## Systematic Review

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# Effect of Ramadan fasting on glycaemic parameters & body mass index in type II diabetic patients: A meta-analysis

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*Background & objectives*: There has been an ongoing debate about the impact of Ramadan fasting (RF) on the health of these individuals who fast during Ramadan. The aim of this meta-analysis was to evaluate the relationship between RF and glycaemic parameters in type 2 diabetes mellitus (T2DM) patients.

*Methods*: Search terms were decided and databases such as MEDLINE EBSCO, Google Scholar and EMBASE were searched for eligible studies. Standardized mean differences and 95 per cent confidence intervals (CIs) of post-prandial plasma glucose (PPG), fasting plasma glucose (FPG), glycated haemoglobin (HbA<sub>10</sub>) (%) and fructosamine levels were calculated for different treatment regimens.

*Results*: Of the 40 studies, 19 were found eligible for inclusion in the meta-analysis. Based on pooled results, significant reductions in FPG were found in single oral antidiabetics (OAD) [standardized weighted mean difference (SMD)=0.47, 95% CI=(0.20-0.74)], multi-OAD [SMD=0.36, 95% CI=(0.11-0.61)] and multitreatment subgroups [SMD=0.65, 95% CI=(0.03-1.27)] and overall [SMD=0.48, 95% CI=(0.27-0.70)]. Furthermore, HbA<sub>1c</sub> (%) [SMD=0.26, 95% CI=(0.03-0.49)] and body mass index (BMI) [SMD=0.18, 95% CI=(0.04-0.31)] were significantly decreased in the multi-OAD group.

*Interpretation & conclusions*: The meta-analysis showed that RF was not associated with any significant negative effects on PPG and fructosamine levels. However, BMI and FPG and HbA<sub>1c</sub> (%) were positively affected by RF.

Key words Fasting plasma glucose - glycated haemoglobin (%) - post-prandial plasma glucose - Ramadan fasting - T2DM

Type 2 diabetes mellitus (T2DM) is the most common type of DM and affects around 95 per cent of people with DM around the world<sup>1,2</sup>. The World Health Organization (WHO) estimated that in 2015, more than 415 million people worldwide were living with diabetes<sup>3</sup>, and in 2014, the International Diabetes Federation estimated that diabetes resulted in five million deaths<sup>4</sup>. It is estimated that around 40 to 50 million individuals with diabetes worldwide fast during Ramadan<sup>5</sup>. During fasting, they abstain from eating, drinking, taking oral medications and smoking from sunrise to sunset. Because people fast from dawn to sunset, they consume substantial quantities of sugary foods and carbohydrate-rich meals during non-fasting hours<sup>5</sup>. It is assumed that these traditionally rich

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foods associated with Ramadan may present a risk of hyperglycaemia and weight gain for diabetic patients<sup>5</sup>. In healthy people, this fasting does not have any harmful consequences on health<sup>6</sup>. However, it can induce several complications in patients with diabetes<sup>7,8</sup>. There is only one previously published meta-analysis that showed the impact of fasting on health parameters in a healthy population<sup>6</sup>. An outcome of interest of other three meta-analysis was the occurrence of hypoglycaemic events in T2DM patients who fast during Ramadan<sup>9-11</sup>. There is perhaps no meta-analysis that included before-after studies to show any effect of RF on glycaemic parameters used for monitoring T2DM patients. For this reason, this meta-analysis was conducted including all recent studies on T2DM with the aim to demonstrate the impact of RF on the most widely reported health outcomes including post-prandial plasma glucose (PPG), fasting plasma glucose (FPG), glycated haemoglobin (HbA<sub>1</sub>,) (%), fructosamine levels and body mass index (BMI).

## **Material & Methods**

*Literature search*: A systematic review protocol was developed for the meta-analysis, and MEDLINE EBSCO, Google Scholar and EMBASE databases were searched from January 2010 to August 2017. Terms such as Ramadan, Ramadan fasting, diabetes, BMI, body weight, fructosamine, PPG, FPG, *etc.*, were used to search appropriate studies in literature.

*Study inclusion/exclusion criteria*: All studies included in the meta-analysis compared the outcomes before and after RF. Studies were included when at least one of the following outcome indicators had been evaluated: PPG, FPG, HbA<sub>1c</sub> (%), fructosamine levels and BMI. Details are shown in Figure 1. Studies on patients with T2DM with co-morbidities such as cardiovascular disease were excluded. Only studies with adult participants were considered.

*Outcome measures*: In this study, results were combined for five outcome indicators: PPG, FPG, HbA<sub>1c</sub> (%), fructosamine levels and BMI. Among the included

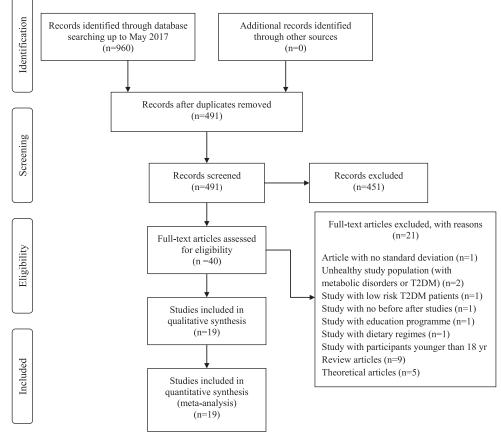


Fig. 1. PRISMA flow diagram of search results.

studies, these were the most commonly used outcomes for which results were available.

*Data extraction and quality assessment*: Authors, publication year, sample size, characteristics of the population studied and outcome measures were recorded. Two authors independently screened the titles, abstracts and keywords to identify eligibility and assessed methodological quality of the included studies and recorded the findings and the studies were included when both agreed. Any disagreement was discussed with a third author. Quality of the paper was assessed based on the Newcastle-Ottawa Scale<sup>12</sup>. All of included studies achieved a score of 7 out of 8 on that scale. All of the outcome variables were used as descriptive statistics.

*Treatment subgroups*: All patients with T2DM participating in the studies included in the meta-analysis were given different therapies. To evaluate the effect of different treatment regimens, studies were classified into three different subgroups: single oral antidiabetics (single OAD), multi-OAD and multitreatment (OAD plus insulin or diet modification).

Data analysis: Data analysis was performed using the guideline for statistical methods as described by the Cochrane Collaboration<sup>13</sup>. Random effect models were used to conduct meta-analysis of continuous outcomes to eliminate the effect of heterogeneity on results for all outcomes<sup>14</sup>. A sensitivity analysis was performed to identify studies with poor quality<sup>15</sup>. The earliest, the largest, the smallest and studies with the most contradictory results were excluded sequentially to see how these affected the meta-analysis when included in the sensitivity analysis. Separate funnel plots to assess potential publication bias for individual outcome variables were plotted. Egger regression test<sup>13</sup> to check funnel plot asymmetry was applied using metaphor package in R package v3.5.1 for windows (https:// cran.r-project.org/bin/windows/base/old/3.5.1/). Meta-analysis results were presented with a forest plot. Since the units for the variables differed between the publications, these were converted into the most commonly used units to be able to combine results. The standardized weighted mean difference (SMD) and 95 per cent confidence intervals (CI) were used as a summary statistic in the meta-analysis to assess the same outcome. SMD can be considered as a uniform scale between 0 and 1 to express intervention effect<sup>14,15</sup>. A SMD less than 0.40 is interpreted as a small effect

size, a SMD between 0.40 and 0.70 as moderate and >0.70 as a large effect size<sup>16</sup>. Analysis was performed using RevMan 5.03<sup>17</sup>.

## Results

The search strategy identified a total of 960 records (Fig. 1). Among the 40 studies identified, 19 publications with 33 independent treatment groups met the study inclusion criteria. Details of all included studies and treatments are given in Table I. A total sample of 2457 patients was included in the meta-analysis. Five of the included studies were performed in Turkey<sup>18-22</sup>, and three were multicentered<sup>23-25</sup>. In studies by Almutari<sup>26</sup> and Belkadir<sup>24</sup> younger population was included compared to the rest of the studies. Not all of the study gave gender information, but majority of the studies included both men and women in the study. Duration of fasting varied between 10 and 30 days. Time of measurements for before and after Ramadan was different for each study.

Effect of Ramadan fasting on PPG: Ten studies were included<sup>19,20,22,27</sup> in the meta-analysis to estimate the pooled reduction in PPG after RF versus before RF. A total of 199 participants were analyzed, including 108 participants in the monotherapy and 56 participants in the oral combination therapy subgroup. RF had no significant effect in the monotherapy group [SMD=0.01, 95% CI=(-0.26, 0.28), P=0.94], and no significant difference was observed in the oral combination therapy group [SMD=0.00, 95% CI=(-0.37, 0.37), P=1.000]. The overall pooled SMD for PPG was 0.06, 95% CI=[(-) 0.14-0.26], which was not significant. SMD estimates and their 95 per cent CIs are shown in Fig. 2.

*Effect of Ramadan fasting on FPG*: Fifteen studies<sup>19,20,22,26-30</sup> reporting estimates for FPG were included. A total of 624 participants were analyzed, including 364 participants in the monotherapy and 135 participants in the insulin combination therapy subgroup. The Figure 3 displays the results of the meta-analysis. FPG values were significantly decreased in single OAD [SMD=0.47, 95% CI=(0.20-0.74), P<0.001], in the multi-OAD group [SMD=0.36, 95% CI=(0.11-0.61), P=0.005] as well as in the insulin combination therapy after Ramadan [SMD=0.65, 95% CI=(0.03-1.27), P=0.04]. Furthermore, the overall result of meta-analysis was significant [SMD=0.48, 95% CI=(0.27-0.70), P<0.001]. There was heterogeneity across studies for FPG ( $I^2$ =61%, P=0.001).

