ORIGINAL | INDEPENDENT JOURNAL OF ALLIED HEALTH SCIENCES

IJAHS-0256

EFFECTS OF NATURAL HONEY ON MODIFIABLE CARDIOVASCULAR RISK FACTORS IN OVERWEIGHT AND OBESE PAKISTANI INDIVIDUALS

Faiza Samad, MBBS, MCPS, FCPS, Professor of Medicine Al Tibri Medical College & Hospital
Aziz-ur Rehman, Assistant Professor, Department of Medicine AL Tibri Medical College &Hospital
Muhammad Faisal Fahim, Statistician ISRA Ophthalmic Research & Development center
Al-Ibrahim Eye Hospital, Isra postgraduate Institute of Ophthalmology
Zaheer Ahmed, MBBS, Medical Officer Al-Tibri Medical College &Hospital

Date of Received: 11/07/2018 **Date of Acceptance:** 23/01/2019

ABSTRACT

Objective: Assess The Effect Of Natural Honey On The Modifiable Cardiovascular Risk Factors In Overweight And Obese Individuals. **Study design:** Open labeled experimental study convenience sampling. **Setting:** Isra University, Karachi Campus, Pakistan, during April 2016 to May 2016. Subjects were enrolled from family members, friends and hospital staff **Methods:** A total of 50 subjects overweight or obese fulfilling WHO South Asian criteria were divided into two groups, 30in the honey group and 20 in the control group. Seventy grams honey in 250 milliliters of water was consumed in the fasting state for 30 days, 27 subjects completed the study period. Fasting glucose, BMI, WC, BP,, TL, TC, LDL-C, HDL-C, VLDL, TG, NHDL-C , TC: HDL-C Ratio, LDL-C:HDL-C Ratio and TG: HDL-C Ratios were measured at baseline and day 31 **Results:** There was a reduction in mean WC 93.93±9.57 to 91.26±9.07 p value< 0.006 (95%CI87.67-94.85), BMI Improved obese n=11 (40.74%) subjects to n=8(29.62%) p value< 0.000. and normal to overweight in 19 (70.37%), mean fasting blood sugar reduced from mean 95.78±9.60 to 92.26±10.92,P< value 0.034 (95% CI 87.94-96.58),both systolic and diastolic blood pressures reduced P value< 0.005 (CI107.74-120.46)and P value <0.0446-78.95) respectively. Hypertension normalized in n=2 (7.46%) p-value<0.024, T Lreduced from mean670.22±256.65 to 620.04±210.82 p< value 0.015(95% C I 536.64-703.43) and at end of 30 days was normal in n=23 (85.18%) p value <0.002.TG were normal to borderline in n=24(88.8%) p value< 0.000. The TC was normal in 24(88.9%) and borderline in 3(11.11%) at the end of 30days and none of the patients remained in high group p value<0.005. Mean TC reduced P value <0.037 (95%CI 168.16-187.7) from 187.07±32.88 to177.96±24.77 The LDL- C was normal to borderline in all n=27 (100%) p value< 0.000..The NHDL-C at the end of 30days was normal inn=21 (77.8%) at end of study compared to n=17(62.96%) at the baseline no patient was in the high group p value<0.000, The HDL- C was normal to desirable in n=11(40.74%) p value< 0.019.In the control group lacked improvements in all parameters. **Conclusion:** Natural honey significantly reduced BMI, WC, fasting blood glucose, systolic and diastolic blood pressures and, hypertension. TG, TC, TL, LDL-C, and NHDL-C. HDL-C did not show a dramatic increase. HDL-Csub types exist in ethnic groups. NHDL-C has emerged as a predictor of CVD risk in South Asian race.

Correspondence Address
Faiza Samad
Professor of Medicine
Al Tibri Medical College & Hospital.
faiza.samad@gmail.com

Keywords: Cholesterol, Triglycerides, BMI

Article Citation: Samad F, Rehman U A, Fahim F M, Ahmed Z. Effects of Natural Honey on Modifiable Cardiovascular Risk Factors in Overweight and Obese Pakistani Individuals. **IJAHS,** Jan-Mar 2019;01(01-10):08-17.

INTRODUCTION

In a Hadithnarrated from Abu Hurairah that the Messenger of Allah (ﷺ)said: "Whoever eats honey three mornings each month, will not suffer any serious calamity."[1]Several studies have been performed forassessing its benefits in a variety of infective diseases, hyperglycemiaand cardiovascular diseases[2,3,4] One of the leading causes of morbidity and mortality is cardiovascular diseases (CVD) worldwide. According to World Health Organization (WHO), 17.3 million people died of CVD in 2008[5]Risk factors that can be modified includediet[6,7]smoking, sedentary lifestyle and

alcohol intake. Increased levels of serum totalcholesterol (TC) along with low-density lipoprotein cholesterol (LDL-C) are one of the most important reversible risk factors for cardiovascular morbidity and mortality[7]. The American College of Cardiology and the American Heart Association (ACC/AHA) have issued guidelines to decrease TC and LDL-C. (Cholesterol Treatment Guidelines, (CTG) to reduce modifiable risk factors)[8].

