Original Article

THE EFFECT OF LACTOSE INTOLERANCE ON PLASMA GLUCOSE LEVELS AND ASSOCIATED BIOCHEMICAL PARAMETERS

Zulfiqar Detho, Sher Ali, Furqan Ahmed Bhatti

ABSTRACT

Aim: To determine the effect of lactose intolerance on serum glucose levels and related biochemical parameters in the adult population who refrain from consuming milk and milk products.

Material and Method: This retrospective, observational study was conducted in a tertiary care hospital between January 2020 and December 2020 with 296 participants. Plasma glucose, calcium, 25-hydroxyvitamin D3, folate, vitamin B12, thyroid- stimulating hormone (TSH), and ferritin levels were controlled. Patients with positive lactose intolerance test results were accepted as the study group and negative results were accepted as the control group, and data of two groups were compared.

Results: Of the total 296 participants 212 (71.7%) were found to have lactose intolerance and 84 (28.3%) were found to be normal. In the lactose intolerant group, blood glucose levels were significantly lower than the control group (5.14±0.53 mmol/L versus 5.47±0.54 mmol/L, p<0.001). In the lactose intolerant group, 29 (13.7%) patients, and in the control group 18 (21.4%) patients were having type 2 diabetes mellitus. In diabetic patients, both fasting blood glucose (5.68±0.49 mmol/L versus 6.30±0.59 mmol/L, p<0.001) and glycated hemoglobin levels were also significantly lower than the control group in the study group (6.78±1.08 versus 7.62±0.96, p<0.001).

Conclusions: In this study, based upon the findings of people with insufficient milk consumption, any decrease in blood calcium or vitamin D levels was not observed. Lactose intolerant people may have lower blood glucose levels compared to lactase persistent people. Larger-scale and long-term studies are needed to demonstrate that persistence of lactase is an independent risk factor for the development of diabetes.

Keywords: Lactose intolerance, plasma glucose, biochemical parameters

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INTRODUCTION

Lactose is a disaccharide, found in milk and milk products, composed of simple sugars, glucose, and galactose. Lactase enzyme is needed in the degradation process. Decreasing enzyme activity during the lifetime may lead to less diabetes risk during adulthood theoretically. Enzyme activity of lactase decrease as time passes and in adulthood, the enzyme capacity decreases down to 30%. [1] Intestinal epithelial lactase enzyme deficiency causes insufficient degradation of lactose into glucose and galactose and results in lactose intolerance. [2-3] Due to flatulence and dyspepsia experienced after ingesting dairy products, many people presume that they have lactase deficiency and refrain from consuming lactose-containing foods, such as milk and milk products, although they, have no lactase enzyme deficiency. [4] According to statistical data of the year 2017, diabetes is an epidemic condition affecting 451 million people. [5] Treating diabetes is very important in many aspects of community health. The majority (over 90%) of diabetic patients are having type 2 diabetes mellitus. [6] Protective measures such as regular physical exercise and losing excess weight, and diet are key points in the treatment of type 2 diabetes mellitus. According to different trials, maltase, sucrase, and lactase enzyme activities are shown to be increased in diabetic patients and treatment of diabetes results in decreases in the activity of those enzymes. [7-8] In addition, high plasma glucose levels cause decreased intestinal motility. [9] Hyperglycemic patients have low duodenojejunal motility index and have longer intestinal transit time, which allows more time for intestinal bacteria to process available nutrients. [10-11] which may result in remarkable dyspeptic complaints in case of concomitant lactose intolerance. Milk and milk products are shown to be protective against the progression of diabetes. [12-14] People who do not have lactose intolerance but refrain from milk and milk products because of dyspeptic symptoms, are at increased risk to develop diabetes and hypertension. [15] This study was designed to observe the effects of lactose intolerance on glycemic control and related biochemical parameters, among lactose intolerance positive and negative patients refraining from milk and milk products.