	ц		29	30	39	12	13	18	17	88	001	100	50		75	23	36	276	26	26	110	21	18	10	Contd
	Subgroups Treatments		Oral antidiabetic agents alone or insulin therapy + oral antidiabetics	Metformin + vildagliptin	Metformin + sulphonylurea	Insulin premix + metformin	Insulin long-acting + metformin	Metformin	Metformin + pioglitazone + acarbose	Glinides + metformin		Ural anuquadencs	Pioglitazone		Oral antidiabetics + insulin	Metformin + vildagliptin	Metformin + suphonylurea	Metformin + glimepiride	Metformin + vildagliptin	Metformin + gliclazide	Gliclazide	Glimepiride	Repaglinide	Glargine	Coi
is	Subgroups		No subgroups	A	В	Α	В	С	D	No suberoun	MI-	subgroup	No	subgroup	No subgroup	V	В	No subgroup	Α	В	No subgroup	A	В	С	
e meta-analys	Time of measurements	After Ramadan	Last day	Last day		29 <sup>th</sup> day				At the end No of Ramadan suboroun		ı	One week	after	seventh day No sub <sub>i</sub>	$\leq six$ week	atter	One month after	10 days	after	29 <sup>th</sup> day	Four days	after		
ncluded in the		Before Ramadan	Before	Before		15 days				Two week hefore	210120	I	One week	before	10 days	One-six	week	One month before	Two days	before	First day	Two days	before		
teristics in	Duration	of fasting (days)	>15	>15		29				27		ı	30		>20	>10		ı	>15		30	ı			
Table I. Summary of the study characteristics included in the meta-analysis	Main outcome		HbA <sub>1c</sub> (%), body weight change, blood pressure, TG	HbA <sub>lc</sub> (%), hypoglycaemic	events, BMI	HbA <sub>1c</sub> (%), body weight,	BMI, PPG			PPG, FPG, HbA <sub>1c</sub> (%), body weight fructosamine		FPG, BIMI, CKP, MAP	FPG, PPG, body weight,	fructosamine, dietary pattern	Glucose level, body weight, lipid profile	Hypoglycaemic events,	$HbA_{lc}$ (%), body weight	Anthropometric characteristics and nutrient intakes	Body weight, hypoglycaemic	event, HbA <sub>1c</sub>	BMI, HbA <sub>1c</sub> (%), fructosamine	FPG, PPG, HbA <sub>1c</sub> (%),	fructosamine		
Table ]	Male/	female	15/14	ı	ı	19/57*				ı		50/0 <del>2</del>	ı		38/37	11/12	15/21	0/276	18/34		58/62*	29/20			
	Age range	or mean age±SD (yr)	57±11	57.0±9.6	54.6±9.2	57.4±10.1				59.93±9.57		10-87	45±9		52.8±8.5	58.3±13.1	57.3±11	49±6	53.2±9.7		48-60	56.5±9.2			
	Country		Singapore	USA		Turkey				Turkey	7	Nuwait	India		Pakistan	UK		Multicenter study/Algeria	UK		Morocco	Turkey			
	First author,	year	Yeoh <i>et al</i> , 2017 <sup>33</sup>	Malha et al,	$2014^{30}$	Karatoprak	<i>et al</i> , 2013 <sup>22</sup>			Şahin <i>et al</i> , 2013 <sup>21</sup>		Almutalitie $et al., 2012^{26}$	Vasan <i>et al</i> ,	2012 <sup>27</sup>	Khan <i>et al</i> , 2012 <sup>34</sup>	Hassanein	<i>et al</i> , 2011 <sup>32</sup>	Khaled & Belbraouet 2009 <sup>25</sup>	Devendra	<i>et al.</i> , 2009 <sup>35</sup>	M'guil <i>et al</i> , 2008 <sup>31</sup>	Cesur et al,	$2007^{20}$		

## AYDIN et al: RAMADAN FASTING & TYPE II DIABETES

549

INDIAN J MED RES	S, DECEMBER 2019
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First author,	Country	Age range	Male/	Main outcome	Duration	Time of me	Time of measurements S	ubgroups	Subgroups Treatments	u
year		or mean age±SD (yr)	female		of fasting (days)	Before Ramadan	After Ramadan			
Patel <i>et al</i> , 2007 <sup>36</sup>	Sultanate of Oman	54.3±11.7 146/1	146/188	88 BMI, sugar intake, food intake, fluid intake	ı	At the beginning of Ramadan	At the end No of Ramadan subgroup	No subgroup	Insulin + oral antidiabetics	334
GLIRA study Lebanon group, 2005 <sup>28</sup>	Lebanon	53.8±9.2	123/109	109 FPG, HbA <sub>1c</sub> (%), BMI	ı	One week before	At the end No of Ramadan subgroup	No subgroup	Glimepiride	232
Gustaviani et al, 2004 <sup>29</sup>	Indonesia	52.6±8	10/14	BMI, FPG, fructosamine	ı	One week before	Two week N after s	No subgroup	Repaglinide	24
Sarı <i>et al</i> , 2004 <sup>19</sup>	Turkey	57.79±7		BMI, PPG, FPG, HbA <sub>lc</sub> (%), fructosamine	ı		- B	B A	Glimepiride Gliclazide	23 17
Mafauzy, 2002 <sup>23</sup>	Multicenter shidv/	52.7±7.4	87/29	FPG, $HbA_{1c}$ (%), BMI	ı	At the heginning	At the end A	_	Repaglinide	116
	Malaysia/UK/ France/Saudi Arabia	9.5±6.9¢	82/3			of Ramadan	9	~	Gilbenclamide	611
Uysal, 1998 <sup>18</sup> Turkey	Turkey	55	11/30	HDL, LDL, HbA <sub>1c</sub> (%), BMI	ı	Two week before	Last week No of Ramadan subgroup	No 1 subgroup	Diabetic diet or single or combined oral anti-diabetics	41
Belkhadir	Multicenter	33-80	391/198*	391/198* Fructosamine, HbA <sub>1c</sub> (%),	ı	One day	day	A	Glibenclamide	78
<i>et al</i> , 1993 <sup>24</sup>	study/Morocco			body weight		before	after <sub>E</sub>	В	Glibenclamide	173
							0		Glibenclamide	95
							Π	~	Glibenclamide	87
							Ē		Glibenclamide	101
*Mismatch in plasma glucos	total number of I e; FPG, fasting I	atients is due 1 dasma glucose	co dropout ; CRP, C-1	"Mismatch in total number of patients is due to dropout. SD, standard deviation; HbA <sub>le</sub> , glycated haemoglobin; TG, triglyceride; BMI, body mass index; PPG, post plasma glucose; FPG, fasting plasma glucose; CRP, C-reactive protein; MAP, mean arterial pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein	A <sub>1c</sub> , glycated arterial press	haemoglobi sure; HDL, h	n; TG, triglycer igh-density lipc	ide; BMI, pprotein; L	Mismatch in total number of patients is due to dropout. SD, standard deviation; HbA <sub>16</sub> , glycated haemoglobin; TG, triglyceride; BMI, body mass index; PPG, post-prandial plasma glucose; FPG, fasting plasma glucose; CRP, C-reactive protein; MAP, mean arterial pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein	andial

	Before	Rama	After F	Ramad	an		Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% Cl	
1.1.1 Single OAD										
Sarı B,2004	210	57	17	196	53	17	8.5%	0.25 [-0.43, 0.92]		
Sari A,2004	162	49	23	161	51	23	11.6%	0.02 [-0.56, 0.60]		
Vasan,2012	232.56	70.74	50	242.28	78.3	50	25.2%	-0.13 [-0.52, 0.26]		
Karatoprak C,2013	156.6	37.8	18	150.3	37.8	18	9.1%	0.16 [-0.49, 0.82]	_ <u>+</u>	
Subtotal (95% CI)			108			108	54.5%	0.01 [-0.26, 0.28]	<b>•</b>	
Heterogeneity: Chi <sup>2</sup> =	1.17, df=	3 (P = (	).76); I <sup>z</sup>	= 0%						
Test for overall effect:	Z = 0.08 (	(P = 0.9	4)							
1.1.2 Multi OAD										
Cesur B,2007	159.7	68.1	18	177.7	73.2	18	9.0%	-0.25 [-0.91, 0.41]		
Cesur A,2007	211.1	55.9	21	202.1	78.2	21	10.6%	0.13 [-0.48, 0.74]		
Karatoprak D.2013	201.6	109.8	17	191.88	70.2	17	8.6%	0.10 [-0.57, 0.78]		
Subtotal (95% CI)			56			56	28.2%	0.00 [-0.37, 0.37]	<b>•</b>	
Heterogeneity: Chi <sup>2</sup> =	0.82, df=	2 (P = (	).66); I <sup>z</sup>	= 0%						
Test for overall effect:	Z = 0.00 (	(P = 1.0)	) ((							
1.1.3 Multi treatment										
Cesur C,2007	224	69.3	10	200.4	80.5	10	5.0%	0.30 [-0.58, 1.18]		
Karatoprak A,2013	264.6	10.8	12	226.8	86.4	12	5.8%	0.59 [-0.23, 1.41]		
Karatoprak B,2013	171	72	13	163.8	64.8	13	6.6%	0.10 [-0.67, 0.87]		
Subtotal (95% CI)			35			35	17.3%	0.32 [-0.15, 0.80]		
Heterogeneity: Chi <sup>2</sup> =	0.73, df=	2 (P = (	).69); I <sup>z</sup>	= 0%						
Test for overall effect:	Z=1.33 (	(P = 0.1)	3)							
Total (95% CI)			199			199	100.0%	0.06 [-0.14, 0.26]		
Heterogeneity: Chi <sup>2</sup> =	4.14, df=	9 (P = (	).90); I <sup>z</sup>	= 0%						
Test for overall effect:	Z=0.61 (	P = 0.5	4)						-2 -1 U 1 2 Before Ramadan After Ramadan	
Test for subaroup diffe		•		- 2 (P = 0	49) 12	- 0%			Belore Ramadan Alter Ramadan	

Fig. 2. Forest plot for pre-post Ramadan changes in post-prandial plasma glucose (mg/dl).

