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POSTPRANDIAL GLYCEMIC RESPONSE TO MANGO (MANGIFERA INDICA) INGESTION AND ITS IMPLICATIONS FOR GLUCOSE HOMEOSTASIS

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ABSTRACT
Background: Mango (Mangifera indica), a commonly consumed tropical fruit contains plenty of essential vitamins, dietary fibre content, and phytochemicals. Postprandial glycemic response has an important role in the regulation of glucose homeostasis. Despite its various nutritional benefits, concerns remain regarding the glycemic impact of mango consumption particularly in those with diabetes. Therefore, evaluation of the post prandial glycemic response following Mango consumption is important in understanding its role in glucose metabolism and impact on insulin sensitivity and post prandial metabolic response especially in diabetics.
Objectives: The study was planned to evaluate the postprandial glycemic response following mango ingestion as a surrogate marker of glucose homeostasis in diabetics as well as non diabetics.
Methods: We conducted this quasi-experimental study in the department of Medicine, Shifa College of Medicine from 31st January 2023 to 31st January 2024. A total of 222 participants included in our study using WHO sample size calculator. Fasting sugar was recorded and then random sugar levels 2 hours after consumption of a specified quantity of mango. The data was analyzed using SPSS version 26.
Results: Correlation analysis demonstrated no significant association between post-mango increment in blood glucose and age, HbA1c, or fasting blood glucose (p was more than 0.05). Multiple linear regression analysis was performed to identify factors independently associated with the rise in blood glucose following mango ingestion. After adjusting for age, gender, diabetes and HbA1c, body mass index (BMI) was the only variable which was independently associated with rise in blood sugar after mango ingestion. ($\beta = -0.228$, $p = 0.001$). Age, gender, HbA1c, and the presence of diabetes were not significantly associated with rise in glucose levels after mango ingestion. ($p > 0.05$).
Conclusion: While taken alone and in specific amount, the consumption of mangoes in diabetics and non-diabetics is not associated with incremental postprandial glycemic excursion (ΔRBS)

KEYWORDS: Endocrine metabolism, Glucose homeostasis, Glycemic index, Mangiferin, Type 2 diabetes

INTRODUCTION
Mango is among the commonly consumed fruit that contains various essential minerals, vitamins, dietary fibre and carbohydrates. Mango is considered as one of the sweetest among all fruits however despite that it has anti-oxidant properties and good impact on glucose metabolism[1]. Many fruits have a sweet taste but the sugar or carbohydrate content is not much high in fact some sweet taste food have excellent health benefits and anti-oxidant functions[2].It has been observed that consumption of fresh fruits can positively impact the post prandial glucose responses and glucose homeostasis as they contain certain bio active compounds and high fiber content that assists in prevention of post prandial abrupt rise in sugar levels, therefore beneficial in diabetics as well. The high fiber content of fruits including mango helps in slowing down the digestion process of carbohydrates[3].
Glycemic index, portion control and glycemic load are necessary parameters which a doctor must be aware of now before restricting the patients from ingestion of certain foods. A few parameters of Glycemic Index ranking of foods have been defined to define the carbohydrate content[4]. The glycemic index tells us about how quickly a food item affects the blood sugar levels when that food is taken alone in fasting state. The foods with a low and medium glycemic index lead to a gradual rise in blood sugars rather than abrupt. A combination of portion eating and glycemic index leads to a more useful parameter called glycemic load which is considered good between 11 to 19[5]. So, a serving of 100 gm of Mango has 15 grams carbohydrates, 48 glycemic index and glycemic load of 8 as its nutritional value[6]. On the basis of these facts, researchers now found that eating appropriate recommended quantity of mangoes on daily basis under the surveillance of a nutritionist helps in controlling blood sugars, blood