Statinsi.e.3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors reduce CVD events and are used both for secondary and primary prevention[9]. However natural honey with its rich constituents of vitamins, enzymes, and minerals also has a lipid lowering effect.[2]This study was undertaken to evaluate the effects of honey in lowering modifiable CVD risk factors when taken in the fasting state in overweight and obese adults.

MATERIAL AND METHODS

Subjects: A total of 50 subjects, were selected, 30 subjects in the honey group of whom 3 dropped out leaving 27,mean age 35.81 SD± 11.2ranges 21-64,12 were females and 15 males. Ofthe 20 in the control group mean age was 35.85± 14.01 ranges 24-72. Females were 12 and males 8.Subjects were selected according to South Asian criteria for BMI categories.[10] Individuals included were overweight if their BMI was found to be> 23 kg/$m^2$and obese if BMI was 27.5 kg/m^2or more and represented high risk. Diabetics and patients with co-morbidities,chronic and debilitating diseases and pregnancy were excluded.

Participants in this open labeled experimental study convenience sampling were allocated to honey group from friends, family and from staff of Isra University who were reliable and motivated for taking honey in the fasting state. Controls were selected from the friends of staff of and staff of Isra University**.** Height without shoes (in meters) and weight (in kilograms) was taken and BMI was calculated as weight divided by height in meters squared (kg/m^2)[11] Waist Circumference (WC) was measured at the mid-point between the lower costal margin and the level of the anterior superior iliac crest as recommended by WHO[12].Therecommended criteria for South Asian was abnormal for Men if 90 cm and for Women if 80 (13).Blood pressure (BP) was measured with the patient in the sitting position; the right arm BP was measured with a mercury sphygmomanometer with an appropriate cuff size. Hypertension was defined as a systolic BP ≥140mmHg and/or diastolic BP ≥90mmHg according to the criteria of The Joint National Committee on Hypertension 7(JNC 7)[14]. Demographics included sex, age, marital status, household income, and address. Subjects in intervention group were given thirty 250 mL bottles containing 70 grams honey measured on an electronic balance and were asked to dissolve it in water to the top and consume it in the fasting state each day. Honey used was 100% natural clover honey brand name Sue Bee Honey[15]and control group received no intervention. All subjects provided Informed consent and approval was taken from the Al Ibrahim Ethical Committee. As Isra University had no committee. Anonymity was maintained

Biochemical Analysis

A 5 ml blood sample was obtained from all subjects after a14 hour overnight fast and collected into the test tubes to obtain serum, which was obtained by low speed centrifugation at 1500 × g for 10 min. Serum was separated and used for the assessment of fasting blood glucose. Lipid profile included total lipids,(TL)total cholesterol (TC)Triglycerides(TG),low density lipoprotein cholesterol(LDL- C),high density lipoprotein cholesterol(HDL- C),non- high density lipoprotein Cholesterol (NHDL-C)**,** Cholesterol: HDL-C Ratio, Cholesterol: LDL-C Ratio, Triglycerides: HDL C-Ratio Test was done on Beckman CoulterAU480 completely automated, random access Clinical Chemistry analyzer[16].

Statistical analysis

Data was analyzed through the software SPSS version 20.0. The continuous variables (Age, Height, Weight, and Systolic and Diastolic Blood Pressure) were presented in Mean Standard Deviation. All categorical variables (Gender, BMI, Ethnic group, and Hypertension) were presented in frequencies and percentages. To see the significance one way ANOVA, ANCOVA or Chi Square test was applied for different variables. P-value < 0.05 was considered to be statistically significant.

RESULTS

Comparing the results of both groups at end of 30 days, there was a significant reduction in mean waist circumference 93.93±9.51 (95% CI 90.16-97.69) to91.26±9.07 (95% CI87.67-94.85), P value<0.006.(Table I) and (Table II), Fasting blood sugar reduced from mean 95.78±9.60 (95% CI 91.98-99.58) to 92.26±10.92 (95% CI 87.94-96.58), P value<0.034.

In the honey group both mean systolic and diastolic blood pressures reduced P value <0.005(95%CI107.74-120.46)and P value <0.04(95% CI 71.46-78.95) respectively.

T Lreduced P value< 0.015 from mean 670.22±256.65 (95% CI 568.69-771.75)to 620.04±210.82 (95% CI 536.64-703.43) TC dropped from mean187.07±32.88 (95% CI 174.07-200.08) to177.96±24.77 (95% CI 168.16-187.76)P value <0.037.

VLDL-C was 29.56±12.02 (CI 20.84-38.27) and reduced to27.33±13.44 (CI27.33±13.44) P value <0.24.