Effect of Ramadan fasting on HbA<sub>1c</sub>: A total of 22 studies<sup>18-20,22,24,28,30-33</sup> provided data for the metaanalysis for HbA<sub>1c</sub> (%) change (1173 participants, 884 in single OAD, 254 in multi OAD and 35 in multitreatment). In the subgroup analysis, there was no significant difference in monotherapy group [SMD=0.03, 95%] CI=([-]0.23-0.28), P=0.84] and oral combination therapy group [SMD=0.18, 95% CI=([-]0.29-0.65), P=0.45]. However, in multi-OAD subgroup, small significant reduction was observed [SMD=0.26, 95% CI=(0.03-(0.49), P=0.03. The overall results of random effects model showed that RF did not lead to significant changes in HbA<sub>1c</sub> (%) levels [SMD=0.13, 95% CI=([-]0.04-0.30), P=0.13] (Fig. 4). There was heterogeneity across studies for HbA<sub>1c</sub> (%) ( $l^2=71\%$ , P=0.01), but there was no difference between subgroups (P=0.72).

Effect of Ramadan fasting on fructosamine: Fifteen studies<sup>19,20,23,24,27,29,31</sup> were included in the meta-analysis to estimate the pooled changes in fructosamine after RF compared to before RF. A total of 998 participants were analyzed to evaluate changes in fructosamine levels. Most of the participants received monotherapy (n=943). RF had no significant effect [SMD=(-)0.08, 95% CI=([-]0.24, 0.08), P=0.320]. SMD estimates

and their 95 per cent CIs are shown in Fig. 5. There was heterogeneity across studies for fructosamine ( $l^2=65\%$ , P=0.001).

Effect of Ramadan fasting on body mass index: Nine<sup>18,26,27,30,31,33-36</sup> studies representing T2DM population of 959 participants reported BMI scores before and after RF. Overall, meta-analysis results of the random effects model showed marginally significant reduction in BMI levels compared to pre-Ramadan levels as shown in Fig. 6 [SMD=0.09, 95% CI=([-]0.00-0.18), P=0.06]. Furthermore, in the multi-OAD group, there was a significant decrease in BMI values [SMD=0.18, 95% CI=(0.04-0.31), P=0.01].

#### Discussion

One major finding of our meta-analysis was the reduction in the HbA<sub>1c</sub> (%) and FPG in the multi-OAD subgroup after Ramadan. In addition to these glycaemic parameters, BMI values were lower after Ramadan in this subgroup. Another meta-analysis on healthy controls also reported significant decrease in body weight after RF<sup>6</sup>. Body weight reduction might have led to improvement in these glycaemic parameters. Norris

#### INDIAN J MED RES, DECEMBER 2019

	Before Ramadan		After	Ramad	an		Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl	
5.2.1 Single OAD										
Sarı A,2004	118	20	23	117	24	23	6.5%	0.04 [-0.53, 0.62]	+	
Sarı B,2004	150	42	17	142	46	17	5.5%	0.18 [-0.50, 0.85]		
Gustaviani,2004	130.8	27.3	24	110.8	15.7	24	6.3%	0.88 [0.29, 1.48]		
GLIRA,2005	163.8	59.4	232	127.8	34.2	232	11.5%	0.74 [0.55, 0.93]	-	
Vasan,2012	154.62	55.26	50	133.56	55.08	50	8.8%	0.38 [-0.02, 0.77]		
Karatoprak C,2013 Subtotal (95% CI)	113.4	25.2	18 364	108	16.2	18 364	5.7% 44.3%	0.25 [-0.41, 0.91] 0.47 [0.20, 0.74]	•	
Heterogeneity: Tau <sup>2</sup> =	= 0.05; Ch	i <sup>2</sup> = 10.4	0, df = 5	5 (P = 0.0	6); I <sup>2</sup> = 9	52%				
Test for overall effect	Z = 3.39	(P = 0.0)	007)							
5.2.2 Multi OAD										
Cesur A,2007	140.6	32.6	21	137.7	44.6	21	6.2%	0.07 [-0.53, 0.68]	-	
Cesur B,2007	133.9	29.1	18	131.9	33	18	5.7%	0.06 [-0.59, 0.72]		
Karatoprak D,2013	160.2	54	17	135	30.6	17	5.4%	0.56 [-0.13, 1.25]	<u>+</u>	
Malha B, 2014	150.18		30		25.11	30	7.3%	0.41 [-0.10, 0.93]	+	
Malha A, 2014 Subtotal (95% Cl)	170.85	64.46	39 125	139.89	47.3	39 125	8.0% 32.6%	0.54 [0.09, 0.99] 0.36 [0.11, 0.61]	◆	
Heterogeneity: Tau <sup>2</sup> =	= 0.00; Chi	i <sup>2</sup> = 2.65	, df = 4	(P = 0.62	); $ ^2 = 0^4$	%				
Test for overall effect	Z = 2.83	(P = 0.0)	05)							
5.2.3 Multi treatment	t									
Cesur C,2007	158.6	62.6	10	146.4	32.9	10	4.0%	0.23 [-0.65, 1.11]		
Almutari,2012	151.38	15.76	100	134.82	9.54	100	10.0%	1.27 [0.96, 1.57]		
Karatoprak B,2013	118.8	46.8	13	104.4	25.2	13	4.7%	0.37 [-0.41, 1.15]		
Karatoprak A,2013	168.3	48.6	12	149.4	41.4	12	4.4%	0.40 [-0.41, 1.21]		
Subtotal (95% CI)			135			135	23.1%	0.65 [0.03, 1.27]	◆	
Heterogeneity: Tau <sup>2</sup> =				3 (P = 0.0	2); l² = 1	71%				
Test for overall effect	Z = 2.07	(P = 0.0-	4)							
Total (95% Cl)			624			624	100.0%	0.48 [0.27, 0.70]	•	
Heterogeneity: Tau <sup>2</sup> =	= 0.09; Ch	i² = 35.9	0, df = 1	4 (P = 0.	001); l²	= 61%			-4 -2 0 2 4	
Test for overall effect	Z= 4.50	(P < 0.0)	0001)						Before Ramadan After Ramadan	
Test for subgroup dif	ferences:	Chi <sup>2</sup> = 0	.86, df=	= 2 (P = 0	.65), I <sup>2</sup> :	= 0%			Bolore Ramadan Alter Ramadan	

Fig. 3. Forest plot for pre-post Ramadan changes in fasting plasma glucose (mg/dl).

et al37 showed that relatively modest weight loss was significantly associated with improvement in FPG and HbA<sub>10</sub>. Fujioka<sup>38</sup> showed that even the intention to lose weight, without significant success, improved outcomes in patients with diabetes and moderate weight loss had positive effects on metabolic control. However, another meta-analysis examining non-pharmacological weight loss in adults with T2DM did not report significant changes in HbA1639. Another meta-analysis which assessed the benefit of low calorie diet programmes in obese patients reported dramatic reductions in FPG values after two weeks and relative improvement in FPG over the course of a single week, when three per cent decrease was achieved in body weight<sup>40</sup>. Overall results of our meta-analysis also showed significant FPG reductions after Ramadan and overall BMI result was marginally significant. We did not find a significant FPG reduction in the single OAD group. Fasting patients consume substantial amounts of sugary foods

and carbohydrate-rich meals during non-fasting hours<sup>5</sup>. Therefore, monotherapy alone for the treatment of diabetes may not be sufficient for FPG control.

Since smoking is not permitted during RF, there is a consequential reduction in smoking and tobacco consumption among fasting diabetic patients. Another explanation for the improvement in FPG and HbA<sub>1c</sub> (%) could be cessation or reduction of smoking during Ramadan. In healthy young males, an increased insulin resistance was observed in acute smokers<sup>41</sup>. Other studies showed that smoking reduced insulin-mediated glucose uptake by 10-40 per cent when compared to non-smokers<sup>42,43</sup>. Other studies showed a positive association between HbA<sub>1c</sub> and total smoking exposure as measured by pack-years<sup>44,45</sup>. One of the reasons for positive outcomes of our meta-analysis could be increased treatment adherence during Ramadan. It has been shown that in most of the countries, non-