pressure and HbA1c in diabetic patients[7].
Glucose homeostasis has traditionally been considered a process with pancreatic beta cells as mainly responsible for its endocrine regulation. The fluctuations in blood glucose levels is a factor leading to the secretion of insulin and other hormones. Some other regulatory mechanisms are also acting in place involving both central and peripheral pathways[8]. The Insulin signaling pathway plays a key role in regulation of glucose homeostasis in the body which is carried out in a stepwise manner. Initially the insulin and insulin like growth factors (IGF-1) binds to their receptors, which in turn bind to various substrates[9]. The islet cells of Pancreas are responsible for secreting Insulin, a peptide hormone that exerts the metabolic response by binding with specific target receptors. The insulin signaling mechanism is well regulated so as to keep the glucose homeostasis under control and is affected by various phosphatases and stress kinases. Mango as a fruit has been included in the list of deliquescent drupe type of fruits, with a thick green to yellow skin peel, a fibrous juicy pulp and a hard endocarp inside. Mango peel is also used as an antioxidant in food items and it has anti-cancer properties as well due to its phenol rich compounds. The Polyphenols such as phenolic acid and flavonoids are rich in mango with anti-oxidant activities[10]. Similarly, the Phytosterols are rich in mangoes that has anti-inflammatory as well as cholesterol reduction properties hence can be helpful in improving the metabolic profile[10]. Mangoes are also rich in Tocopherols that exhibit strong anti-oxidative activities.
Insulin resistance develops when there is reduced responsiveness to the actions of insulin in the body promoting the uptake of glucose even after its disposal. It is mainly found to be linked with blockade in insulin signaling mechanisms and glycogen synthesis dysregulation[11]. Mangiferin, found in mango has anti-oxidant as well as blood sugar lowering properties. Mangiferin activates AMPK (activated protein kinase) and enhances sensitivity to insulin in the body and the derivatives of Mangiferin like 1,3,6,7-tetrapropylene acyloxy-ketone (TPX) has been found to improve the insulin sensitivity and improvement in the glycemic control[11]. The natural activators of AMPK signaling like Mangiferin in mango has the potential to be used for management of Type 2 Diabetes due to its anti-oxidant and sugar lowering actions[12].The rationale behind planning this study was to see the Glycemic patterns after mango ingestion in diabetics and non-diabetic patients.

METHODOLOGY

This Quasi-experimental study was done in the Medicine department (OPD) of Shifa College of Medicine (SFCHC), Shifa International hospital, Islamabad from 31st January 2023 to 31st January 2024 after taking the ethical approval from the institutional review board (IRB#0179-22). Using WHO Calculator, 222 participants were enrolled (111 in 2 groups) by following: 2-sided level of significance 95, Power (1 beta) 80%, ratio of sample size exposed vs unexposed 1:1, percentage of unexposed with outcome 5, percentage of exposed with outcome 17, Odds ratio 4, Risk/Prevalence ratio 3.5 and Risk/prevalence difference of 12. Subjects from age 15 years above, presenting in Medical Opd were included in the study with following characteristics including 50% non-insulin dependent diabetic patients in whom recent (within last 3months) HbA1c was <8 while the rest of 50% were non-diabetic subjects with recent HbA1c < 5.6. Patients with end stage liver, renal, pulmonary or cardiac diseases, those on steroids, using alcohol or using XR (extended release) anti-diabetic oral drugs, patients receiving insulin, having HbA1c >8 (done within last 3 months) and those who were not willing to participate, were excluded from our study.
Fasting blood sugars (after 8 to 10 hours of fasting) were checked using capillary glucometer (Accu-check (Roche)) then One portion of mango, that is 120 grams (using same measuring scale "Sinba") of most commonly grown variety of mangoes from the same batch of mangoes were given to the patients to eat and were advised not to eat anything else till the second blood sugar was checked. Patients were advised not to do any strenuous work for 2 hours. (a comfortable waiting area was also provided to stay for 2hours). Blood sugars were checked again by using same glucometer after 2 hours (from the start of mango ingestion). Patient's demographic features, BMI, prior metabolic status (diabetic/non-diabetic) and both sugars was entered on prescribed Performa.
Statistical analysis of our collected data was performed using SPSS software version 26 (IBM Corp). Continuous variables were summarized as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages (n (%)).
The glycaemic patterns were analysed for both diabetics and non-diabetics. Mean of HbA1c, fasting blood glucose, and post-mango random blood glucose levels were compared between the two groups using appropriate statistical tests.The primary physiological endpoint was the incremental postprandial glucose response, used as a surrogate marker of endocrine regulation of glucose metabolism. Categorical variables were assessed and compared by using the chi-square test, while continuous variables were assessed and compared using the independent samples t-test. A p-value < 0.05 was considered statistically significant.

