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Original article

Honey and diabetes mellitus: Obstacles and challenges – Road to be repaired

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ABSTRACT

Background and objective: Since ancient times, honey has been used due to its nutritional and therapeutic value. The role of honey has been acknowledged in the scientific literature however, its use has been controversially discussed and has not been well accepted in modern medicine especially for diabetic patients. This study aimed to investigate the role of honey in diabetic patients.

Methods: In this study, we identified 107 research articles from data based search engines including "PubMed", "ISI-Web of Science", "Embase" and "Google Scholar". The research papers were selected by using the primary key-terms including "Honey", "Honey bee" and "Diabetes Mellitus". The research documents in which "Honey" and "Diabetes Mellitus" were debated are included. After screening, we reviewed 66 papers and finally we selected 35 studies which met the inclusion criteria and the remaining documents were excluded.

Results: This study investigated the preclinical, clinical, human and animal model studies on honey and diabetes mellitus and found that honey decreases the fasting serum glucose, increases the sting C-peptide and 2-h postprandial C-peptide. Although, there is a dearth of data and literature also contrary discussed the use of honey in diabetic patients.

Conclusion: Honey decreases the fasting serum glucose, increases fasting C-peptide and 2-h postprandial C-peptide. Honey had low glycemic index and peak incremental index in diabetic patients. The use of honey in diabetic patients still has obstacles and challenges and needs more large sample sized, multicenter clinical controlled studies to reach better conclusions.

1. Introduction

Honey is a sweet viscous substance made by honey bees using the nectar part of the flowers. Honey has various physical, physiological and chemical characteristics. The consumption of honey has a very long history among human beings. It has been used in numerous ancient cultures as a complete nourishing food, beverages as sweetening and flavoring agent as well as a remedy for many illnesses (Ismail et al., 2015). Since ancient times, honey has been known for its nutritive and therapeutic values. The global production of honey is approximately 1.20 million tons per annum (Bogdanov et al., 2008). China, Turkey, Argentina, Mexico and United States are the main makers of honey. The most important ingredient of honey is carbohydrates present in the form of monosaccharides, fructose, glucose and disaccharides, maltose and sucrose. The sweetness of honey is due to the presence of these ingredients. Furthermore, honey contains amino acids, vitamin B, Vitamin B6, Vitamin C, niacin, folic acid, minerals, iron, zinc and

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antioxidants (David Ball, 2007; Fatimah et al., 2013). Honey is commonly used as an anti-inflammatory, anti-oxidant and anti-bacterial agent (Noori et al., 2014).

The health promoting characteristics of honey bee are mainly due to the presence of multiple metabolites including vitamins and essential minerals besides enzymes and co-enzymes. In principle, honey is a valuable supplement for a healthy population (Denisow and Denisow-Pietrzyk, 2016). Recent advances in research, literature highlight that honey has potential biological activities with promising health promoting properties (Muhammad et al., 2016). The data are limited and findings are inconclusive about the valuable impact of honey and generalization of honey samples from various geographical corners of the globe remain controversial especially in the metabolic compromised patients including diabetic patients. This study aimed to investigate the role of honey in diabetic patients.

2. Research methodology

2.1. Selection of studies

In this study, we acknowledged 107 documents from data based search engines including "PubMed", "Institute of Scientific Information" (ISI) "Web of Science", "EMBASE" and "Google Scholar". Two investigators searched, reviewed and collected the literature using the primary key-terms including "Honey", "Honey bee" and "Diabetes Mellitus". The research documents in which "Honey" and "Diabetes Mellitus" were debated were also included. After screening, out of 107, we reviewed 66 papers and finally we selected 35 studies which met the inclusion criteria and remaining documents were excluded.

2.2. Data extraction

The eligibility of the research papers was considered by two investigators and the differences were determined by a third member. Research documents which were included in the study were peer-reviewed cross sectional, cohort studies, clinical trials and all studies were mainly included enough sample size. The findings were entered into the computer, tabulated and analyzed using the Statistical Package for Social Sciences [SPSS for Windows, version 21.0].

2.3. Ethics approval

For this study, we collected data on "Honey bee" "Diabetes Mellitus" from the research articles already published in databases, hence ethical approval was not required.