#### AYDIN et al: RAMADAN FASTING & TYPE II DIABETES

3.1.2 Single OAD Belkadir (A 1993 11.7 3.7 Belkadir (C, 1993 14.1 3.7 Belkadir (C, 1993 15 2.8 101 15.4 2.5 101 10 2.5 102 102 102 102 102 102 102 102	Before Ramadan				After	Ramad	lan	:	Std. Mean Difference	Std. Mean Difference
Belkadir Å 1993 11.7 3.7 78 11.8 3.1 78 5.9% -0.03 [-0.24, 0.28] Belkadir $P_1$ 993 14 3.8 173 14.2 3.1 173 6.7% -0.03 [-0.24, 0.28] Belkadir $D_1$ 993 14 3.8 173 14.2 3.1 173 6.7% -0.31 [-0.06, 0.02] Belkadir $D_1$ 993 14 1 3.7 87 14.6 3.1 87 6.0% -0.15 [-0.44, 0.15] Belkadir $D_1$ 993 15 2.8 101 15.4 2.5 101 6.2% -0.15 [-0.44, 0.13] GURA, 2005 8.4 1.8 222 7.3 1.3 222 6.8% 0.70 [0.51, 0.89] Karatoprak C, 2013 6.9 0.7 18 6.9 0.8 18 3.5% 0.00 [-0.56, 0.65] San A, 2004 6.6 0.9 23 6.4 1.1 23 3.9% 0.20 [-0.38, 0.78] San A, 2004 7.5 1 1.7 7.5 0.9 17 3.4% 0.00 [-0.67, 0.67] Subtoal (95% CI) 884 884 54.2% 0.03 [-0.23, 0.28] Heterogeneity. Tau <sup>2</sup> = 0.15; Ch <sup>2</sup> = 56.12, df = 9 (P < 0.00001); P = 84% Test for overall effect $Z = 0.20$ (P = 0.84) Xaratoprak 0, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.04 [-0.60, 0.71] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.04 [-0.60, 0.71] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.04 [-0.02, 1.00] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.04 [-0.20, 0.71] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.04 [-0.60, 0.71] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.04 [-0.20, 0.71] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.04 [-0.60, 0.71] Hassanein B, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.04 [-0.60, 0.71] Hassanein A, 2014 7.93 1.47 30 7.1 0.84 30 4.3% 0.08 [0.16, 1.21] Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% -0.15 [-0.61, 0.31] Karatoprak 0, 2013 8.1.5 1.7 7.6 0.9 17 3.4% 0.25 [-0.30, 0.99] Maiha B, 2014 8.47 1.75 3 9.751 1.16 39 4.8% 0.48 [-0.27, 0.77] Subtotal (95% CI) 2.5 1.7 41 5.0% 0.00 [-0.88, 0.88] Karatoprak 2,013 8.3 1.8 12 8.1 1.1 12 2.8% 0.37 [-0.41, 1.15] Subtotal (95% CI) 1.7 1.3 4.7 10.0.13 [-0.76, 0.93] Karatoprak 2,013 8.2 1.5 13 7.7 1.2 13 2.9% 0.37 [-0.41, 1.15] Subtotal (95% CI) 1.7 1173 107.3 100.0% 0.13 [-0.04, 0.30] Heterogeneity. Tau <sup>2</sup> = 0.01; Ch <sup>2</sup> = 0.44; Te = 0.9 Color); P = 0% Test for overall effect $Z = 1.51$ ( $P = 0.13$ ) Heterogeneity. Tau <sup>2</sup> = 0.01; Ch <sup>2</sup> = 0.41, df = 21 (P < 0.00001); P = 71% Test for ove	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Belkadir E 1993 14 3.8 173 14.2 3.1 173 6.7% -0.06 [ $0.27$ 0.15] Belkadir E 1993 14.1 3.7 87 14.6 3.1 87 6.7% -0.06 [ $0.27$ 0.15] Belkadir E 1993 14.1 3.7 87 14.6 3.1 87 6.7% -0.05 [ $0.27$ 0.15] Belkadir E 1993 14.1 3.7 87 14.6 3.1 87 6.7% -0.15 [ $0.44$ , 0.15] Belkadir E 1993 15 2.8 101 15.4 2.5 101 6.2% -0.15 [ $0.44$ , 0.15] Belkadir E 1993 15 2.8 101 15.4 2.5 101 6.2% -0.15 [ $0.44$ , 0.15] Belkadir E 1993 15 2.8 101 15.4 2.5 101 6.2% 0.01 [ $0.51$ , 0.89] Karatoprak C, 2013 6.9 0.7 18 6.9 0.8 18 3.5% 0.00 [ $0.65$ , 0.67] San A, 2004 6.6 0.9 23 6.4 1.1 23 3.9% 0.20 [ $0.33$ , 0.38] San A, 2004 7.5 1 17 7.5 0.9 17 3.4% 0.00 [ $0.67$ , 0.67] Subtotal (95% CI) 884 884 54.2% 0.03 [ $0.23$ , 0.28] Heterogeneily: Tau" = 0.13; Chi" = 56.12, df = 9 ( $P < 0.00001$ ); P = 84% Test for overall effect: $Z = 0.20$ ( $P = 0.84$ ) 3.1.3 Multi OAD Cesur A, 2007 6.81 0.75 18 6.56 0.97 18 3.5% 0.06 [ $0.06$ 10.31] Karatoprak D, 2013 7.1 0.84 17.55 1.7 41 5.0% -0.15 [ $0.05$ , 0.03] Maiha A, 2014 7.93 1.6 41 7.55 1.7 41 5.0% -0.15 [ $0.05$ , 0.28] Heterogeneily: Tau" = 0.05; Chi" = 13.46, df = 8 ( $P = 0.10$ ); $P = 41\%$ Test for overall effect: $Z = 2.23$ ( $P = 0.82$ ); $P = 0\%$ Test for overall effect: $Z = 2.73$ ( $P = 0.45$ ) Total (95% CI) 17.2 $0.9$ 10 7.76 0.91 10 2.5% 0.00 [ $-0.88$ , 0.88] Karatoprak A, 2013 8.3 1.8 12 ( $P = 0.10$ ); $P = 14\%$ Test for overall effect: $Z = 2.23$ ( $P = 0.45$ ) Total (95% CI) 117.3 1173 100.0% 0.13 [ $-0.04$ , 0.30] Heterogeneily: Tau" = 0.01; Chi" = 72.14, df = 21 ( $P < 0.0000$ 1); $P = 71\%$ Test for overall effect: $Z = 1.51$ ( $P = 0.100$ ); $P = 1\%$ Total (95% CI) 117.3 1173 100.0% 0.13 [ $-0.04$ , 0.30] Heterogeneily: Tau" = 0.01; Chi" = 72.14, df = 21 ( $P < 0.0000$ 1); $P = 71\%$ Total (95% CI) 117.3 1173 100.0% 0.13 [ $-0.04$ , 0.30] Heterogeneily: Tau" = 0.01; Chi" = 72.14, df = 21 ( $P < 0.0000$ 1); $P = 71\%$ Test for overall effect: $Z = 1.51$ ( $P = 0.100$ ); $P = 10\%$ Total (95% CI) 1173 1173 100.0% 0.13 [ $-0.04$ , 0.30] Heterogeneily: Tau" = 0.01; Chi" = 72.14, df = 21 ( $P < 0.0000$ );	3.1.2 Single OAD									
Belkadir C, 193 14.1 3.7 87 14.6 3.1 87 6.0% -0.31 $[0.04, 0.02]$ Belkadir C, 193 14.1 3.7 87 14.6 3.1 87 6.0% -0.15 $[-0.44, 0.15]$ Belkadir E, 193 15 2.8 101 15.4 2.5 101 6.2% -0.15 $[-0.43, 0.13]$ GLRA, 2005 8.4 1.8 232 7.3 1.3 232 6.8% 0.70 $[0.51, 0.89]$ MrSul, 2008 6.65 0.81 60 6.83 0.86 60 5.5% 0.03 $[-0.33, 0.38]$ San A, 2004 7.5 1 17 7.5 0.9 17 3.4% 0.00 $[-0.67, 0.67]$ Subtotal (95% CI) 884 884 884 54.2% 0.03 $[-0.32, 0.28]$ Heterogeneity, Tau <sup>2</sup> = 0.13; Chi <sup>2</sup> = 56.12, df = 9 (P < 0.00001); P = 84% Test for overall effect Z = 0.20 (P = 0.84) 3.1.3 Multi CAD Cesur A, 2007 6.93 1.33 21 6.68 1.06 21 3.8% 0.20 $[-0.40, 0.81]$ Cesur A, 2007 6.63 1.33 21 6.68 1.06 21 3.8% 0.06 $[-0.60, 0.71]$ Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% -0.15 $[-0.64, 0.31]$ Karatoprak D, 2013 8 15 17 7.6 0.9 17 3.4% 0.32 $[-0.56, 0.28]$ Walha A, 2014 7.93 1.47 30 7.1 0.84 30 4.3% 0.68 $[0.16, 1.21]$ Malha A, 2014 7.93 1.64 17.55 1.7 16 0.91 72.44 % 0.25 $[-0.27, 0.77]$ Subtotal (95% CI) 254 2254 37.7% 0.26 $[0.03, 0.49]$ Heterogeneity, Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 13.46, df = 8 (P = 0.10); P = 44% Test for overall effect Z = 0.23 (P = 0.82); P = 0.% Test for overall effect Z = 0.00; Chi <sup>2</sup> = 0.44, df = 8 (P = 0.10); P = 41% Test for overall effect Z = 0.00; Chi <sup>2</sup> = 0.41, df = 2 (P = 0.82); P = 0.% Test for overall effect Z = 0.75 (P = 0.45) Total (95% CI) 177 1173 1173 100.0% 0.13 $[-0.04, 0.30]$ Heterogeneity, Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 7.14, df = 2 (P = 0.002); P = 1% Test for overall effect Z = 0.75 (P = 0.45) Total (95% CI) 177 1173 1173 100.0% 0.13 $[-0.04, 0.30]$ Heterogeneity, Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 7.14, df = 2 (P = 0.002); P = 7% Test for overall effect Z = 1.57 (P = 0.45) Total (95% CI) 177 1173 1173 100.0% 0.13 $[-0.04, 0.30]$ Heterogeneity, Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 7.14, df = 2 (P = 0.002); P = 7% Test for overall effect Z = 1.57 (P = 0.45)	Belkadir A,1993	11.7	3.7	78	11.8	3.1	78	5.9%	-0.03 [-0.34, 0.28]	-