RSEULTS

A total of 222 patients were included in the study. Out of these 91 were males (40.99%) while the rest were females. Half (50.0%) among them were diabetic and other half (50.0%) were non-diabetic. The mean age of the study patients was 45.20 ± 12.736 years. Baseline demographic, clinical, and biochemical characteristics including age, gender, weight, height, body mass index (BMI), HbA1c, fasting blood glucose (FBS), and random blood glucose (RBS), were compared between diabetic and non-diabetic subjects. Categorical variables including the

age and gender are presented in Table 1, while continuous variables are presented in Table 2.
Distribution of diabetes varies significantly among different age groups and different comorbidities as shown by p-value less than 0.05. Comparisons of continuous variables between the two groups were performed using the independent samples t-test. There was significant difference in means value of age, weight, height, HbA1C, fasting blood sugar and random blood sugar among diabetic and no-diabetic groups (P value less than 0.05). On the other hand Postprandial glycemic excursion after mango ingestion was not statistically significant between diabetics and non-diabetic groups. (p value > 0.05).

Table 1: Baseline demographic, clinical and biochemical characteristics (categorical)

Group	**Sub group**	**Overall**	**Diabetics**	**Non Diabetics**	**p-value**
Total count	Count (n)	222(100%)	111(50.0%)	111(50.0%)	
Gender	Male	91 (40.99%)	39(42.85%)	52(57.14%)	0.051
	Female	131(59.00%)	72(54.96%)	59(45.03%)	
Age Groups (Years)	15-30	28(12.61%)	6(21.42%)	22(78.57%)	0.002
	31-50	130(58.55%)	66(50.76%)	64(51.53%)	
	50-90	64(28.82%)	39(60.93%)	25(39.06%)	
Comorbidities	None	181(81.53%)	84(46.40%)	97(53.59%)	0.000
	CVD	34(15.31%)	27(79.41%)	7(20.58%)	

Table 2: Baseline demographic, clinical and biochemical characteristics

	Diabetics	**Non-Diabetics**	**t**	**Df**	**p-valve**
Age	47.92±12.123	42.49±12.808	-3.245	220	0.001
Weight	70.57±11.919	66.08±12.930	-2.682	219	0.008
Height	1.581±0.1116	1.544±0.0844	-2.773	218	0.006
Body mass index (BMI)	28.668±5.5004	27.766±5.4446	-1.210	214	0.228
HbA1c	7.770±2.1318	5.792±1.1638	-8.582	170.216	0.000
Fasting blood glucose	152.27±60.703	104.19±20.462	-7.908	134.679	0.000
Random blood glucose	164.14±60.731	106.14±19.494	-9.579	132.430	0.000
Increment in blood sugar	7.1351±27.23250	3.2019±18.79288	-1.239	196.127	0.217

Association of incremental post-mango glucose rise with different categorical and non- categorical variables was calculated and the results are highlighted in table 3.

Table 3: Spearman’s correlation of rise in blood sugar with Different variables

	Age	Weight	Height	HbA1C	Fasting sugars	Post mango sugars	BMI
Correlation Coefficient	-0.090	-.143*	0.138*	0.063	-0.026	.201**	-.245**
Sig. (2-tailed)	0.189	0.037	0.054	0.360	0.709	0.003	0.000

Correlation analysis demonstrated no significant association between post-mango increment in blood glucose and age, HbA1c, or fasting blood glucose (p was more than 0.05). Weight and height and Post mango random blood glucose showed statistically significant correlations with glucose increment ($r = -0.143$, $p = 0.037$; $r = 0.138$, $p = 0.044$; $r = 0.201$, $p = 0.003$ respectively). Body mass index exhibited a moderate negative correlation with post-mango glycemic rise ($r = -0.245$, $p < 0.001$), representing the strongest observed association.
Multiple linear regression analysis was performed to identify factors independently associated with the rise in blood glucose following mango ingestion. After adjusting for age, gender, diabetes and HbA1c, body mass index (BMI) was the only variable which was independently associated with rise in blood sugar after mango ingestion. ($\beta = -0.228$, $p = 0.001$). Age, gender, HbA1c, and the presence of diabetes were not significantly associated with rise in glucose levels after mango ingestion. ($p > 0.05$ for all). The regression model demonstrated modest explanatory power (adjusted $R^2 = 0.037$).

