



Ramadan Fasting and Maternal Perspectives in Healthy Pregnant Women: Systematic Review

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Authors' contributions

This work was carried out in collaboration between all authors. Authors IES and IMT reviewed the literature independently and wrote the first draft of the manuscript. Author MMH managed to review the manuscript and helped in publication. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Background: Practicing fasting during Ramadan by pregnant women might be risky. Controversies still exist about the nature and the magnitude of metabolic changes in healthy pregnant women who practice fasting.

Objectives: To systematically review literature pertaining to the practice of Ramadan fasting and the effect of fasting on maternal health.

Methods: Relevant literature was obtained through searches of PubMed, and Cochran's. Incidence and duration of fasting, reasons for non-fasting, dietary changes, physical activity, weight changes, symptoms with fasting, and metabolic parameters for healthy pregnant women who fasted during Ramadan were extracted. Synthesis of data was performed when appropriate.

Results: Out of 56 English-language studies, 21 addressed maternal perspectives, 85.57% women experienced fasting during pregnancy, 76.26% fasted the whole month or ≥ 20 days, 80.9% perceived fasting as obligatory, 63.1% perceived no harm in fasting during pregnancy,

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and 17.6% broke their fast because of harm. The reasons for non- fasting included pregnancy (25%), coexisting medical problems (20.6%), symptoms (16.2%), daily commitments (16.2%), personal, family reasons (13.2%), and belief that fasting is not compulsory (8.8%). Common symptoms were hunger or thirst (16.82%), nausea or vomiting (7.47%), giddiness (6.66%), fatigue (17.01%), and fever or headache (2.72%). Accelerated starvation was reported in many studies; whereas hyperglycemia was reported in only 2 studies. Negative impact of fasting on lipids and hormones was reported in a few studies.

Conclusion: There are large gaps in knowledge, and more large interventional clinical trials are needed. In the light of available research, the majority of pregnant women showed a strong sense of religious obligation and chose to fast, even though some of them did not fully recognize their right to be exempted. There is still no definite evidence that accelerated starvation due to Ramadan fasting during an uncomplicated pregnancy can adversely affect maternal health.

Keywords: Ramadan; fasting; pregnancy; maternal health; accelerated starvation.

1. INTRODUCTION

Religious fasting during the Holy Month of Ramadan entails abstinence from food, water, smoking, and drugs from dawn to sunset. Fasting is obligatory for healthy adult individuals according to a strong statement in the holy Quran [1]. Recent evidence pointed at the great religious interest and enthusiasm by a large percentage of Muslim people who insist on observing Ramadan fasting even if they are exempted by clear indications [2,3]. The marked alterations in the pattern and amount of activity, meals and fluid intake, and even sleeping hours during this month [4,5] could affect the metabolic condition both during the fasting hour and after breaking the fast. During their periods of menstruation, women are definitely exempted from fasting. The situation for pregnant women may be different from that for non-pregnant women even they are healthy. From a religious perspective, healthy pregnant women are exempted from fasting if they believe it will harm their own or their fetal health. This blurred guidance could make some women believe that fasting is an obligation [6] and that they need to practice Ramadan fasting, at least partly during Ramadan. Multiple social, religious, and cultural reasons could explain why these women prefer to fast. Family and societal situations along with the lack of proper religious information probably represent the major reasons for their will to fast, irrespective of strong medical reasons for exemption [3]. In general, published literature addressing the physiology of Ramadan fasting in healthy pregnant or breastfeeding women is very limited. Ramadan fasting is considered by some researchers as a natural model of prolonged intermittent fasting in humans [7] that is presumed to be beneficial [8,9]. Intermittent

fasting due to religious reasons adds to the improved compliance than calorie restriction models. Researchers described the underlying mechanisms of intermittent fasting to involve lipolysis inhibition and increased insulin sensitivity in muscle and fat tissue and plasma adiponectin levels [10]. However, there is no available evidence that allows application of the concepts of intermittent fasting in cases of pregnancy, who insist to fast. Instead, other concepts such as nutritional disruptions and accelerated starvation could be applied on fasting during pregnancy and can represent the scientific evidence of exemption of pregnant women from fasting [9]. Accelerated fasting was reported in late normal pregnancy if breakfast was skipped and in pregnant women compared with non- pregnant women after 12 hours of fasting [11,12]. Prolonged periods without food intake during pregnancy were found to increase the risk for elevated maternal corticotropin-releasing hormone concentrations with possible maternal and fetal health consequences in both human [13] and animal studies [14].

