*Original Article*

# Glycemic Effects of Honey Compared to Glucose Using Standard OGTT

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### Abstract

***Background***: *Honey, though rich in fructose and glucose, had been shown to have plasma glucose lowering effect. It may be as a result of insulin sensitization, enhanced insulin secretion and anti-oxidant activity.* ***Objective***: *This study was designed to assess the glycemic effects of honey comparing to glucose.* ***Materials and Methods***: *The study was carried out at Armed Forces Institute of Pathology (AFIP), Dhaka cantonment from September, 2015 to October, 2015 on 35 individuals who reported to AFIP for 'Oral Glucose Tolerance Test (OGTT)'. They were categorized to three groups based on OGTT ─ Normal, Impaired glucose homeostasis (IGT or IFG), and Diabetes mellitus. On the subsequent day they were subjected to 52 mL honey load (equivalent to 75 gm by weight) to assess plasma glucose level after 1 hour and 2 hours post-honey load state. Student t-test was done to compare between means of plasma glucose level 1 hour after 75 gm glucose load and 1 hour after 75 gm honey load and also between means of plasma glucose level 2 hours after 75 gm glucose load and 2 hours after 75 gm honey load in the same individuals.* ***Results***: *In all the three groups mean plasma glucose level in post-honey load state was found declined compared to post-glucose load state in both 1 hour and 2 hours specimens of HTT (Honey Tolerance Test) versus OGTT (Oral Glucose Tolerance Test) and this reduction was statistically significant ($p<0.05$).* ***Conclusion***: *The study findings provide evidence that honey consumption causes less change in plasma glucose level than the equivalent quantity of oral glucose load regardless of status of glucose homeostasis. Further well designed researches are needed to determine the long term effects and beneficial quantity of honey, particularly in relation to diabetes mellitus.*

***Key words***: *Honey; Fructose; Glucose; Oral glucose tolerance test*

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## Introduction

History says that honey had been used more as a drug than a nutrient. Aristotle[1] (350 BC) wrote of honey being a salve for wounds and sore for eyes. Hippocrate[2] said, "I eat honey and use it in the treatment of many diseases because honey offers good food and good health." Avicenna (Ebne Sina), the famous Persian philosopher and physician about 1,000 years ago, mentioned the therapeutic effect of honey in Ghanoon, his published book.[3] It was used as an alternative to gold to pay taxes by the Romans, in matrimonial ceremonies by the Greeks, and in the treatment of wounds by the Egyptians.[2-4] In modern medicine, honey has been used for the treatment of respiratory

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disease, urinary disease, gastrointestinal disease, skin ulcers, wounds, eczema, psoriasis, dandruff, diaper dermatitis, and radiation mucositis.[4,5] Blood glucose lowering effect of honey may be due to multifactorial mechanisms, including insulin sensitization[4,5], enhanced insulin secretion in diabetic patients[3] and its anti-oxidant activity[5]. Yaghoobi et al[3] found that natural honey lowers fasting blood glucose, improves lipid profile (i.e. decreases total cholesterol, LDL-C, VLDL-C, triglycerides and increases HDL-C), lowers normal and elevated C-reactive protein (CRP), lowers homocysteine and thus reduces cardiovascular risks.

Carbohydrate is the major component (82%) of honey.[2,3,6-8] Monosaccharides, fructose and glucose are the dominant fractions of honey sugars, of which 38.2% is from fructose and 31% from glucose.[6,8] Besides, there are about 25 different disaccharides and oligosaccharides accounting for 5−10% of the total carbohydrates.[7] So, it is puzzling that how honey would lower blood glucose levels in patients having diabetes mellitus. Although honey is rich in carbohydrate, its glycemic index (GI) varies within a wide range from 32 to 85, lower than sucrose (60 to 110) depending on its botanical source.[7] Research has shown that foods with a low GI cause a small rise in blood glucose, may provide reduced risk of coronary heart disease and type 2 diabetes.[6]

## Materials and Methods

This study was carried out at Armed Forces Institute of Pathology (AFIP), Dhaka Cantonment from September 2015 to October 2015. Informed consent was taken from all the participating subjects. Total 35 individuals, who reported to AFIP for 'Oral Glucose Tolerance Test (OGTT)', were enrolled in this study. On the first day, OGTT with 75 gm oral glucose load was carried out and blood sugar readings were taken at fasting state, 1 hour and 2 hours post-glucose load state. Test results were interpreted as per WHO criterion and thus they were grouped into three groups ─ Group 1: Normal, Group 2: Impaired glucose homeostasis (IGT or IFG), and Group 3: Diabetes mellitus. On the subsequent day, blood glucose was estimated in 1 hour and 2 hours post-load of 52 mL honey (equivalent to 75 gm by weight) in same study subjects, who reported at AFIP in fasting state. Individuals known to have kidney disease, hepatic disorders, endocrinopathy, and pregnancy were excluded from the study. Quantitative variables were described as mean ± standard deviation (SD). Student t-test was done to compare between means of plasma glucose level 1 hour after 75 gm glucose load and 1 hour after 75 gm (= 52 mL) honey load and also between means of plasma glucose level 2 hours of post-glucose load and 2 hours of post-honey load state in the same individuals. $p \le 0.05$ was considered statistically significant.