Belkadir D, 1933 14.1 3.7 87 14.6 3.1 87 0.0% $-0.15[-0.44, 0.15]$ Belkadir D, 1933 15 2.8 101 15.4 2.5 101 6.2% $-0.15[-0.43, 0.15]$ Belkadir E, 1993 15 2.8 101 15.4 2.5 101 6.2% $-0.15[-0.43, 0.15]$ Belkadir E, 1993 15 2.8 101 15.4 2.5 101 6.2% $-0.15[-0.43, 0.15]$ Karatoprak C, 2013 6.9 0.7 18 6.9 0.8 18 3.5% $0.00[-0.65, 0.35]$ San A, 2004 6.6 0.81 6.0 6.63 0.66 00 5.6% $0.03[-0.33, 0.38]$ San A, 2004 6.6 0.9 23 6.4 1.1 23 3.9% $0.20[-0.38, 0.78]$ San B, 2004 7.5 1 17 7.5 0.9 17 3.4% $0.00[-0.67, 0.67]$ Subtotal (9% CI) 884 884 54.2% $0.00[-0.67, 0.67]$ Subtotal (9% CI) 884 884 54.2% $0.00[-0.60, 0.71]$ Hessanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% $-0.15[-0.81, 0.31]$ Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% $-0.15[-0.81, 0.31]$ Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% $-0.15[-0.81, 0.31]$ Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% $-0.15[-0.81, 0.31]$ Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% $-0.15[-0.81, 0.31]$ Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% $-0.15[-0.81, 0.31]$ Hassanein B, 2014 7.93 1.47 30 7.1 0.84 30 4.3% $0.68[016, 1.21]$ Malha A, 2014 7.93 1.47 30 7.1 0.8 4.9% $0.04[018, 1.10]$ Uysal, 1988 7.3 1.6 4(1 7.55 17 7.16 0.91 10 2.5% $0.00[-0.88, 0.88]$ Karatoprak A, 2013 8.3 1.8 12 8.1 1.1 12 2.8% $0.13[-0.67, 0.93]$ <b>3.1.4 Multi treatment</b> Cesur C, 2007 7.76 0.91 10 7.76 0.91 10 2.5% $0.00[-0.88, 0.88]$ Karatoprak A, 2013 8.3 1.8 12 8.1 1.1 12 2.8% $0.13[-0.27, 0.05]$ Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 13.46, df = 8 (P = 0.10); P = 41\% Test for overall effect Z = 0.75 (P = 0.45) Total (95% CI) 173 1173 100.0% $0.13[-0.04, 0.30]$ Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.14, df = 2 (P < 0.00001); P = 71\% Test for overall effect Z = 1.5f (P = 0.13)	Belkadir B,1993	14	3.8	173	14.2	3.1	173	6.7%	-0.06 [-0.27, 0.15]	-
Belkadir $E_1^{1}$ 1993 15 2.8 101 15.4 2.5 101 6.2% -0.15 $\begin{bmatrix} -0.43 \\ 0.13 \\ 0.178,2005 8.4 1.8 232 7.3 1.3 232 6.8% 0.70 \begin{bmatrix} -0.65 \\ 0.58 \\ 0.00 \end{bmatrix} = \begin{bmatrix} -0.68 \\ 0.58 \\ 0.58 \\ 0.58 \\ 0.00 \end{bmatrix} = \begin{bmatrix} -0.68 \\ 0.58 \\ 0.$	Belkadir C,1993	13	3	95	13.9	2.8	95	6.1%	-0.31 [-0.60, -0.02]	
GLIRA,2005 8.4 1.8 232 7.3 1.3 232 6.8% 0.70 [0.51, 0.89] Karatoprak C,2013 6.9 0.7 18 6.9 0.8 18 3.5% 0.00 [-0.65, 0.65] Moriul,2008 6.65 0.81 6.60 6.63 0.66 60 5.6% 0.03 [-0.33, 0.38] San A,2004 6.6 0.9 23 6.4 1.1 23 3.9% 0.20 [-0.38, 0.78] San B,2004 7.5 1 17 7.5 0.9 17 3.4% 0.00 [-0.67, 0.67] Subtotal (9% CI) 884 884 5.2% 0.03 [-0.23, 0.28] Heterogeneity: Tau <sup>2</sup> = 0.13; ChP = 56.12; df = 9 (P < 0.00001); P = 84% Test for overall effect Z = 0.20 (P = 0.4) 3.1.3 Multi OAD Cesur A,2007 6.61 0.75 18 6.56 0.97 18 3.5% 0.06 [-0.60, 0.71] Hassanein A,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.06 [-0.60, 0.71] Hassanein B,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.06 [-0.60, 0.71] Hassanein A,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.06 [-0.60, 0.71] Hassanein A,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.06 [-0.60, 0.71] Hassanein B,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.06 [-0.60, 0.71] Hassanein B,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.06 [-0.60, 0.71] Hassanein B,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.06 [-0.60, 0.71] Hassanein B,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.05 [-0.61, 0.31] Karatoprak D,2013 8 1.5 17 7.6 0.9 17 3.4% 0.32 [-0.36, 0.99] Maiha A, 2014 8.47 1.75 39 7.51 1.16 39 4.4% 0.64 [0.18, 1.10] Uysal,1988 7.3 1.6 41 7.55 1.7 41 5.0% -0.15 [-0.58, 0.28] Yeoh, 2015 8.6 2.4 29 8 2.3 29 4.4% 0.25 [-0.27, 0.77] Subtotal (9% CI) 254 254 7.7% 0.26 [0.03, 0.49] Heterogeneily: Tau <sup>2</sup> = 0.00; ChP = 13.46; df = 8 (P = 0.10); P = 41% Test for overall effect Z = 2.23 (P = 0.43) Total (9% CI) 253 5 35 8.1% 0.18 [-0.29, 0.65] Heterogeneily: Tau <sup>2</sup> = 0.00; ChP = 0.41, df = 2 (P = 0.82); P = 0% Test for overall effect Z = 0.15 (ChP = 72.14, df = 21 (P < 0.00001); P = 71% Test for overall effect Z = 1.51 (P = 0.13) Heterogeneily: Tau <sup>2</sup> = 0.10; ChP = 72.14, df = 21 (P < 0.00001); P = 71% Test for overall effect Z = 1.51 (P = 0.13) Heterogeneily: Tau <sup>2</sup> = 0.10; ChP = 72.14, df = 21 (P < 0.00001); P = 71% Test for overall effect Z = 1.51 (P = 0.13) Heterogeneily: Tau <sup>2</sup> = 0.10; ChP = 72.14, df = 21 (P < 0.00001); P = 71% Test for overall	Belkadir D,1993	14.1	3.7	87	14.6	3.1	87	6.0%	-0.15 [-0.44, 0.15]	
GURA 2005 8.4 1.8 232 7.3 1.3 232 6.8% 0.70 [0.51,0.89] Karatoprak C, 2013 6.9 0.7 18 6.9 0.8 18 3.5% 0.00 [0.65, 0.65] Moul, 2006 6.65 0.81 6.0 6.63 0.66 60 5.6% 0.03 [0.33, 0.38] San A, 2004 6.6 0.9 23 6.4 1.1 23 3.9% 0.20 [0.38, 0.78] San B, 2004 7.5 1 17 7.5 0.9 17 3.4% 0.00 [0.67, 0.67] Subtotal (9% CI) 884 884 54.2% 0.03 [-0.23, 0.28] Heterogeneity. Tau <sup>2</sup> = 0.13; ChP = 56.12; df = 9 (P < 0.00001); P = 84% Test for overall effect Z = 0.20 (P = 0.84) 3.1.3 Multi OAD Cesur A, 2007 6.61 0.75 18 6.56 0.97 18 3.5% 0.06 [-0.60, 0.71] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.66 [0.06, 0.71] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.66 [0.06 [0.10, 1.20] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.66 [0.68, 0.71] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.66 [0.68, 0.71] Hassanein A, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.66 [0.68, 0.99] Malha A, 2014 7.93 1.47 30 7.1 0.84 30 4.3% 0.68 [0.16, 1.21] Malha B, 2014 8.47 1.75 39 7.51 1.16 39 4.4% 0.48 (0.18, 1.10] Uysal, 1998 7.3 1.6 41 7.55 1.7 41 5.0% -0.15 [-0.58, 0.28] Yeoh, 2015 8.6 2.4 29 8 2.3 29 4.4% 0.25 [-0.27, 0.77] Subtotal (9% CI) 254 254 254 3.7% 0.26 [0.03, 0.49] Heterogeneity. Tau <sup>2</sup> = 0.00; ChP = 13.46; df = 8 (P = 0.10); P = 41% Test for overall effect Z = 2.23 (P = 0.43) 3.1.4 Multi treatment Cesur C, 2007 7.76 0.9 10 7.76 0.91 10 2.5% 0.00 [-0.88, 0.88] Karatoprak A, 2013 8.3 1.8 12 8.1 1.1 12 2.8% 0.13 [-0.67, 0.93] 3.1.4 Multi treatment Cesur C, 2007 7.76 0.9 10 7.76 0.91 10 2.5% 0.01 [-0.88, 0.88] Karatoprak A, 2013 8.3 1.8 12 (P = 0.82); P = 0% Test for overall effect Z = 0.75 (P = 0.45) Total (95% CI) 35 35 8.1% 0.18 [-0.29, 0.65] Heterogeneity. Tau <sup>2</sup> = 0.00; ChP = 72,14, df = 21 (P < 0.00001); P = 71% Test for overall effect Z = 1.51 (P = 0.13) Heterogeneity. Tau <sup>2</sup> = 0.10; ChP = 72,14, df = 21 (P < 0.00001); P = 71% Test for overall effect Z = 1.51 (P = 0.13) Heterogeneity. Tau <sup>2</sup> = 0.10; ChP = 72,14, df = 21 (P < 0.00001); P = 71% Test for overall effect Z = 1.51 (P = 0.13) Heterogeneity.	Belkadir E,1993	15	2.8	101	15.4	2.5	101	6.2%	-0.15 [-0.43, 0.13]	
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	GLIRA,2005	8.4	1.8	232	7.3	1.3	232	6.8%	0.70 [0.51, 0.89]	-