3. Results

In this study we investigated the preclinical, clinical, human and animal model studies and potential impact of honey on diabetes mellitus. It was established that honey decreases the fasting "serum glucose", increases "fasting C-peptide" and 2-h postprandial "C-peptide". Honey had low "glycemic index" and "peak incremental index" in diabetic patients. In addition, honey significantly increases "High Density Lipoprotein (HDL)" decrease "hyperglycemia", "triglycerides (TGs)", "very low density lipoprotein (VLDL)", "non–HDL cholesterol", "coronary risk index (CRI)" and "cardiovascular risk index (CVRI)". Moreover, honey paralleled to sucrose had a lesser "glycemic index (GI)" and "peak incremental index (PII)" and honey made substantially higher "C-peptide" level when compared to glucose or sucrose (Table 1).

Table 1
Honey and diabetes mellitus.

Authors and year of study	Type of study	Study outcome
Abdulrhman et al. (2013)	Randomized crossover clinical trial	Significant decreases in "fasting blood glucose", "triglycerides", "total cholesterol" "low-density lipoprotein" noteworthy rises in "fasting C-peptide" and "2-h postprandial C-peptide"
Khedekar et al. (2016)	Cross sectional Study	Traditional medicine Shadguna Balijarita Makaradhwaja (SBM) and honey with T-cordifolia markedly decreases the blood glucose and demonstrates anti-diabetic impact
Erejuwa et al. (2016)	Cross sectional study	Honey significantly reduce "hyperglycemia", "triglycerides (TGs)", "very low density lipoprotein (VLDL)", "non-HDL cholesterol", "coronary risk index" (CRI) and "cardiovascular risk index" (CVRI)"
Erejuwa et al., 2010	Cross sectional study	Honey has hypoglycemic impact in "streptozotocin" induced diabetic rats
Erejuwa et al. (2011)	Cross sectional study	Honey significantly increased insulin, decreased hyperglycemia. Addition of "glibenclamide" or "metformin" with honey increases the glycemic control and provides supplementary metabolic benefits.
Fasanmade and Alabi (2008)	Cross sectional study	Honey significantly decreased blood glucose in rats. Honey reduced hyperglycemia persuaded by long-term ingestion of fructose. However, honey not decreased blood glucose in controlled rats. Use of honey in diabetes may be due to abundant antioxidants in honey
Shambaugh et al. (1990)	Cross sectional study	Fructose showed minor alterations in blood sugar, sucrose showed higher blood sugar values than honey, producing significantly greater glucose intolerance
Prasetyo and Safitri (2016)	Cross sectional study	Honey could have possible honey-induced pancreatic beta cell regeneration
Abdulrhman et al. (2013)	Case control cross sectional study	Honey had low "glycemic index" and "peak incremental index" and honey increases "C-peptide" compared to glucose or sucrose
Abdulrhman (2016)	Cohort prospective study, Non-randomized, open clinical trial	Honey ingestion caused more hyperglycemia in type 2 diabetic patients but no diabetic ketoacidosis or hyperglycemic hyperosmolar condition. Long duration use of honey resulted in decreased weight and control of the blood pressure
Whitfield et al. (2016)	open-label, randomised controlled trial	Combination of chromium, cinnamon and magnesium with honey was not linked with progress in glycaemic control in type 2 diabetics. Ingestion of honey was allied with decreased in weight and improvement in lipid parameters
Behroozi et al. (2014)	cross-over design	Honey bee venom (HBV) has significant anti-glycation impact and avoid glycation-induced change in the structure and function of hemoglobin, HBV can be established as a medication against glycation-associated complications in diabetes
Nazir et al. (2014)	The experimental study	Honey swiftly decreases the plasma glucose levels compared to glucose
Abdulrhman et al. (2011)	case-control cross-sectional study	Honey as compared to sucrose had low "glycemic index (GI) and peak incremental index (PII)". Honey resulted higher "C-peptide" level, as compared with glucose or sucrose

Table 1 also demonstrates that honey ingesting causes hyperglycemia in type 2 diabetic patients but no diabetic ketoacidosis or hyperglycemic hyperosmolar state. Long duration of honey ingestion is associated with decreased body weight and control of the blood pressure in the patients who had high blood pressure earlier the honey mediation (Table 1).