HDL- C decreased from 41.74±8.89,(95% CI38.22-45.26)to 38.07±9.07(95% CI I34.49-41.66) P value< 0.000

The AHA recommended Cholesterol: HDL-C Ratio and LDL-C: HDL-C Ratio showed no improvement.

Honey Group (n=27)			
Parameters	Baseline	After 30 days	P-value
SBP(mmHg)	117.6±11.5	114.1±13.7	0.005
95% Confidence Interval	112.11-123.25	107.74-120.46	
DSBP(mmHg)	74.8±19.8	75.2±7.7	0.04
95% Confidence Interval	65.34-84.44	71.46-78.95	
Waist Circumference (cm)	93.93±9.51	91.26±9.07	0.006
95% Confidence Interval	90.16-97.69	87.67-94.85	
BMI (kg/m2)	27±4.69	26.81±4.54	0.134
95% Confidence Interval	25.14-28.86	25.02-28.61	
Fbs (mg/dl)	95.78±9.60	92.26±10.92	0.034
95% Confidence Interval	91.98-99.58	87.94-96.58	
Cholesterol (mg/dl)	187.07±32.88	177.96±24.77	0.037
95% Confidence Interval	174.07-200.08	168.16-187.76	
Triglycerides (mg/dl)	148±54.22	137.41±95.20	0.26
95% Confidence Interval	104.46-191.54	99.74-175.07	
HDL (mg/dl)	41.74±8.89	38.07±9.07	0.000
95% Confidence Interval	38.22-45.26	34.49-41.66	
LDL (mg/dl)	115.81±27	113.07±23.84	0.424
95% Confidence Interval	105.13-126.50	103.64-122.51	
VLDL (mg/dl)	29.56±12.02	27.33±13.44	0.24
95% Confidence Interval	20.84-38.27	20.02--34.65	
Total lipids (mg/dl)	670.22±256.65	620.04±210.82	0.015
95% Confidence Interval	568.69-771.75	536.64-703.43	
Cholesterol: HDL-C Ratio	4.56±1.42	5.0±1.33	0.003
95% Confidence Interval	3.99-5.12	4.47-5.53	
LDL-C: HDL-C Ratio	2.89±0.84	3.22±0.97	0.01
95% Confidence Interval	2.55-3.22	2.84-3.61	
Triglyceride: HDL-C Ratio	4.0±1.7	4.15±1.81	0.637
95% Confidence Interval	2.13-5.87	2.60-5.70	
NHDLC (mg/dl)	145.37±32.92	140.0±27.66	0.155
95% Confidence Interval	132.35-158.39	129.06-150.94	

Honey Group (n=27)			
Parameters	Baseline	After 30 days	P-value
SBP(mmHg)	111.6±12.7	110.74±17.6	0.355
95% Confidence Interval	105.52-117.84	101.74	
DSBP(mmHg)	75.9±7.9	75.7±7.6	0.421
95% Confidence Interval	72.10-79.78	72.09-79.37	
Waist Circumference (cm)	93.56±9.81	94.51±9.11	0.41
95% Confidence Interval	88.97-98.15	90.25-98.78	
BMI (kg/m2)	26.55±3.37	26.84±3.72	0.3
95% Confidence Interval	24.97-28.13	25.09-28.58	
Fbs (mg/dl)	93.55±8.92	95.54±12.1	0.287
95% Confidence Interval	89.37-97.72	89.87-101.22	

Cholesterol (mg/dl)	172.60±31.35	171.85±35.04	0.844
95% Confidence Interval	157.92-187.27	155.44-188.25	
Triglycerides (mg/dl)	128.6±55.2	123±55.1	0.54
95% Confidence Interval	102.72-154.47	97.18-148.81	
HDL (mg/dl)	45.35±20.10	41.85±17.22	0.301
95% Confidence Interval	35.94-54.75	33.79-49.90	
LDL (mg/dl)	109.5±27.2	112.35±27.92	0.508
95% Confidence Interval	96.76-122.33	99.27-125.42	
VLDL (mg/dl)	26.6±11.5	24.9±10.9	0.349
95% Confidence Interval	21.19-32.00	19.78-30.01	
Total lipids (mg/dl)	615.7±166.02	597±165.57	0.35
95% Confidence Interval	537.99-693.44	519.50-571.00	
Cholesterol: HDL-C Ratio	4.46±0.83	4.55±1.01	0.368
95% Confidence Interval	4.07-4.85	4.07-5.02	
LDL-C: HDL-C Ratio	2.93±0.71	2.93±0.84	0.512
95% Confidence Interval	2.60-3.26	2.59-3.38	
Triglyceride: HDL-C Ratio	3.36±1.37	3.21±1.46	0.614
95% Confidence Interval	2.71-4.00	2.52-3.89	
NHDLC (mg/dl)	135.3±27.1	134.9±30.8	0.903
95% Confidence Interval	122.57-148.02	120.47-149.32	