San A 2004 6.6 0.9 23 6.4 1.1 23 3.9% 0.20 [ $0.38, 0.78$ ] San B 2004 7.5 1 17 7.5 0.9 17 3.4% 0.00 [ $0.67, 0.67$ ] 0.03 [ $0.23, 0.28$ ] Heterogeneity: Tau <sup>2</sup> = 0.13; Chi <sup>2</sup> = 56.12, df = 9 ( $P < 0.00001$ ); $P = 84\%$ Test for overall effect: $Z = 0.20$ ( $P = 0.84$ ) <b>3.1.3 Multi OAD</b> Cesur A 2007 6.61 0.75 18 6.66 0.97 18 3.5% 0.06 [ $0.60, 0.71$ ] Hassanein A,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.61 [ $0.02, 1.20$ ] Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% -0.15 [ $0.61, 0.31$ ] Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% -0.15 [ $0.61, 0.31$ ] Hassanein B, 2011 7.2 0.6 36 7.3 0.7 1 0.84 30 4.3% 0.68 [ $0.16, 1.21$ ] Malha A, 2014 7.93 1.47 30 7.1 0.84 30 4.3% 0.68 [ $0.16, 1.21$ ] Malha A, 2014 7.93 1.47 30 7.1 0.84 30 4.3% 0.68 [ $0.16, 1.21$ ] Malha B, 2014 8.47 1.75 39 7.51 1.16 39 4.8% 0.25 [ $0.27, 0.77$ ] Subtotal (95% Cl) 254 254 37.7% 0.26 [ $0.03, 0.49$ ] Heterogeneity: Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 13.46, df = 8 ( $P = 0.10$ ); $P = 41\%$ Test for overall effect: $Z = 2.23$ ( $P = 0.03$ ) <b>3.1.4 Multi treatment</b> Cesur C, 2007 7.76 0.9 10 7.76 0.91 10 2.5% 0.00 [ $-0.88, 0.88$ ] Karatoprak A, 2013 8.3 1.8 12 8.1 1.1 12 2.8% 0.13 [ $-0.67, 0.93$ ] Karatoprak B, 2013 8.22 1.5 13 7.7 1.2 13 2.9% 0.37 [ $-0.41, 1.16$ ] Subtotal (95% Cl) 35 3.1% 0.27 [ $0.41, df = 2$ ( $P = 0.82$ ); $P = 0\%$ Test for overall effect: $Z = 0.75$ ( $P = 0.45$ ) Total (95% Cl) 1173 1173 100.0% 0.13 [ $-0.04, 0.30$ ] Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.41, df = 21 ( $P < 0.0000$ ); $P = 71\%$ Test for overall effect: $Z = 0.75$ ( $P = 0.45$ ) Total (95% Cl) 1173 173 100.0% 0.13 [ $-0.04, 0.30$ ] Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 7.21.4, df = 21 ( $P < 0.00001$ ); $P = 71\%$ Test for overall effect: $Z = 0.75$ ( $P = 0.45$ ) Total (95% Cl) 1173 173 100.0% 0.13 [ $-0.04, 0.30$ ] Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 7.21.4, df = 21 ( $P < 0.00001$ ); $P = 71\%$ Test for overall effect $Z = 1.51$ ( $P = 0.13$ )	Karatoprak C,2013	6.9	0.7	18	6.9	0.8	18	3.5%	0.00 [-0.65, 0.65]	
San B 2004 7.5 1 17 7.5 0.9 17 3.4% 0.00 [-0.67, 0.67] Subtotal (95% CI) 884 654.2% 0.03 [-0.23, 0.28] Heterogeneily: Tau <sup>2</sup> = 0.13; Ch <sup>2</sup> = 5 (P < 0.00001); P = 84% Test for overall effect: Z = 0.20 (P = 0.84) 3.1.3 Multi OAD Cesur A,2007 6.93 1.33 21 6.68 1.06 21 3.8% 0.20 [-0.40, 0.81] Cesur B,2007 6.61 0.75 18 6.56 0.97 18 3.5% 0.06 [-0.60, 0.71] Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% -0.15 [-0.61, 0.31] Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% -0.15 [-0.61, 0.31] Karatoprak D,2013 8 1.5 17 7.6 0.9 17 3.4% 0.32 [-0.36, 0.99] Maiha A, 2014 7.33 1.47 30 7.1 0.84 30 4.3% 0.68 [0.16, 1.21] Maiha A, 2014 8.47 1.75 39 7.51 1.16 39 4.8% 0.64 [0.18, 1.10] Uysal, 1998 7.3 1.6 41 7.55 1.7 41 5.0% -0.15 [-0.58, 0.28] Yeoh, 2015 8.6 2.4 29 8 2.3 29 4.4% 0.25 [-0.27, 0.77] Subtotal (95% CI) 254 254 37.7% 0.26 [0.03, 0.49] Heterogeneity: Tau <sup>2</sup> = 0.05; Ch <sup>2</sup> = 13.46, df = 8 (P = 0.10); P = 41% Test for overall effect: Z = 2.23 (P = 0.41), df = 2 (P = 0.82); P = 0% Test for overall effect: Z = 0.75 (P = 0.44], df = 2 (P = 0.82); P = 0% Test for overall effect: Z = 0.75 (P = 0.44], df = 2 (P = 0.82); P = 0% Test for overall effect: Z = 0.75 (P = 0.42) Heterogeneity: Tau <sup>2</sup> = 0.01; Ch <sup>2</sup> = 7.214, df = 21 (P < 0.00001); P = 71% Test for overall effect: Z = 1.51 (C = 0.75) Total (95% CI) 1173 1173 100.0% Heterogeneity: Tau <sup>2</sup> = 0.10; Ch <sup>2</sup> = 7.214, df = 21 (P < 0.00001); P = 71% Test for overall effect: Z = 1.51 (C = 0.13) Heterogeneity: Tau <sup>2</sup> = 0.10; Ch <sup>2</sup> = 7.214, df = 21 (P < 0.00001); P = 71% Test for overall effect: Z = 1.51 (C = 0.713) Heterogeneity: Tau <sup>2</sup> = 0.10; Ch <sup>2</sup> = 7.214, df = 21 (P < 0.00001); P = 71% Test for overall effect: Z = 0.75 (P = 0.45) Total (95% CI) 1173 1173 100.0% Heterogeneity: Tau <sup>2</sup> = 0.10; Ch <sup>2</sup> = 7.214, df = 21 (P < 0.00001); P = 71% Test for overall effect: Z = 1.51 (P = 0.13)	M'Guil,2008	6.65	0.81	60	6.63	0.66	60	5.6%	0.03 [-0.33, 0.38]	+
Subtotal (95% CI) 884 884 54.2% 0.03 [-0.23, 0.28] Heterogeneity: Tau <sup>2</sup> = 0.13; Ch <sup>2</sup> = 56.12, df = 9 (P < 0.00001); P = 84% Test for overall effect: Z = 0.20 (P = 0.84) <b>3.1.3 Multi OAD</b> Cesur A,2007 6.63 1.33 21 6.68 1.06 21 3.8% 0.20 [-0.40, 0.81] Cesur A,2007 6.61 0.75 18 6.56 0.97 18 3.5% 0.06 [-0.60, 0.71] Hassanein A,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.61 [0.02, 1.20] Hassanein A,2011 7.7 0.9 23 7.2 0.7 36 4.8% -0.15 [-0.61, 0.31] Karatoprak D,2013 8 1.5 17 7.6 0.9 17 3.4% 0.32 [-0.36, 0.99] Malha A, 2014 7.93 1.47 30 7.1 0.84 30 4.3% 0.68 [0.16, 1.21] Malha B, 2014 8.47 1.75 39 7.51 1.16 39 4.8% 0.64 [0.18, 1.10] Uysal, 1998 7.3 1.6 41 7.55 1.7 41 5.0% -0.15 [-0.56, 0.28] Yeoh, 2015 8.6 2.4 29 8 2.3 29 4.4% 0.25 [-0.27, 0.77] Subtotal (95% CI) 254 254 37.7% 0.26 [0.03, 0.49] Heterogeneity: Tau <sup>2</sup> = 0.05; Ch <sup>2</sup> = 1.34, df = 8 (P = 0.10); P = 41% Test for overall effect: Z = 2.23 (P = 0.03) <b>3.1.4 Multi treatment</b> Cesur C,2007 7.76 0.9 10 7.76 0.91 10 2.5% 0.00 [-0.88, 0.88] Karatoprak A,2013 8.3 1.8 12 8.1 1.1 12 2.8% 0.13 [-0.67, 0.93] Karatoprak B,2013 8.22 1.5 13 7.7 1.2 13 2.9% 0.37 [-0.41, 1.15] Subtotal (95% CI) 35 35 8.1% 0.18 [-0.29, 0.65] Heterogeneity: Tau <sup>2</sup> = 0.00; Ch <sup>2</sup> = 0.441, df = 2 (P = 0.82); P = 0% Test for overall effect: Z = 0.75 (P = 0.45) Heterogeneity: Tau <sup>2</sup> = 0.00; Ch <sup>2</sup> = 0.71 (P < 0.00001); P = 71% Test for overall effect: Z = 1.51 (P = 0.13)	Sari A,2004	6.6	0.9	23	6.4	1.1	23	3.9%	0.20 [-0.38, 0.78]	
Heterogeneity: Tau <sup>2</sup> = 0.13; Ch <sup>2</sup> = 56.12, df = 9 (P < 0.00001); P = 84% Test for overall effect: $Z = 0.20$ (P = 0.84) 3.1.3 Multi OAD Cesur A,2007 6.93 1.33 21 6.68 1.06 21 3.8% 0.20 [-0.40, 0.81] Cesur B,2007 6.61 0.75 18 6.56 0.97 18 3.5% 0.06 [-0.60, 0.71] Hassanein A,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.61 [0.02, 1.20] Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% -0.15 [-0.61, 0.31] Karatoprak D,2013 8 1.5 17 7.6 0.9 17 3.4% 0.32 [-0.36, 0.99] Malha A, 2014 7.93 1.47 30 7.1 0.84 30 4.3% 0.68 [0.16, 1.21] Malha B, 2014 8.47 1.75 39 7.51 1.16 39 4.8% 0.64 [0.18, 1.10] Uysal, 1998 7.3 1.6 41 7.55 1.7 41 5.0% -0.15 [-0.58, 0.28] Yeoh, 2015 8.6 2.4 29 8 2.3 29 4.4% 0.25 [-0.27, 0.77] Subtotal (95% CI) 254 254 37.7% 0.26 [0.03, 0.49] Heterogeneity: Tau <sup>2</sup> = 0.05; Ch <sup>2</sup> = 13.46, df = 8 (P = 0.10); P = 41% Test for overall effect: $Z = 2.23$ (P = 0.03) 3.1.4 Multi treatment Cesur C, 2007 7.76 0.9 10 7.76 0.91 10 2.5% 0.00 [-0.88, 0.88] Karatoprak A,2013 8.3 1.8 12 8.1 1.1 12 2.8% 0.13 [-0.67, 0.93] Karatoprak B,2013 8.22 1.5 13 7.7 1.2 13 2.9% 0.37 [-0.41, 1.15] Subtotal (95% CI) 35 35 8.1% 0.18 [-0.29, 0.65] Heterogeneity: Tau <sup>2</sup> = 0.00; Ch <sup>2</sup> = 0.41, df = 2 (P = 0.82); P = 0% Test for overall effect: $Z = 0.75$ (P = 0.45) Total (95% CI) 1173 1173 100.0% 0.13 [-0.04, 0.30] Heterogeneity: Tau <sup>2</sup> = 0.10; Ch <sup>2</sup> = 72.14, df = 21 (P < 0.00001); P = 71% Test for overall effect: $Z = 1.51$ (P < 0.00001); P = 71% Test for overall effect: $Z = 1.51$ (P = 0.13)	Sarı B,2004	7.5	1	17	7.5	0.9	17	3.4%	0.00 [-0.67, 0.67]	