4. Discussion

Honey is highly nutritional with favorable properties of antioxidant, anti-inflammatory and anti-bacterial characteristics. The role of honey depends on its concentration and its geographic origin. As an antioxidant, honey has numerous preemptive properties against many clinical conditions such as inflammatory disorders, coronary artery diseases, neurological worsening and aging (Kishore et al., 2011). In various cultures and vicinities, patients suffering from diabetes mellitus use honey. Honey is useful for diabetic patients as honey contains lesser calories than sugar and providing vitamin "B_2, B_4, B_5, B_6, B_{11}, C" and minerals such as "Iron, Zinc, calcium, potassium, phosphorous, magnesium, selenium and manganese". The nutritional values of honey depends on the types, feeding, regional and geographical conditions of the bees (Ediriweera and Premarathna, 2012).

The impact of carbohydrate diet on human health has been debated particularly to understand in what way carbohydrate diet changes the blood glucose. Presently, the importance of carbohydrate is frequently demonstrated as "glycemic index (GI)". Carbohydrates with minimum and maximum GI provide low and high blood glucose correspondingly. It is an established fact that unifloral honeys have variable fructose and glucose contents (Persano and Piro, 2004). Acacia and yellow box types of honey have comparatively high concentration of fructose with lower GI (Ludwig, 2000). The diet with low GI provides advantages with respect to metabolic including diabetes mellitus and in coronary artery disease (Jenkins et al., 2016). The ingesting of honey with a low GI, such as acacia honey, has physiological advantages and may be used among patients with impaired endocrine functions (Peretti et al., 1994; Al-Wali, 2004).

Al-Waili et al., 2013 reported that honey bee is commonly used in traditional medicine for various illnesses. Honey is re-positioned in modern medicine with its well acknowledged benefits including "antioxidant", "anti-inflammatory" and "antimicrobial" activities. The scientific findings also sustain the use of honey in diabetic patients.

Abdulrhman et al. (2013a, 2013b) investigated the metabolic effect of three month honey ingestion in type 1 diabetic patients. The authors found a decrease in fasting serum glucose, serum triglycerides, total cholesterol, low-density lipoprotein and marked increase in fasting C-peptide and 2-h postprandial C-peptide. Long-term ingestion of honey caused significant reductions in fasting serum glucose, 2-h postprandial serum glucose, serum triglycerides and HbA1C. This clinical trial provides evidence that prolonged ingestion of honey has positive impacts on the metabolic imbalances of type 1 diabetes mellitus. Similarly, Khedekar et al. (2016) reported that, honey with T-cordifolia significantly decreases blood glucose and demonstrates anti-diabetic impact.

Erejuwa et al. (2016) established the animal model of alloxan-induced diabetes and determined the outcome of Nigerian honey on hyperglycemia and hyperlipidemia. The authors administered 1.0, 2.0 and 3.0 gm/kg honey in diabetic rats for the period of three weeks. 1.0 or 2.0 gm/kg honey markedly enhanced "high density lipoprotein (HDL)" and decreased "hyperglycemia", "triglycerides (TGs)", "very low density lipoprotein (VLDL)", "non-HDL cholesterol", "coronary risk index (CRI)" and "cardiovascular risk index (CVRI)". The authors also claimed that their study findings confirmed the reproducibility of glucose minimizing and hypolipidemic effects of honey. They also found that Nigerian honey improves hyperglycemia and dyslipidemia in alloxan-induced diabetic rats. Study findings showed that glucose minimizing and hypolipidemic effects of honey have not been limited to the types of honey of various geographical origins. The study showed that a minimum dose of 1.0 gm/kg body weight improves the glycemic control and hyperlipidemia (Erejuwa et al., 2011; Bahrami et al., 2009).