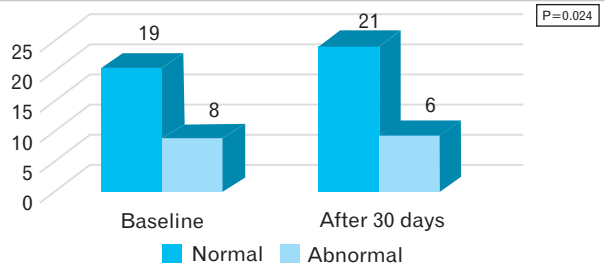

Figure 1: Systolic blood pressure mmHg (Honey Group)

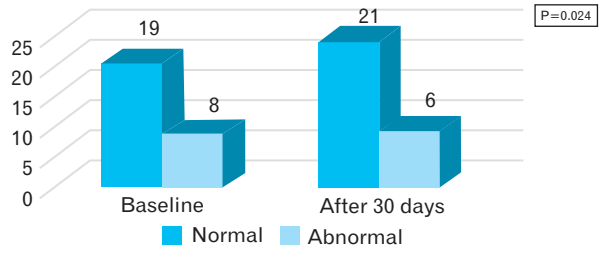

Figure 2: Diastolic blood pressure mmHg (Honey Group)

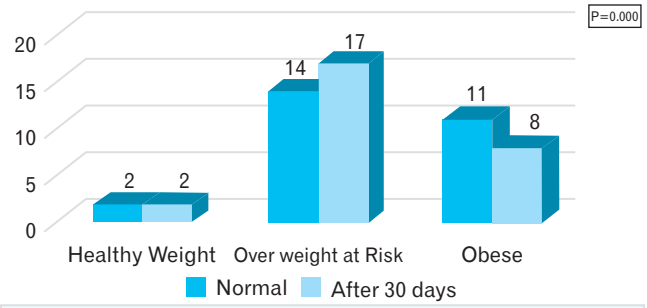

Figure 3: BMI (kg/m2): South Asian Criteria (Honey Group)

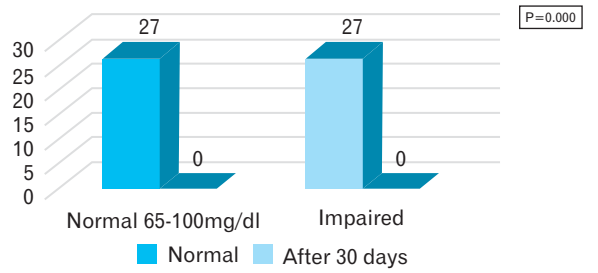

Figure 4: Triglycerides: mg/dl (Honey Group)

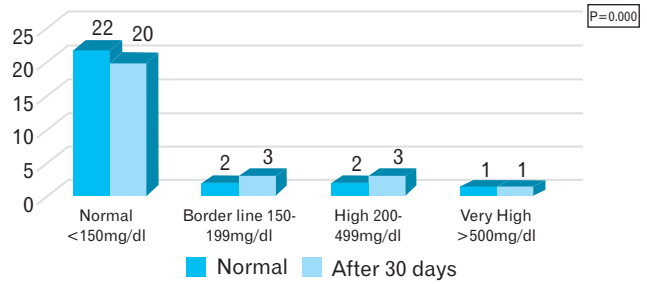

Figure 5: Fasting Blood Sugar mg/dl: (Honey Group)

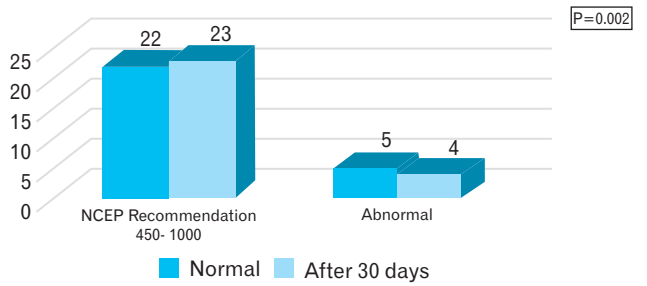

Figure 6: Total LIPIDS mg/dl (Honey Group)

Hypertension (Figure I) became normal in n=2(7.41%)P-value< 0.024. BMI improved obese subjects at end of 30 days were n=8(29.62%) as compared to n=11 (40.74%) P value<0.000 and normal to overweight in 19 (70.37%).Triglycerides were normal to borderline in n=24(88.8%), P value <0.000. Total lipids were normal at the end of 30 days in n=23 (85.18%) P value< 0.002.The NHDL-C in n=21(86.8%) was in the desired range at end of study as compared to n=17(61.3%),on day 1P value <0.000.