## Results

Oral glucose tolerance test (OGTT) shows that among 35 individuals, 15 had normal, 10 had impaired and 10 had diabetic range of plasma glucose level. Table I shows the glycemic status and mean age of the study subjects. Table II shows sex distribution in different groups.

No significant ($p>0.05$) age difference was observed between normal and impaired glucose groups. But, age was significantly ($p<0.005$) higher in diabetic group in contrast to normal or impaired glucose groups.

Among the participating males 27.3% were normal, 18.2% had impaired glucose homeostasis and 54.5% had diabetes. Among the participating females 50% were normal, 33.3% had impaired glucose homeostasis and 16.7% had diabetes (Table III). Table IV shows the OGTT results in different groups of subjects.

It is observed in 'normal group' that following 75 gm (52 mL) honey administration mean plasma glucose level decreased in comparison to post-glucose load from 8.7 ± 1.6 to 6.4 ± 0.7 ($p<0.0001$) and from 6.5 ± 0.7 to 5.5 ± 0.4 ($p<0.0001$) after 1 hour and 2 hours respectively. In 'impaired group' mean plasma glucose level of post-honey load state also decreased in comparison to post-glucose load state from 11.5 ± 1.1 to 8.5 ± 0.8 ($p<0.0001$) and from 8.9 ± 0.6 to 6.5 ± 0.7 ($p<0.0001$) after 1 hour and 2 hours respectively. In 'diabetic group' mean plasma glucose level of post-honey load state decreased too in comparison to post-glucose load state from 17.5 ± 3.7 to 13.4 ± 4.0 ($p<0.05$) and from 14.7 ± 4.4 to 10.5 ± 3.9 ($p<0.05$) after 1 hour and 2 hours respectively. So, in all groups regardless the pattern of glucose homeostasis, post-honey load state glucose level was found significantly decreased in comparison to post-glucose load state both after 1 hour and 2 hours.

Table I: Frequency and mean age of different groups

| Groups | Glycemic status | Frequency | Age in years Mean ± SD (Range) |
|---|---|---|---|
| Group 1 | Normal | 15 | 34.1 ± 5.9 (22−42) |
| Group 2 | Impaired (IGT/ IFG ) | 10 | 35.1 ± 8.8 (20−48) |
| Group 3 | Diabetes | 10 | 45.8 ± 5.4 (35−54) |

Normal: FPG, 3.33–6.1 mmol/L; 2 hrs after 75 gm glucose load, <7.8 mmol/L
Impaired (IGT/IFG): FPG, 6.1–6.9 mmol/L; 2 hrs after 75 gm glucose load, 7.8–11.1 mmol/L
Diabetic: FPG, ≥7.0 mmol/L; 2 hrs after 75 gm glucose load: ≥11.1 mmol/L

**Level of Significance**
Group 1 versus Group 2: p=0.9296 (insignificant)
Group 1 versus Group 3: p=0.0005 (significant)
Group 2 versus Group 3: p=0.0033 (significant)

Table II: Sex distribution in different groups

| Groups | Glycemic status | Frequency | Sex distribution | |
|---|---|---|---|---|
| | | | Male | Female |
| Group 1 | Normal | 15 | 3 (20%) | 12 (80%) |
| Group 2 | Impaired (IGT/ IFG ) | 10 | 2 (20%) | 8 (80%) |
| Group 3 | Diabetes | 10 | 6 (60%) | 4 (40%) |
| Total | | 35 | 11 (31.4%) | 24 (68.6%) |

Table III: Pattern of glucose homeostasis in male and female

| Sex | Normal | Impaired (IGT/ IFG ) | Diabetes | Total |
|---|---|---|---|---|
| Male | 3 (27.3%) | 2 (18.2%) | 6 (54.5%) | 11 (100%) |
| Female | 12 (50%) | 8 (33.3%) | 4 (16.7%) | 24 (100%) |