Table 4. Multi variable linear regression analysis showing independent predictors of post-mango blood glucose increment

Variable	Unstandardized Coefficients		St. Coefficient	t	sig	95.0% Confidence Interval for B		Collinearity Statistics	
	B	Std. Error	beta			Lower Bound	Upper Bound	Tolerance	VIF
(Constant)	36.665	12.168		3.013	0.003	12.673	60.656		
Age	-0.096	0.139	-0.050	-0.695	0.488	-0.370	0.177	0.897	1.115
Gender	-2.693	3.333	-0.056	-0.808	0.420	-9.264	3.878	0.966	1.035
BMI	-0.995	0.301	-0.228	-3.304	0.001	-1.589	-0.401	0.974	1.027
HbA1C	-0.069	0.942	-0.006	-0.073	0.942	-1.927	1.789	0.724	1.381
Diabetes	4.768	3.822	0.100	1.247	0.214	-2.769	12.305	0.715	1.399

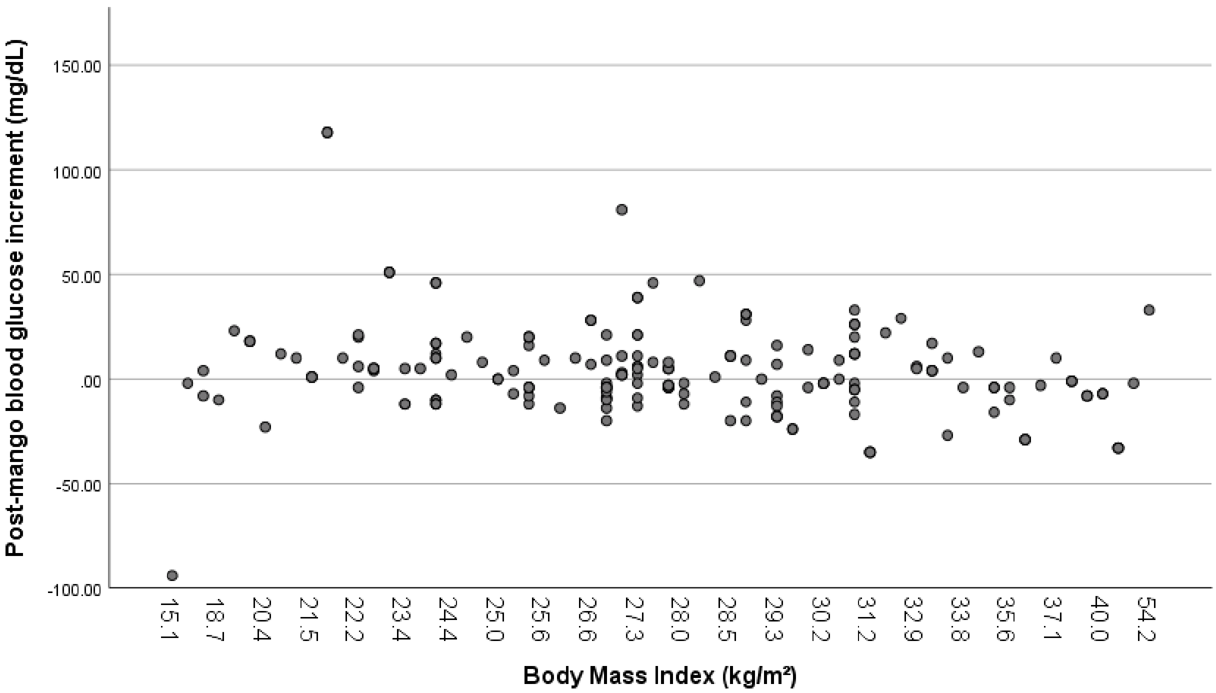

Figure 1: Relationship between body mass index and incremental postprandial glucose response following mango ingestion.