The TC was normal in 24(88.9%) and borderline in 3(11.11%) at the end of 30days and none of the patients remained in high group P value<0.005. (Figure II) The LDL Cholesterol was normal to

borderline in all n=27 (100%) P value <0.000.The HDL -C Cholesterol however was normal to desirable in n=11(40.74%)Pvalue<0.019.

The NHDL-C at the end of30days was in normal range n=21 (77.8%) at end of study compared to n=17(62.96%) and no patient was in the high group P value<0.000, The AHA recommended ratio showed no improvement in 2of the three categories, Cholesterol: HDL-C Ratio p-value 0.003 and LDL-C: HDL-C Ratiop value <0.01.

In the control group there were no improvements in all parameters.

DISCUSSION

Cardiovascular diseases have a number of risk factors, some are not modifiable like age, gender and family history[17,18] the modifiable ones are hypertension, dyslipidemia, diabetes mellitus , lifestyle modifications such as a healthy diet , giving up smoking and alcohol, physical activity and control of obesity[6,7]

Honey was used to assess its role in ameliorating the modifiable risk factors in CVD. Elevated waist circumference (WC) is an important risk factoras compared to BMI as it reflects the distribution of visceral body fat[19,20]. It is manifested as central obesity leading to a higher risk of developing hypertension, diabetes mellitus, and hyperlipidemia[21]. In the present study both BMI and WC improved, obese subjects at end of 30 days as compared to baseline were 29.62% as compared to40.74% and normal to overweight in 70.37%,P value< 0.000. There was a reduction in mean WC from 93.93±9.57 to 91.26±9.07 P value< 0.006 (95%confidence interval 87.67-94.85)
A United States study showed that leptin levels were lowered in the serum of honey fed ratswith subsequent reduction in weight gain and obesity compared to a diet of equal energy[22]. Similar results were found in 2 studies in New Zealand in rats[23,24] An Iranian study found that 70 g of natural honey reduced body weight by 1.3% and body fat by 1.1%in overweight and obese subjects[25]. A study from Quetta Baluchistan showed that 70 g of honey had a favorable response in weight reduction and lipid profile.[26]

The meanfasting blood sugar reduced from 95.78±9.60 to 92.26±10.92 P value <0.034 (95% CI 87.94±96.58.) Two patients with impaired fasting glucose were normal at the end of the study period. Other studies have shown that honey reduces fasting glucose[19,27,28] by 5 %. Honey lowers fasting glucose, by increasing fasting and 2-h postprandial C-peptide[29]. A study by the author[30] on 97 patients with type2 diabetes in a honey tolerance test showed that the rise in blood glucose level at 60 and 180 minutes was significantly lower in the honey group compared to the standard 75g grams glucose tolerance test moreover low dose honey 30 grams reduced sugar levels to normal in 10% of patients. Honey significantly decreased blood glucose level in diabetic rats and TC, TG, LDL, VLDL in another study.[31]

Comparing the blood pressure results of both groups at end of 30 days in the honey group both systolic and diastolic blood pressures were reduced P value< 0.005 (CI107.74-120.46)and P value <0.04(95% CI 71.46-78.95) respectively. In the honey group 7.46% patients with hypertension became normotensive P-value<0.024.They were asked not to take anti –hypertensives.

A Malaysian study usedtualang honey for 3 weeks in diabetic rats with hypertension with reduction in systolic blood pressure[32,33] another group found that inhalation of honey reduced systolic and diastolic blood pressure60 and 120 min after inhalation.[34]

Total lipids were normal at the end of 30 days in 85.18% P value< 0.002,Triglycerides were normal to borderline in 88.8% p value

<0.000.Although mean VLDL –C reduced after honey P values, were not significant. The TC was normal in 88.9% and borderline in 11.11% at the end of 30days and none of the patients remained in high group P value<0.005. The LDL- C was normal to borderline in 100% P value <0.000.The AHA recommended ratio showed no improvement in 2of the three categories. In the control group there were no improvements in all parameters.

Several studies support the improvement in lipid profile. In Iran, 48 patients with type 2 Diabetes Mellitus received natural honey for eight weeks; with a resultant decrease in TC, LDL-C, and TG and increased HDL-C)[34]. Two more Iranian studies showed that Honey improved the lipid profile such as TC, TG and LDL and HDL[24,35]A study from Quetta found a decrease in TC, LDL –C and TG, and increase in HDL-C in young healthy adults[36].The NHDL-C was in the desired range in 86.8% at end of study as compared to 61.3% P value <0.000. The importance of NHDL-C should not be overlooked .There are ethnic differences in the various lipid parameters, are trospective study found that low levels of NHDL-C was a risk factor for CVD.[39]

HDL -C was normal to desirable in 40.74%pvalue <0.019 but the mean value decreased from 41.74±8.89, (95% CI 38.22-45.26) to 38.07±9.07 (95% CI34.49-41.66) p value< 0.000.