Erejuwa et al. (2010) investigated the hypoglycemic and antioxidant effects of honey in streptozotocin-induced diabetic rats. The authors concluded that honey has hypoglycemic effect streptozotocin-induced diabetic rats. Erejuwa et al. (2011) reported that honey significantly increased insulin, decreased hyperglycemia. They found that anti-diabetic drugs such as glibenclamide or metformin combined with honey significantly lower blood glucose and fructosamine levels. This remedy with honey increased insulin levels. These results demonstrate that combination of glibenclamide or metformin with honey improves the glycemic control and provides better metabolic benefits which cannot be attained by either glibenclamide or metformin alone. Similarly, Fasanmade and Alabi (2008) conducted a study and examined the impact of honey on alloxan and fructose induced diabetic rats. The authors reported that daily intake honey for three weeks efficiently decreased blood glucose level in alloxan induced diabetic rats. Honey resulted in reduction in hyperglycemia induced by long-term use of fructose. It is thus established that honey may be beneficial in the management of diabetes. The effective use of honey in diabetes is advised due to its multi-characteristics constituents mainly the presence of abundant antioxidants.

Shambaugh et al. (1990) recruited 33 students for oral glucose tolerance test comparing sucrose, fructose and honey. Fructose showed slight adjustment in blood sugar, while sucrose gave upper blood sugar readings than honey at every measurement producing significantly greater glucose intolerance and this concludes that honey has effect on blood sugar levels.

Abdulrhman et al. (2013a, 2013b) conducted study on 50 type 1 diabetic patients and 30 control subjects. The author determined the fasting and postprandial serum C-peptide levels. Honey compared to sucrose had lower glycemic index and peak incremental index in both patients and control subjects. The increase in C-peptide levels after honey was significant compared to glucose or sucrose groups. This impact most probably was due to secretion of more insulin. It is a well-established fact that, hydrogen peroxide produced when honey is dissolved in water, helps in stimulating the beta-cells to secrete insulin which provide possible mechanism of the hypoglycemic activity of honey in diabetes (Al-Waili (2003)). Moreover, honey has been known to cause regeneration of damaged beta cells (Prasetyo and Safitri, 2016) and its effect on the beta cell enhances the repair of these cells thereby increasing insulin secretion.

Abdulrhman (2016) conducted a non-randomized open clinical trial single arm phase I cohort prospective study and investigated the usefulness of honey in a group of type 2 diabetic patients. They reported that honey ingestion caused hyperglycemia in type 2 diabetic patients. However, long-term honey consumption resulted in decreased weight and blood pressure.

Whitfield et al. (2016) conducted a randomized controlled trial and investigated the effect of daily ingestion of honey combined with "cinnamon", "chromium" and "magnesium" on glucose metabolism and lipid variables in type 2 diabetics. The combination of "cinnamon", "chromium" and "magnesium" mixing to honey was not allied with significant improvement in glycemic control in type 2 diabetic patients. Although, honey was allied with decrease in body weight and improvements in lipid variables.

Behroozi et al. (2014) reported that that honey bee venom (HBV) has antiglycation impact and HBV can be act as a natural medication against glycation-associated complications in diabetes. Nazir et al. (2014) compared the glycemic effect of honey in type 2 diabetics. The authors reported that the serum glucose level was decreased with ingestion of honey compared to glucose and indicating a lower glycemic response with honey.

Abdulrhman et al. (2011) reported that honey compared to sucrose had lowest glycemic index (GI) and peak incremental index (PII) in type 1 diabetic patients and control subjects. In the patients the upsurge in C-peptide levels after using honey was not significant compared to subjects using glucose or sucrose. However, in control group, honey produced a significant higher C-peptide level compared to glucose or sucrose. The authors reported that honey has lower GI and PII compared to sucrose, hence honey may be used as a substitute of sugar in diabetic patients.

5. Conclusion

This study investigated the preclinical, clinical, human and animal model studies on honey and diabetes mellitus and found that honey decreases the fasting blood glucose, increases fasting C-peptide and 2-h postprandial C-peptide and had lower glycemic index and peak incremental index. No doubt there is a dearth of data and literature implying the possible impact of honey in diabetes mellitus is moderate at an early stage. Moreover, the findings of animal studies may not be justly generalized to human condition, before endorsing honey as a preferred sugar substitute, therapeutic or dietary supplement in diabetic or any metabolic compromised patients, further studies are required to investigate the effects of long term consumption of honey in these patients. The dietary or therapeutic use of honey in diabetic patients still has some obstacles and challenges and needs more large sample sized, multi-center clinical controlled studies to reach better conclusions.

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