DISCUSSION

We planned this study to see the effects of Mango use in diabetics, to evaluate the metabolic response particularly the postprandial glycemic excursion. Rationale behind our plan was to see the glucose homeostasis after consumption of Mango, a fruit that contains essential minerals and vitamins with anti-oxidant properties. Glycemic index (GI) of a food indicates its ability to produce postprandial glucose excursion compared to that of a reference food[13]. Food with a Glycemic index of <55 is considered as low GI while those with a glycemic index of 70 or more are categorized as high GI foods. American Diabetes Association (ADA) recommends and encourages diabetics to consume food with low glycemic index[14] and mangoes are included in the list of common fruits having low Glycemic index. Glycemic index and glycemic load are useful parameters that can be utilized as a guide to select the appropriate food plan in diabetics. Low Glycemic index food actually helps in maintaining a good health with a preventive role in chronic diseases[15]. The metabolic regulation of the body is also improved with low GI diet particularly in diabetics, one of the main pathophysiological contributors in diabetes is insulin resistance which is reduced by the food with low glycemic index. We found the similar results as mango is included in low GI food and its consumption was not associated with postprandial hyperglycemia both in diabetics as well as in non-diabetics. This observation has also been found in other studies, that showed that mango use actually improves the glycemic control[16]. Among all the variables including Age, gender, HbA1c there was no signification association with the rise in blood sugars post mango ingestion except for the BMI showing significant association. This observation reflects that mango consumption in those diabetic patients who are overweight or obese may cause elevated blood sugars, however literature review showed that mangoes can actually be helpful in obese people in reducing blood sugars as well as improvement in their blood pressure. Adipose tissue functions as an endocrine organ secreting adipokines which affect insulin signaling as well as glucose metabolism. Pancreatic poly peptide (PP) helps as a hepatic blood glucose regulator which has various actions including delaying the gastric emptying and improving the insulin sensitivity. In obese diabetic individuals, there is impaired secretion of pancreatic poly peptide therefore leading to postprandial hyperglycemia[17]. Ren Y et Al conducted a study in China which showed increasing the fruit intake actually lowers the blood sugar levels in diabetics[18]. Majority of the fruits particularly the mangoes have useful micro nutrients as well as the anti-oxidant properties that have good effects on the glucose homeostasis and insulin signaling so they can be safely utilized by diabetics. Mango contains bio active compounds particularly Mangiferin that help regulate glucose balance in the body. These compounds can increase plasma insulin levels, improve lipid regulation, and support healthy microcirculation[19]. Mangoes are considered to reduce the oxidative stress that helps in metabolic regulation, improved glycemic response as well as reduction of atherosclerosis risk[20]. Mangiferin helps control postprandial glucose levels by reducing the expression of TNF-alpha and nitric oxide synthase, while also increasing pancreatic beta-cell mass and enhancing insulin uptake[21]. These beneficial effects and anti-diabetic properties of Mango has been found in our results with no post prandial hyperglycemia following mango consumption both in diabetics as well as non diabetics.

Our study had a few strengths, first is that it highlights and focused on the clinically relevant important topic

which remained debatable among the healthcare workers regarding use of Mango in diabetics, as we observed the glycemic effects following mango ingestion the results clearly indicate its safety without significant postprandial glucose excursion. Secondly, the use of standardized portion sizes of mango in our study ensured consistency across participants and improved reproducibility.
We noted a few limitations as well. Only a single postprandial time point was measured, it would be appropriate to do further studies by checking the postprandial results on more than one time. Mango contains fiber, natural sugars and Polyphenols that may affect insulin sensitivity and incretin secretion. Without measuring these hormones, the study cannot explain how mango consumption affects metabolic pathways,therefore we suggest measurement of these important hormones in future studies. We measured post prandial glycemic response at one point of time while much better would be continuous glucose monitoring. Continuous monitoring allows more accurate measurements like time to peak glucose, the duration of hyperglycemia,transient glucose metabolism changes and overall glycemic exposure, which provide a more comprehensive understanding of the food's glycemic impact.

CONCLUSION

Mango consumption is safe in diabetics and its use is not associated with significant rise in blood sugars both in diabetics as well as in non-diabetics, therefore can be consumed by diabetic patients.

Conflict of Interest: None
Consent: Informed consent was obtained from participants
Funding: No funding was obtained from any institution or organization
Acknowledgment: None
Ethical Standards: The study was performed after the ethical approval by the IRB/Institutional review board of Shifa International hospital with approval number (IRB#0179-22)
Declaration of Generative AI and AI-assisted technologies: No assistance was taken from AI tools during the manuscript preparation

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