The decrease in mean HDL-C value may seem unexpected as it is believed to remove excess cholesterol from peripheral cells and atherosclerotic plaques to the liver[3]. This view has been challenged[40,41,42]), as elevated HDL-C that is genetically raised does not protect against myocardial infarction[43,44]. Variant apolipoproteins are responsible low HDL-C[43].A study from Multan[26] found honey to have a lowering effect on lipids as a whole but only an imperceptible increase of HDL-C in some ethnic groups. This supports the presence of subtypes of HDL in Pakistan as well.[45] High level of HDL-C alone is not a predictor of low risk in the presence of high levels of LDL-C and TG[45]. The current concept of HDL-C is that molecules may either be functional or dysfunctional [46,47] and qualitative molecules are more important than the quantitative ones. It is highly likely that HDL-C molecules in this study despite the decrease in mean value became more functional as seen by the improvement in all modifiable risk factors. Studies[47,48,49] have looked into dysfunctional HDL--Cin groups of patients with high risk factors and studied the different subtypes of HDL for predicting risk for CVD. Qualitative molecules are less important quantitative ones.[48]

CONCLUSION

Natural honey was effective in improving all the modifiable risk factors for CVD significantly. The HDL –C although did not increase as expectations but as the concept of HDL-C has changed ethnicsub types differ in levels, high HDL-Cin isolation is not protective in the presence of elevated TG and LDL-C. Furthermore dysfunctional molecules exist, and honey most likely made them functional. There is now a role for NHDL-C as well for in identifying subjects at high risk for CVD especially in South Asians.

LIMITATIONS

The number of patients were limited as it was difficult to rely on subjects to take honey in a fasting state .It would be interesting to study the different subtypes of HDL-C in ethnic groups in Pakistan and dysfunctional molecules where facilities are available.

CONFLICT OF INTEREST

None

FUNDING

NONE

REFERENCES

1. Sunan ibn majah .Chapters on medicine: Vol. 4, Book 31, Hadith 3450

2. Al-Waili, N. S. 2004. "Natural Honey Lowers Plasma Glucose, C-Reactive Protein, Homocysteine, and Blood Lipids in Healthy, Diabetic, and Hyperlipidemic Subjects: Comparison with Dextrose and Sucrose." J. Med. Food 7: 100-7.

3. Nazir N, Samad F, Kidwai SS, Wahid H,Siddiqi S,Zehravi M. Comparison of glycaemic response to honey and glucose in type 2 diabetes. JPMA 201464: 69; 72-74.

4. Shivkumar Y. Herbs used in Management of Obesity. International Journal of Institutional Pharmacy and Life Science. 2011 1(1):7-17

5. Siri-Tarino PW, Sun Q, Hu FB,and KraussRM. Saturated fat, carbohydrate, and cardiovascular disease. Am J ClinNutr 2015; 91:502-9

6. WORLD HEART FOUNDATION 2017 Cardiovascular risk factor)https://www.world-heart-federation.org/resources/risk-factors

7. Bertoluci MC and Rocha VZ Cardiovascular risk assessment in patients with diabetes.DiabetolMetabSyndr (2017)9(1):25 doi: 10.1186/ s13098-017-0225-1.

8. Martin SS, Abd TT, Jones SR,Michos ED, Blumenthal RS, Blaha MJ. ACC/AHA cholesterol treatment guideline, what was done well and what could be done better. J Am CollCardiol 2014; 63:2674-8.

9. Stone NJ, Robinson J, Lichtenstein AH, Merz CNB, Lloyd-Jones DM, Blum CB, ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults, J Am CollCardiol. 2014; 63(25 Pt B):2889-934 .doi: 10.1016/j.jacc.2013.11.002

10. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004; 363(9403): 157-163.

11. Must A and Anderson S. Body mass index in children and adolescents: considerations for population-based applications. International Journal of Obesity. 2005; 30(4): 590-4. doi:10.1038/sj.ijo.0803300

12. Bodicoat DH, Gray U, Henson J, Webb D, Guru *A*, Misra A. Body Mass Index and Waist Circumference Cut-Points in Multi-Ethnic Populations from the UK and India PLOS ONE 2014 9(3) 1-6

13. Ma WA, Yang CY, Shih SR, Hsie HJ, Hung CS, Chiu FC. Measurement of Waist Circumference Midabdominal or iliac crest? Diabetes Care 2013. 36:1660–1666,

14. National Institutes of Health (NIH). Reference Card from the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7). 2003, NIH; US Department Of Health And Human Services.