METHODS AND MATERIALS

The study was carried out with the permission of the Institutional Ethics Committee. Study Setting, Design, Duration, Population This single-center, retrospective study was conducted in a tertiary care hospital, at tertiary care hospital between January 2020 to December 2020. A total of 296 patients, 176

(59.5%) female, and 120 (40.5%) male, who suffered from abdominal pain, dyspepsia, and diarrhea, were included. The ages of participants were between 18 to 77 (mean 35.61±13.9). Patients who become symptomatic after ingesting milk and milk products were tested for lactose intolerance, and positive results were accepted as the study group and negative results were accepted as the control group. Participants, who had >126 mg/dl fasting glucose, glycated hemoglobin (HbA1c) levels above % 6.5, or who were taking anti-diabetic medications were accepted to have diabetes mellitus. Plasma glucose, calcium, 25-hydroxyvitamin D3, folate, vitamin B12, thyroid- stimulating hormone (TSH), and ferritin levels were controlled in all patients included in this study. All tests were performed at the time of admission. Patients who were under 18 years, who had additional diseases other than diabetes mellitus and hypertension,

who were using other drugs other than anti-diabetics and anti-hypertensives (such as drugs for inflammatory bowel diseases, any antibiotic and probiotic usage), who had unregulated diabetes (HbA1c > 8, Type 1 diabetes mellitus or Brittle diabetes), who had hypothyroidism or hyperthyroidism were excluded.

Lactose Tolerance Test All patients enrolled in this study were tested for lactose intolerance. After 12 hours of fasting, patients ingested a solution containing 50 gr of lactose. Plasma glucose levels were checked at the beginning, 30th, 45th, 60th, and 90th minutes. An increase, lower than 20 mg/dL in plasma glucose level from the baseline, during the test, was accepted as lactose intolerance. The standard lactose tolerance test, which measures blood glucose, may be unreliable in insulin- dependent diabetics, but it can be reliable in non-insulin-dependent diabetics. Thus, standard lactose tolerance test can be used in Type 2 diabetic patients under oral anti- diabetic treatments whose blood sugar is regulated.

Statistical Analysis

All data were analyzed by the computer software program SPSS, version 20 (SPSS Inc.,Chicago, Illinois, USA, 2016). Results were reported as means standard deviation. Group analyses were made with Pearson's chi-square test. Within and between-group differences were analyzed by students paired and unpaired t-tests. A p-value <0.05 was considered statistically significant.

RESULTS

All patients were tested for lactose intolerance and 212 (71.7%) patients were found to have lactose intolerance, whereas 84 (28.3%) patients were found to be normal. There was no statistical difference between the study group and control group in age, gender, calcium, 25- hydroxyvitamin D3, folate, vitamin B12, TSH, ferritin levels, and duration of diabetes and hypertension. Both groups were distributed homogeneously according to demographic and some biochemical and hormonal levels (Table 1).

Table1.Demographiccharacteristicsandlaboratoryresultsofstudyparticipants (n=296)

	Lactose intolerance group(n=212)	**Control group(n=84)**	P value
Age	35.40±13.20	37.20±13.60	0.308
Gender(Female/Male)	133/79	43/41	0.880
Glucose (mmol/L)(4.0-6.0)	5.14±0.53	5.47±0.54	<0.001
Calcium (mmol/L)(2.12-2.62)	2.35±0.12	2.35±0.07	0.655
25-Hydroxyvitamin D3(nmol/L)(30-100)	44.68±22.96	54.66±29.20	0.227
Folate (nmol/L)(6.12-38.52)	13.63±6.14	14.55±5.90	0.589
VitaminB12(pmol/L)(160-950)	256.83±112.22	293.13±128.23	0.191
TSH* (mIU/L)(0.5-4.5)	2.10±1.10	2.40±1.30	0.251
Ferritin (pmol/L)(24-336)	147.42±113.26	190.79±152.14	0.248
Hypertension (%)	19(9.0%)	12 (14.3%)	0.255
Diabetes Mellitus (%)	29 (13.7%)	18 (21.4%)	0.001
*Thyroid stimulating hormone			

In the lactose in tolerant group, blood glucose levels were significantly lower than in the control group(5.14±0.53 mmol/L versus 5.47±0.54 mmol/L, p<0.001).Among study participants, 47 patients were having type2 diabetes mellitus. In the lactose intolerant group, 29(13.7%) patients, and in the control group 18 (21.4%) patients were having type2 diabetes mellitus. In diabetic patients, both fasting blood glucose (5.68±0.49 mmol/Lversus6.30±0.59mmol/L,p<0.001)

andglycated hemoglobin levels were also significantly lower than the control group in the study group (6.78±1.08 versus7.62±0.96, p<0.001). However, the was no significant difference in the frequency of hypertension between the lactose intolerant (9%) and control group (14.3%)(p=0.255) (Table2).