Table IV: Mean plasma glucose levels during OGTT in different groups of glucose homeostasis (normal, impaired and diabetes)

| Groups | Glycemic status | Fasting (in mmol/L) | 1 hr after 75 gm glucose (in mmol/L) | 2 hrs after 75 gm glucose (in mmol/L) |
|---|---|---|---|---|
| Group 1 | Normal | 5.3 ± 0.2 | 8.7 ± 1.6 | 6.5 ± 0.7 |
| Group 2 | Impaired (IGT/IFG ) | 5.8 ± 0.5 | 11.5 ± 1.1 | 8.9 ± 0.6 |
| Group 3 | Diabetes | 8.5 ± 2.6 | 17.5 ± 3.7 | 14.7 ± 4.4 |

Table V: Change in plasma glucose level from 1 hour post-glucose load to 1 hour post-honey load state

| Glycemic status | Plasma glucose level (mmol/L) | | Decrease in % in mean value from 1-hour post-glucose load to 1-hour post-honey load |
|---|---|---|---|
| | 1 hour after 75 gm glucose (Mean ± SD) | 1 hour after 75 gm glucose (Mean ± SD) | |
| Normal | 8.7 ± 1.6 | 6.4 ± 0.7 | 26.4 (p<0.0001) |
| Impaired (IGT/IFG ) | 11.5 ± 1.1 | 8.5 ± 0.8 | 26.1 (p<0.0001) |
| Diabetes | 17.5 ± 3.7 | 13.4 ± 4.0 | 23.4 (p=0.0313) |

Table VI: Change in plasma glucose level from 2 hour post-glucose load to 2 hour post-honey load state

| Glycemic status | Plasma glucose level (mmol/L) | | Decrease in % in mean value from 2-hour post-glucose load to 2-hour post-honey load |
|---|---|---|---|
| | 2 hours after 75 gm glucose (Mean ± SD) | 2 hours after 75 gm glucose (Mean ± SD) | |
| Normal | 6.5 ± 0.7 | 5.5 ± 0.4 | 15.4 (p<0.0001) |
| Impaired (IGT/IFG ) | 8.9 ± 0.6 | 6.5 ± 0.7 | 26.9 (p<0.0001) |
| Diabetes | 14.7 ± 4.4 | 10.5 ± 3.9 | 28.6 (p=0.0362) |

## Discussion

Honey is sweet to taste, rich in monosaccharides and usually is not expected to lower plasma glucose level. But some studies showed that honey decreases plasma glucose level.[3-5] This surprising finding is explained by the fact that the fructose and oligosaccharides present in honey might contribute to the observed blood glucose lowering effect.[9] In fact, the monosaccharide, fructose or glucose in honey need not to be hydrolyzed by GIT enzymes and hence are ready for absorption.[8] In gut, glucose is absorbed by $Na^+$ dependent secondary active transport, employing SGLT1 at luminal membrane and GLUT2 along basolateral membrane of enterocyte.[10] But fructose utilizes a different mechanism independent of $Na^+$. Fructose is absorbed by facilitated diffusion from the intestinal lumen into the enterocytes by GLUT5 and from the enterocytes into the interstitium by GLUT2.[10] The glucose and/or fructose can upregulate GLUT2 mRNA expression. In contrast, GLUT5 mRNA transcription is upregulated by fructose only and thereby fructose absorption is enhanced over glucose. Besides, it is suggested that in the presence of glucose, there is combined absorption of the two monosaccharides, through disaccharidase-related transport system.[11] All these findings could be very important with regard to honey, which is primarily consisting of fructose and glucose. Moreover, recent data indicate that gut microbiota enhance the intestinal absorption of monosaccharides including fructose. Interestingly, honey comprises of oligosaccharides which enhance the activity and growth of gut microorganisms, might also contribute to increased intestinal absorption of honey fructose.[11] Following absorption, monosaccharide is transported to the liver, where the uptake and initial steps of metabolism of glucose and fructose differ. For instance, insulin is required for the hepatic uptake of glucose, but not for fructose.[11] Hence, larger amounts of fructose than glucose are extensively metabolized in the liver. Again, the catalytic reactions of glucose through glycolysis are also insulin dependent.[11] However in case of fructose, the high hepatic extraction results in excessive production of fructose 1-phosphate which in turn inhibits glycogenolysis.[11] Unlike glucose metabolism, all the catalytic reactions of fructose occur independently of insulin and the rate-limiting steps are also bypassed. These differences in metabolism result in about 50% to 70% of the absorbed fructose being metabolized in the liver, compared to only about 20% to 30% of the absorbed glucose.[11] Besides, fructose activates glucokinase and other enzymes involved in glycogenesis. Thus, unmetabolized glucose might be taken up from the circulation into the liver to be stored as glycogen. In other words, honey supplementation via its fructose might enhance glucose uptake, and synthesis as well as storage of glycogen in the liver, and inhibit glycogenolysis resulting in improved glycemic control.[11] Besides, studies have also shown that honey administration ameliorates hepatic oxidative stress and produces hepatoprotective effect, which might be beneficial to the liver, especially in diabetes mellitus.[11] These effects thereby contribute to hypoglycemic effect of honey via improved hepatic enzymes involved in glucose metabolism.