15. FAQ Section Available from URL www.suebee.com/honey_101Faq Section

16. Miller M, Ginsberg HN,Schaefer FJ: Relative atherogenecity and value of non-high-density lipoprotein cholesterol for coronary heart disease. Am J. Cardiol 2008, 101:1003-8

17. Fryar CD, Chen T, Li X. Prevalence of Uncontrolled Risk Factors for Cardiovascular Disease: 2012. United States, 1999–2010. NCHS Data Brief, No. 103. Hyattsville, MD: National Center for Health Statistics, Centers for Disease Control and Prevention, US Dept. of Health and Human Services

18. Steven G. Chrysant MD, George S. Chrysant MD.Treatment of Modifiable Risk Factors Is Associated with Decrease in Coronary Heart Disease Incidence: Time to Use the Polypill. JCH 2016.18(9) 840-842 https://doi.org/10.1111/jch.12827

19. Adegbija O, Wendy ,Hoy W and Wang Z. Prediction of cardiovascular disease risk using waist circumference among Aboriginals in a remote Australian community. BMC Public Health2015.15:57 1-9https://doi.org/10.1186/s12889-015-1406-1

20. **Dijk SB, Takken T, Prinsen EC, and,** Wittink H. **Different anthropometric adiposity measures and their association with cardiovascular disease risk factors: a meta-analysis. Neth Heart J 2012;20:208-18.**doi:10.1007/s12471-011-0237-7

21. Ma, WY , Yang CY, Shih SR, Hsieh HJ, Hung CS, Chiu FC, Measurement of Waist Circumference Midabdominal or iliac crest? Diabetes Care 2013; 36(6): 1660-1666.https://doi.org/10.2337/dc12-1452

22. Nemoseck TM, Carmody EG, Furchner-Evanson A, Gleason M, Li A, Potter H,: Honey promotes lower weight gain, adiposity, and triglycerides than sucrose in rats. Nutr Res 2011; 31:55–60

23. Chepulis L, and Starkey N: The long-term effects of feeding honey compared with sucrose and a sugar-free diet on weight gain, lipid profiles, and DEXA measurements in rats. J Food Sci 2008; 73:H1–H7

24. Chepulis L: The effect of honey compared to sucrose, mixed sugars, and a sugar-free diet on weight gain in young rats. J Food Sci 2007; 72:S224–S229.

25. Yaghoobi N, Al-Waili N, Ghayour-Mobarhan M, Parizadeh S, Abasalti Z, Yaghoobi Z,: Natural honey and cardiovascular risk factors; effects on blood glucose, cholesterol, triacylglycerole, CRP, and body weight compared with sucrose. Scientific World Journal 2008; 8:463–469.

26. Mushtaq R, Mushtaq R, Khan TS. Effects of Natural Honey on Lipid Profile and Body Weight in Normal Weight and Obese Adults: A Randomized clinical trial. Pakistan. J Zool, 2011; 43(1), 161-169

27. Al-Waili NS: Effects of daily consumption of honey solution on hematological indices and blood levels of minerals and enzymes in normal individuals. J Med Food 2003; 6:135–140

28. Al-Waili N: Natural honey lowers plasma glucose, C-reactive protein, homocysteine, and blood lipids in healthy, diabetic, and hyperlipidemic subjects: comparison with dextrose and sucrose. J Med Food 2004; 7:100–107

29. Meo SA, Ansari MJ, Sattar K, Chaudhary HU, Hajjar W, Alasiri S. Honey and diabetes mellitus: Obstacles and challenges - Road to be repaired Saudi J Biol Sci. 2017; 24(5):1030-1033. doi: 10.1016/j.sjbs.2016.12.020. Epub 2017 Jan 11.

30. Nazir L, Samad F, Kidwai SS, Haroon W, Siddiqi S, Zehravi M. Comparison of glycaemic response to honey and glucose in type 2 diabetes JPMA 2014; 64: 69; .72-74

31. Asaduzzaman M , Rahman M S, Munira S , Rahman MM, Hasan M , Siddique MAet al. Effects of Honey Supplementation on Hepatic and Cardiovascular Disease (CVD) Marker in Streptozotocin-Induced Diabetic Rats , J Diabetes Metab 2015, 6:9 DOI: 10.4172/2155-6156.1000592

32. Erejuwa O, Sulaiman SA, Wahab MSA, Sirajudeen KNS, Salleh MSM, Gurtu S: Differential responses to blood pressure and oxidative stress in streptozotocin-induced diabetic Wistar- Kyoto rats and spontaneously hypertensive rats: effects of antioxidant (honey) treatment. Int J MolSci 2011;12:1888–1907.

