, Umgelter A, et al. Clinical manifestations and treatment options in patients with cirrhosis and diabetes mellitus. Digestion. 2013;87:75–84.
9. Khan R, Foster G, Chowdhury T. Managing diabetes in patients with chronic liver disease. Postgrad Med. 2012;124:130–7.
10. Nishida T. Diagnosis and Clinical Implications of Diabetes in Liver Cirrhosis: A Focus on the Oral Glucose Tolerance Test. J Endocr Soc.2017;1:886–96.
11. Lee J. Alternative biomarkers for assessing glycemic control in diabetes: fructosamine, glycated albumin, and 1,5-anhydroglucitol. Ann Pediatr Endocrinol Metab. 2015;20:74–88.
12. Ancona P, Eastwood GM, Lucchetta L, Ekinci EI, Bellomo R, Martensson J. The performance of flash glucose monitoring in critically ill patients with diabetes. Crit Care Resusc.2017;19:167–74.
13. Rodbard D. Continuous Glucose Monitoring: A Review of Recent Studies Demonstrating Improved Glycemic Outcomes. Diabetes Technol Ther. 2017;19:S25-S37.