Test for overall effect: $Z = 0.20$ (P = 0.84) 3.1.3 Mutti OAD Cesur A 2007 6.83 1.33 21 6.68 1.06 21 3.8% 0.20 [-0.40, 0.81] Cesur B 2007 6.81 0.75 18 6.56 0.97 18 3.5% 0.06 [-0.60, 0.71] Hassanein B, 2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.61 [0.02, 1.20] Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% -0.15 [-0.61, 0.31] Karatoprak D, 2013 8 1.5 17 7.6 0.9 17 3.4% 0.32 [-0.36, 0.99] Maiha A, 2014 7.93 1.47 30 7.1 0.84 30 4.3% 0.68 [0.16, 1.21] Maiha B, 2014 8.47 1.75 39 7.51 1.16 39 4.8% 0.64 [0.18, 1.10] Uysal, 1998 7.3 1.6 41 7.55 1.7 41 5.0% -0.15 [-0.58, 0.28] Yeoh, 2015 8.6 2.4 29 8 2.3 29 4.4% 0.25 [-0.27, 0.77] Subtoral (95% CI) 254 254 37.7% 0.26 [0.03, 0.49] Heterogeneity: Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 13.46, df = 8 (P = 0.10); P = 41% Test for overall effect: $Z = 2.23$ (P = 0.03) 3.1.4 Multi treatment Cesur C, 2007 7.7.6 0.9 10 7.7.6 0.91 10 2.5% 0.00 [-0.88, 0.88] Karatoprak A, 2013 8.3 1.8 12 8.1 1.1 12 2.8% 0.13 [-0.67, 0.93] Karatoprak B, 2013 8.2 1.5 13 7.7 1.2 13 2.9% 0.37 [-0.41, 1.15] Subtoral (95% CI) 35 7.7 35 8.1% 0.18 [-0.29, 0.65] Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.41, df = 2 (P = 0.82); I <sup>2</sup> = 0% Test for overall effect: $Z = 0.75$ (P = 0.45) Total (95% CI) 173 1173 100.0% 0.13 [-0.04, 0.30] Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 72.14, df = 2 (P < 0.00001); I <sup>2</sup> = 71% Test for overall effect: $Z = 1.51$ (P = 0.13) Before Ramadan After Ramadan	Subtotal (95% CI)			884			884	54.2%	0.03 [-0.23, 0.28]	<b>•</b>
3.1.3 Multi OAD Cesur A,2007 6.93 1.33 21 6.68 1.06 21 3.8% 0.20 [-0.40, 0.81] Cesur B,2007 6.61 0.75 18 6.56 0.97 18 3.5% 0.06 [-0.60, 0.71] Hassanein A,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.61 [0.02, 1.20] Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% -0.15 [-0.61, 0.31] Karatoprak D,2013 8 1.5 17 7.6 0.9 17 3.4% 0.32 [-0.36, 0.99] Malha A, 2014 7.93 1.47 30 7.1 0.84 30 4.3% 0.68 [0.16, 1.21] Malha B, 2014 8.47 1.75 39 7.51 1.16 39 4.8% 0.64 [0.18, 1.10] Uysal, 1998 7.3 1.6 41 7.55 1.7 41 5.0% -0.15 [-0.58, 0.28] Yeoh, 2015 8.6 2.4 29 8 2.3 29 4.4% 0.25 [-0.27, 0.77] Subtotal (95% Cl) 254 254 37.7% 0.26 [0.03, 0.49] Heterogeneily: Tau" = 0.05; Chi <sup>p</sup> = 13.46, df = 8 (P = 0.10); P = 41% Test for overall effect $Z = 2.23$ (P = 0.03) 3.1.4 Multi treatment Cesur C, 2007 7.76 0.9 10 7.76 0.91 10 2.5% 0.00 [-0.88, 0.88] Karatoprak A,2013 8.22 1.5 13 7.7 1.2 13 2.9% 0.37 [-0.41, 1.15] Subtotal (95% Cl) 355 35 8.1% 0.13 [-0.29, 0.65] Heterogeneily: Tau" = 0.00; Chi <sup>p</sup> = 0.41, df = 2 (P = 0.82); P = 0% Test for overall effect $Z = 0.75$ (P = 0.45) Total (95% Cl) 1173 1173 100.0% 0.13 [-0.04, 0.30] Heterogeneily: Tau" = 0.10; Chi <sup>p</sup> = 72.14, df = 21 (P < 0.00001); P = 71% Test for overall effect $Z = 1.51$ (P = 0.13) Before Ramadan After Ramadan	Heterogeneity: Tau <sup>2</sup> =	0.13; Ch	i <sup>2</sup> = 56.	12, df=	9 (P < 0	0.00001	$ ; ^2 = 8$	34%		
Cesur A,2007 6.93 1.33 21 6.68 1.06 21 3.8% 0.20 [-0.40, 0.81] Cesur B,2007 6.61 0.75 18 6.56 0.97 18 3.5% 0.06 [-0.60, 0.71] Hassanein A,2011 7.7 0.9 23 7.2 0.7 23 3.9% 0.61 [0.02, 1.20] Hassanein B, 2011 7.2 0.6 36 7.3 0.7 36 4.8% -0.15 [-0.61, 0.31] Karatoprak D,2013 8 1.5 17 7.6 0.9 17 3.4% 0.32 [-0.36, 0.99] Malha A, 2014 7.93 1.47 30 7.1 0.84 30 4.3% 0.68 [0.16, 1.21] Malha B, 2014 8.47 1.75 39 7.51 1.16 39 4.8% 0.64 [0.18, 1.10] Uysal, 1998 7.3 1.6 41 7.55 1.7 41 5.0% -0.15 [-0.58, 0.28] Yeoh, 2015 8.6 2.4 29 8 2.3 29 4.4% 0.25 [-0.27, 0.77] Subtotal (95% Cl) 254 254 37.7% 0.26 [0.03, 0.49] Heterogeneity: Tau <sup>2</sup> = 0.05; Chi <sup>2</sup> = 13.46, df = 8 (P = 0.10); P = 41% Test for overall effect: Z = 2.23 (P = 0.03) 3.1.4 Multi treatment Cesur C, 2007 7.76 0.9 10 7.76 0.91 10 2.5% 0.00 [-0.88, 0.88] Karatoprak A, 2013 8.3 1.8 12 8.1 1.1 12 2.8% 0.13 [-0.67, 0.93] Karatoprak A, 2013 8.22 1.5 13 7.7 1.2 13 2.9% 0.37 [-0.41, 1.15] Subtotal (95% Cl) 173 1173 100.0% 0.13 [-0.04, 0.30] Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.41, df = 2 (P = 0.82); P = 0% Test for overall effect: Z = 0.75 (P = 0.45) Total (95% Cl) 1173 1173 100.0% 0.13 [-0.04, 0.30] Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 72.14, df = 21 (P < 0.00001); P = 71% Test for overall effect: Z = 1.51 (P = 0.13) Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 72.14, df = 21 (P < 0.00001); P = 71% Test for overall effect: Z = 1.51 (P = 0.13)	Test for overall effect:	Z=0.20	(P = 0.8	84)						
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Karatoprak A, 2013 8.3 1.8 12 8.1 1.1 12 2.8% 0.13 [-0.67, 0.93]   Karatoprak B, 2013 8.22 1.5 13 7.7 1.2 13 2.9% 0.37 [-0.41, 1.15]   Subtotal (95% Cl) 35 35 8.1% 0.18 [-0.29, 0.65]   Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.41, df = 2 (P = 0.82); i <sup>2</sup> = 0% 0.13 [-0.04, 0.30]   Total (95% Cl) 1173 1173 100.0% 0.13 [-0.04, 0.30]   Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 72.14, df = 21 (P < 0.00001); i <sup>2</sup> = 71% 0.13 [-0.04, 0.30] -2   Test for overall effect: Z = 1.51 (P = 0.13) 0.13 [-0.04, 0.30] -2 1	Cesur C.2007	7.76	0.9	10	7.76	0.91	10	2.5%	0.00 (-0.88, 0.88)	
Karatoprak B, 2013 8.22 1.5 13 7.7 1.2 13 2.9% 0.37 [-0.41, 1.15]   Subtotal (95% Cl) 35 35 8.1% 0.18 [-0.29, 0.65]   Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.41, df = 2 (P = 0.82); l <sup>2</sup> = 0%   Test for overall effect: Z = 0.75 (P = 0.45)   Total (95% Cl) 1173 1173 100.0%   Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 72.14, df = 21 (P < 0.00001); l <sup>2</sup> = 71% 0.13 [-0.04, 0.30]   Test for overall effect: Z = 1.51 (P = 0.13) 2	Karatoprak A,2013									<del></del>
Subtotal (95% Cl) 35 35 8.1% 0.18 [-0.29, 0.65] Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.41, df = 2 (P = 0.82); i <sup>2</sup> = 0% Test for overall effect: Z = 0.75 (P = 0.45) Total (95% Cl) 1173 1173 100.0% 0.13 [-0.04, 0.30] Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 72.14, df = 21 (P < 0.00001); i <sup>2</sup> = 71% Test for overall effect: Z = 1.51 (P = 0.13) Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 72.14, df = 21 (P < 0.00001); i <sup>2</sup> = 71% Test for overall effect: Z = 1.51 (P = 0.13)	Karatoprak B,2013									
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 0.41, df = 2 (P = 0.82); i <sup>2</sup> = 0% Test for overall effect: Z = 0.75 (P = 0.45) Total (95% Cl) 1173 100.0% 0.13 [-0.04, 0.30] Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 72.14, df = 21 (P < 0.00001); i <sup>2</sup> = 71% Test for overall effect: Z = 1.51 (P = 0.13) Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 72.14, df = 21 (P < 0.00001); i <sup>2</sup> = 71% Test for overall effect: Z = 1.51 (P = 0.13)	Subtotal (95% CI)									+
Heterogeneity: Tau <sup>2</sup> = 0.10; Chi <sup>2</sup> = 72.14, df = 21 (P < 0.00001); l <sup>2</sup> = 71% Test for overall effect: Z = 1.51 (P = 0.13) Before Ramadan After Ramadan					2 (P = 0.3	82); l² =	:0%			
Test for overall effect: Z = 1.51 (P = 0.13)	Total (95% CI)			1173			1173	100.0%	0.13 [-0.04, 0.30]	*
Test for overall effect: Z = 1.51 (P = 0.13)	Heterogeneity: Tau <sup>2</sup> =	0.10; Ch	i² = 72.	14, df=	21 (P <	0.0000	01); l² =	71%		
	-									2 1 0 1 2
					= 2 (P =	: 0.39).	<sup>2</sup> = 0%	5		beiore Ramadan Alter Ramadan