Besides, evidence also suggests that fructose consumption prolongs gastric emptying, which may slow down the rate of intestinal absorption.[8] In addition to fructose, oligosaccharides such as palatinose (isomaltulose) present in honey have been reported to delay digestion and intestinal absorption of glucose and thus also may contribute to reduced glycemia.[8]

In this study, there was a statistically significant decrease in 1-hour and also in 2-hour post-honey load blood glucose levels in comparison to post-glucose load levels in normal, impaired and also diabetic group. Our study findings match with that of Agrawal et al1[2] who conducted a study on thirty adults with a proven parental history of type II diabetes mellitus, who were subjected simultaneously to an oral glucose tolerance test (GTT) and a honey tolerance test (HTT). Among them, 24 had impaired glucose tolerance and six had diabetes mellitus and both the groups exhibited significantly lower plasma glucose concentrations after consumption of honey at all time points of the HTT in comparison to the GTT.

Another study was carried out on 97 adult T2DM patients of Jinnah Medical College Hospital, Karachi in 2011 to compare the glycemic response to low (30 grams) quantity of honey and high (75 grams) quantity of honey in comparison to 75 gm glucose in diabetic patients.[13] The glucose response was significantly lower at 2 hours in '30 gram honey group' (p<0.001) compared to '75 gram honey group' or '75 gram glucose group'. Plasma glucose level was also significantly low in '75 gram honey group' than '75 gram glucose group' (p<0.0001).

Our study finding is also strengthened by Majid et al[4] who carried out a randomized controlled trial in Army Medical College, Rawalpindi, Pakistan. They found that the experimental group, provided with 70 gm of honey daily for a period of four weeks, had significantly (p=0.011) lower serum fasting glucose level than that of control group kept on the same diet except honey.

Another study by Yaghoobi et al[3] on 55 overweight or obese patients over a period of 30 days also showed that honey compared with sucrose caused significant reduction of BMI (1.14%, p=0.02) and FBG (4.2%, p=0.04).

Another study also reported that even though glibenclamide or metformin reduced hyperglycemia, the administration of these drugs in combination with honey resulted in much lower glycemic levels in diabetic patients.[9]

In this study, there was no significant age difference between 'normal' and 'impaired' group. But, age was significantly (p<0.005) higher in 'diabetic group' in comparison to both 'normal' and 'impaired' group. So, advanced age appears as a risk factor for diabetes mellitus. Our finding is supported by 'The DECODA (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Asia) Study Group'[14] which conducted 11 studies in 4 countries, comprising 24,335 subjects (10,851 men and 13,484 women) aged 30–89 years. The study observed that the prevalence of diabetes increased with age up to 70–89 years of age in Chinese and Japanese subjects and up to 60–69 years of age in Indian subjects. In India and Singapore, the prevalence was about 10% among subjects aged 40–49 years and over 30% were aged 50–69 years.

In our study, among 35 participating subjects, 11 (31.4%) were male and 24 (68.6%) were female. Among the male 54.5% were diabetic, in comparison to 16.7% in female. So, male sex is more susceptible to develop diabetes mellitus. This finding is also supported by the data derived from the second cycle of the National Population Health Survey[15] conducted in 1996–1997 over 39,021 subjects (17730 males and 21291 females). It was reported that the prevalence of diabetes was higher among men than women, 6.6% (95% CI: 5.8–7.5%) versus 5.1% (95% CI: 4.6–5.7%).

The study findings provide evidence that honey consumption of limited quantity is useful regardless of status of glucose homeostasis. So, honey can be a useful adjunct in impaired glucose tolerance and diabetes mellitus for managing blood sugar level. Low dose of honey thus can be a valuable sugar substitute for healthy, impaired glucose tolerant or diabetic patients. However, further large scale studies should be carried out to assess other effects of honey on different metabolic derangements in association of diabetes mellitus. Besides, assessment of long term effects of honey on glycemia using HbA1c is also important. Otherwise honey cannot be recommended for routine consumption, particularly in diabetic patients. Moreover, what quantity of honey would be beneficial should also be assessed by well-designed rigorously controlled studies to recommend definite quantity of honey in diabetes mellitus.

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