Table2.Fasting blood glucose and glycated hemoglobin levels of participants who have diabetes mellitus (n=296)

Lactose Intolerance Group(n:29)		Control Group (n:18)	P Value
Fasting blood glucose(mmol/L)	5.68±0.49	6.30±0.59	<0.001
Glycated hemoglobin(%)	6.78±1.08	7.62±0.96	<0.001

DISCUSSION

To the best of our knowledge, for the first time in literature, the results of this study demonstrate that; diabetes was less common in lactose-intolerant patients and diabetic lactose- intolerant patients had lower blood glucose and glycated hemoglobin levels compared to the diabetic participants who do not have lactose intolerance.

In this presented study, 296 patients expressed symptoms after consuming milk, and for this reason; they were refraining from consuming milk. But 84 of them (28.4%) had no lactose intolerance. This finding guided us to conclude that nearly 25% of people getting symptomatic after milk consumption were suffering from dyspeptic conditions in the absence of lactose intolerance. In this study, based upon the findings of people with insufficient milk consumption, any decrease in blood calcium or vitamin D levels was not observed. It should be taken into consideration that some of the patients examined at outpatient clinics might consume vitamin D supplements when needed. Some vitamin D supplements also contain calcium; this may be the reason that patients included in the study had no vitamin D or calcium deficiency. Some previous studies stated that higher amounts of milk consumption, especially in infants, were correlated with an increased risk of developing diabetes. [16-18] A French study made by Lambri et al. [19] proposed that people having a genetic polymorphism causing lactase enzyme persistency had higher rates of impaired fasting glucose and diabetes. Low consumption of milk and milk sugar may lead to a decrease in plasma glucose levels compared to milk-consuming people. Controversially, in some of the previous studies it was demonstrated that among the adult patients, lactose intolerance was found more frequently than the non-diabetic people. (20)

A study with many participants reported from Denmark showed that there was no significant difference between low and high amounts of milk consumption, in an aspect of diabetes incidence. (21) Similarly, in a Finnish study, designed by Enettah et al, lactase enzyme persistence was not found to be associated with diabetes. [22] In contrast to these studies, the present study showed that blood glucose levels were significantly lower in the lactose intolerant group. However, this does not mean that lactose intolerance alone is a protective factor from diabetes. Larger-scale and long-term studies are needed to demonstrate the persistence of lactase is an independent risk factor for the development of diabetes. Some previous studies proposed that lactose intolerance is correlated with hypertension. A Brazilian study showed that hypertension was more frequently diagnosed among lactose- intolerant patients than normal population. [23] No significant association between lactose intolerance and diabetes or hypertension was documented in this presented study. This may be caused by restrictive diets followed by patients having dyspepsia and flatulence problems and because they refrained from consuming milk products. Many of the participants included in this study were relatively young since both diseases are rarely reported to be diagnosed in younger people; this may be why no association with diabetes mellitus or hypertension was documented in this study. In this study, those people who refrained from consuming milk and milk products were not found to have vitamin D and calcium deficiency. Vitamin D deficiency, usually, is considered; diagnosed and treated in our country; mainly by family physicians. Because of this, although they had low milk consumption, calcium and vitamin D deficiency might not be demonstrated in participants. There are some limitations of this study that should be mentioned. Firstly, no comparison was performed based on body mass index data. The number of diabetic patients was low since the mean age of our study population was relatively young. Also, this study had no genetic analysis of lactase gene constitution, which would give a clearer idea about the presence of lactose intolerance. And lastly, body mass index, duration of diabetes, and medications of the diabetic patients, which may affect the HbA1c values were not recorded and analyzed in this study.

CONCLUSION

Lactose intolerant people may have lower blood glucose levels compared to lactase persistent people. But, assuming to have lactose intolerance and

refraining from consuming milk and milk products without testing for lactose intolerance, would not be the right behavior for any person because milk products are necessary for better bone health. Long-term follow-up of lactose intolerant patients may help us understand whether this condition is protective against diabetes.

Conflict of interest: None.

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Sher Ali	Drafting and methodology, data interpretation
Furqan Ahmed Bhatti	Analysis and interpretation of data for work & Data Collection

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