Fig. 4. Forest plot for pre-post Ramadan changes in glycated haemoglobin (%).

adherence rates are surprisingly high during RF<sup>46-48</sup>. However, the VIRTUE study enrolling 1333 patients from 10 countries reported high treatment adherence during Ramadan, with low or similar number of missed doses compared to other months<sup>49</sup>.

The sensitivity analysis showed similar SMDs for all of the outcomes (Table II). For fructosamine, HbA<sub>1c</sub> (%) and FPG significant heterogeneity were detected among included studies. Not all of the included studies followed the same duration of fasting (Table I). Hence, duration of fasting may be one of the reasons for heterogeneity. Egger regression analysis showed no publication bias for PPG (P=0.068), FBG (P=0.802), BMI (P=0.622) and fructosamine (P=0.950). For HbA<sub>1c</sub> (%), publication bias was detected (P=0.015).

Our study had several limitations. Although studies with co-morbidities were excluded, it was

very difficult to include only those cases of diabetes without co-morbid conditions, and most of the studies did not follow similar inclusion criteria. The reported rates of hypoglycaemic and hyperglycaemic and hyperglycaemic rate events vary between 3.7 and 33.3 per cent<sup>18,19,22</sup>. Since only a small number of studies reported these outcomes, we could not include them in our meta-analysis. Another limitation of our study was related to the fact that most of the included studies investigated the impact of RF just after Ramadan; therefore, sustainability of positive outcomes could not be evaluated.

In conclusion, our meta-analysis showed that RF was not associated with any significant negative effects on PPG and fructosamine levels. However, BMI and FPG and HbA<sub>1c</sub> (%) were positively affected by RF. Although RF showed positive effects on certain

#### INDIAN J MED RES, DECEMBER 2019

	Before Ramadan		After	Ramad	an	:	Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
8.1.1 Single OAD									
Belkadir A,1993	336	78	78	324	80	78	8.0%	0.15 [-0.16, 0.47]	
Belkadir B,1993	381	98	173	380	97	173	9.6%	0.01 [-0.20, 0.22]	+
Belkadir C,1993	358	78	95	396	99	95	8.4%	-0.42 [-0.71, -0.14]	
Belkadir D,1993	365	75	87	403	104	87	8.2%	-0.42 [-0.72, -0.12]	
Belkadir E,1993	410	67	101	419	91	101	8.6%	-0.11 [-0.39, 0.16]	
Gustaviani,2004	344.1	45.7	24	303.9	34.5	24	4.4%	0.98 [0.38, 1.58]	
M'Guil,2008	269.7	25.15	60	282.75	25.15	60	7.3%	-0.52 [-0.88, -0.15]	
Mafauzy A,2002	389.6	84.6	116	370.8	86.43	116	8.9%	0.22 [-0.04, 0.48]	
Mafauzy B,2002	365.9	75.89	119	358.5	70	119	9.0%	0.10 [-0.15, 0.36]	
Sari A,2004	251	37	23	252	34	23	4.7%	-0.03 [-0.61, 0.55]	
Sarı B,2004	331	62	17	330	72	17	3.9%	0.01 [-0.66, 0.69]	
Vasan,2012	316	102.35	50	352.6	94.65	50	6.8%	-0.37 [-0.76, 0.03]	
Subtotal (95% CI)			943			943	87.9%	-0.06 [-0.25, 0.12]	<b>+</b>
Heterogeneity: Tau <sup>2</sup> :	= 0.07; C	hi² = 39.7	4, df = 1	1 (P < 0.	.0001);	l² = 729	6		
Test for overall effect	: Z = 0.69	P = 0.49	9)						
8.1.2 Multi OAD									
Cesur A,2007	258.7	70.2	21	278.8	77.1	21	4.4%	-0.27 [-0.88, 0.34]	
Cesur B,2007	251.5	58.4	18	262	45.1	18	4.0%	-0.20 [-0.85, 0.46]	
Subtotal (95% CI)			39			39	8.4%	-0.23 [-0.68, 0.21]	-
Heterogeneity: Tau <sup>2</sup> :	= 0.00; C	hi² = 0.02	, df = 1	(P = 0.88	i); I <sup>2</sup> = 0'	%			
Test for overall effect	: Z = 1.03	3 (P = 0.30	0)						
8.1.3 Multi treatmen									
Cesur C,2007 Subtotal (95% Cl)	264.4	35.2	16 16	268.8	41.1	16 16	3.7% 3.7%	-0.11 [-0.81, 0.58] - <b>0.11 [-0.81, 0.58]</b>	
Heterogeneity: Not a	pplicable	1							
Test for overall effect	: Z = 0.32	2 (P = 0.75	5)						
Total (95% CI)			998			998	100.0%	-0.08 [-0.24, 0.08]	•
Heterogeneity: Tau <sup>2</sup> :	- 0.06.0	hi² = 40 2		1 (P = 0	00021				
Test for overall effect				4 (1 - 0	.0002),	- 057	•		-2 -1 0 1 2
Test for subgroup dif		•		2 (P = 0	78) 12-	- 0%			Before Ramadan After Ramadan
restion subdroub di	referices	. on = 0	.40, ul -	- 2 (F = 0		- 0 %			



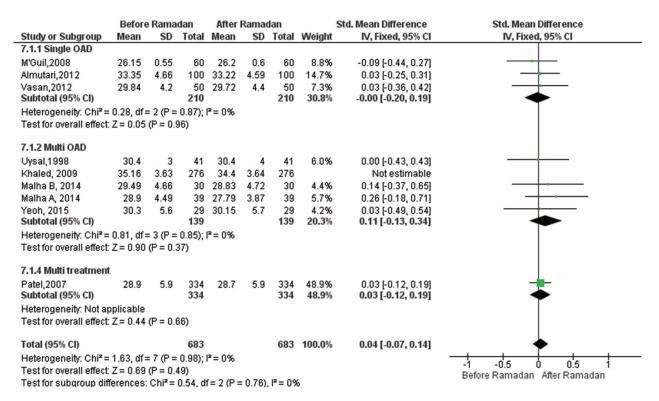


Fig. 6. Forest plot for pre-post Ramadan changes in body mass index.

			Tal	ole II. Result of sensi	tivity analysis		
Outcome	Effect size	Hetero	geneity		Sensitivi	ity analysis	
		<i>I</i> <sup>2</sup> (%)	Р	Excluding the largest	Excluding the smallest	Excluding the earliest	Excluding studies with the most contradictory results
PPG (mg/dl)	0.06 (-0.14-0.26)	0	0.900	0.13 (-0.10-0.35)	0.03 (-0.17-0.23)	0.05 (-0.17-0.27)	0.09 (-0.11-0.30)
FPG (mg/dl)	0.48 (0.27-0.70)	61	0.001	0.44 (0.20-0.69)	0.49 (0.28-0.71)	0.54 (0.32-0.76)	None
HbA <sub>1C</sub> (%)	0.13 (-0.04-0.30)	71	0.001	0.05 (-0.07-0.17)	0.13 (-0.04-0.30)	0.14 (-0.03-0.32)	0.16 (-0.01-0.32)
BMI	0.09 (-0.00-0.18)	0	0.810	0.04 (-0.07-0.14)	0.08 (-0.01-0.18)	0.09 (-0.00-0.18)	0.04 (-0.07-0.14)
Fructosamine	-0.08 (-0.24-0.08)	65	0.001	-0.09 (-0.27-0.09)	-0.08 (-0.25-0.09)	-0.03 (-0.27-0.22)	-0.05 (-0.21-0.11)
HbA <sub>1c</sub> , glycate glucose	ed haemoglobin; TG,	triglyce	ride; BM	II, body mass index;	PPG, post-prandial p	lasma glucose; FPG,	fasting plasma

outcomes, one should consider the limitations of the study and confounders while interpreting the results.

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### Conflicts of Interest: None.

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556