33. Al-Waili N: Intrapulmonary administration of natural honey solution, hyperosmolar dextrose or hypoosmolar distilled water to normal individuals and to patients with type-2 diabetes mellitus or hypertension: their effects on blood glucose level, plasma Insulin and C-peptide, blood pressure and peaked expiratory flow rate. Eur J Med Res 2003; 8:295–303

34. Bahrami M, Ataie-Jafari A, Hosseini S, Foruzanfar MH, Rahmani M, Pajouhi M: Effects of natural honey

consumption in diabetic patients: an 8-week randomized clinical trial. Int J Food Sci Nutr 2009;60:618–626

35. Rasad H, Entezari MH, Ghadiri E, Mahaki B, Pahlavani N. The effect of honey consumption compared with sucrose on lipid profile in young healthy subjects Clin Nutr ESPEN. 2018; 26:8-12. doi: 10.1016/j.clnesp.2018.04.016

36. Erejuwa O, O. Erejuwa OO. Effect of honey in diabetes mellitus: matters arising. Journal of Diabetes and Metabolic Disorders. 2014; 13:23-36. doi:10.1186/2251-6581-13-23.

37. Majid M, Younis MA, Naveed AK, Shah MU, Azeem Z, Tirmizi SH Effects of natural honey on blood glucose and lipid profile in young healthy Pakistani males. J Ayub Med Coll Abbottabad 2013; 25(3-4):44-7

38. Bandeali S, Farmer J. High-density lipoprotein and atherosclerosis: the role of antioxidant activity. Curr Atheroscler Rep. 2012 (2):101-7. doi: 10.1007/s11883-012-0235-2

39. Wongcharoen W, Sutthiwutthichai S, Gunaparn S, Phrommintikul A. Is non-HDL-cholesterol a better predictor of long-term outcome in patients after acute myocardial infarction compared to LDL-cholesterol? : a retrospective study. BMC Cardiovascular Disorders. 2017;17:10.1-16 doi:10.1186/s12872-016-0450-9.

40. Hewing B,. Moore KJ, and. Fisher E A. HDL and Cardiovascular Risk: Time to Call the Plumber? Circ Res. 2012 October 12; 111(9): 1117–1120. doi:10.1161/CIRCRESAHA.112.280958

41. Voight BF, Peloso GM, Orho-Melander M,, Frikke-Schmidt R, Barbalic M, Jensen MK et al. Plasma HDL cholesterol and risk of myocardial Infarction: a mendelianrandomisation study. Lancet. 2012; 380:572–580.

42. Tall AR (2008). Cholesterol efflux pathways and other potential mechanisms involved in the athero-protective effect of high density lipoproteins. J Intern Med 263: 256–273.

43. Singh V, Sharma R, Kumar A, Deedwania P (2010). Low high-density lipoprotein cholesterol: current status and futurestrategies for management. Vasc Health Risk Manag 6: 979–996.

44. Fazio S, Linton MF. High-density lipoprotein therapeutics and cardiovascular prevention. J ClinLipidol. 2010; 4:411–419.

45. Bartlett J, Predazzi IM, Williams SM, et al. Is isolated low high-density lipoprotein cholesterol a cardiovascular disease risk factor? New insights from the Framingham Offspring Study. Circ Cardiovasc Qual Outcomes 2016; 9:206-212.DOI:10.1161/CIRCOUTCOMES.115.002436

46. Singh V, Deedwania P. Dyslipidemia in special populations: Asian Indians,African Americans and Hispanics. Curr Atheroscler Rep. 2006; 8:32–40.

47. Banach M, Rysz J, Rizzo M, Otvos J, Toth P. P. Pencina M. Jet al. Investigating dysfunctional HDL in selected groups of patients at high risk of cardiovascular events (DYS-HDL study): Protocol and organization. *Atherosclerosis* 2014; 235:e171–e172 DOI: https://doi.org/10.1016/j.atherosclerosis.2014.05.496Avaiablehttps://www.atherosclerosis-journal.com/article/S0021-9150(14)00732-1/fulltext accessed June 10 2018.

48. Agouridis AP, Banach M, Dimitri P. Mikhailidis M, Dimitri P. Mikhailidis Dysfunctional high-density lipoprotein: not only quantity but first of all quality? Arch Med Sci. 2015 Mar 16; 11(1): 230–231.doi: 10.5114/aoms.2015.49816

49. American College of Cardiology (ACC.) 2017 Jensen J, Miedema, Expert Analysis: Quality Over Quantity: The Role of HDL Cholesterol Efflux Capacity in Atherosclerotic Cardiovascular Disease, 2017 Available on line :http://www.acc.org/latest-in-cardiology/articles/2017 /02/01/07/34/quality-over-

quantity accessed 21/6/18

50. Gao F. · Ren Y. · Shen X. · Bian Y. · Xiao C. · Li H. Correlation between the High Density Lipoprotein and its Subtypes in Coronary Heart Disease Cell Physiol Biochem 2016; 38:1906-1914https://doi.org/10.1159/000445552.

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Faiza Samad	Concept, design, data collection, preparation of manuscript & Final Manuscript	
2	Aziz-ur Rehman	Recruitment of subjects, Collection of Data and Lab Coordination	
3	Muhammad Faisal Fahim	Data analysis, and preparation of Tables and Graphs	
4	Zaheer Ahmed	Data Collection, blood sampling and Lab Coordination