Since a nutritional environment during prenatal and neonatal periods largely modifies the genetic impact of the morphological and physiological characteristics of the offspring [15,16], there is a need to collect evidence about the nutritional changes during Ramadan fasting in Muslim pregnant women. Currently, there is no available evidence that could delineate the health effects of fasting and the way in which the pregnant women practicing fasting could reflect the metabolic changes. Before we try to collect evidence about pregnancy outcomes, we should first define the practice and the changes during practicing fasting during Ramadan by pregnant women.

Controversies still exist about the nature and the magnitude of metabolic changes in healthy pregnant women who practice fasting. Thus, the aim of this review was to systematically review literature pertaining to the practice of Ramadan fasting and the effect of fasting on maternal health. The objectives were to identify all observational studies and clinical trials testing Ramadan fasting alone or in comparison to non-fasting pregnant healthy women; to assess the quality of those studies; to determine the total number of patients included in such studies to date, and their characteristics; to determine whether non-fasting advice works better than fasting; and, finally, to identify gaps in knowledge where new trials are needed.

2. MATERIALS AND METHODS

Relevant published human studies conducted in healthy pregnant women during Ramadan fasting were searched by using the key words "fasting, Ramadan, pregnancy" either alone or combined. A separate search was performed for "fasting," "Ramadan," and "pregnancy." The 2 researchers independently searched the PubMed, the Cochrane Library, Scopus, Google search, and the reference lists of obtained articles. There was no restriction on the time within which the studies had to be done or on the language used. Inclusion criteria included all original studies of any study design (intervention; observational), involving healthy pregnant women, any reporting of exposure to Ramadan fasting, and reporting on any of the following: incidence and duration of fasting, reasons for non-fasting, dietary changes, physical activity, weight changes, symptoms with fasting, and metabolic parameters for healthy pregnant women. Data extraction included description of study design, inclusion and exclusion criteria, primary and secondary outcome measures, main results, and conclusions. There were no quality assessment criteria. Exclusion criteria included reviews, comments, or incomplete data; published studies in another language and English translation was not available. No authors of any article were contacted for more details. After removal of duplicates, data extraction was performed by 2 independent reviewers who selected studies and extracted data using pre-determined forms: study design, population characteristics, outcomes, results, and

conclusion. Discrepant results were resolved by discussion until a unanimous decision was reached. The diversity of the studies included was allowed.

3. RESULTS

The first search (Ramadan fasting and pregnancy) retrieved 56 related articles. After verification, 26 articles were excluded (1 case report of ruptured peptic ulcer, 7 studies about diabetes with pregnancy, 6 unrelated topics (but related to Ramadan fasting in general), 4 studies with no abstract, 1 consensus and 6 comments to previous studies, and 1 French study with no available English translation). Finally, the researchers retrieved 30 related abstracts, out of which 21 studies were found to address maternal health perspectives with or without fetal health issues. Two summary tables were constructed to include extracted data in 2 subgroups according to outcome measures: the practice of Ramadan fasting by pregnant women (Table 1) and the effect of Ramadan fasting on maternal health (Table 2). Each table gives descriptive information for each included study sorted by the study's primary outcome measures. When appropriate, the overall effect across the different studies was estimated by synthesis of the data and presented in figures.

3.1 Maternal Perception and Practice during Ramadan Fasting

Seven full text studies and 1 abstract addressed the incidence and duration of Ramadan fasting and some aspects of the practice of fasting by pregnant women as the primary or the secondary outcome variables (Table 1). Their design were cross-section (n=4), retrospective (n=1), 1 cohort (n=1), and 1 case control (n=1). Studies were performed in different countries (Pakistan [17], Singapore [18], Yemen [19], United States [20], Iran [2], Iraq [21] Malaysia [22], and Turkish [23] with the largest sample size from Yemen [19] and 3 studies were of a small number [18,20,23]. Many studies addressed incidence of fasting [2,17-21], duration of fasting [2,17,18], and belief / knowledge [17,18,20]. Diet composition and food intake were addressed differently in only 2 studies [2,23]. No study addressed the physical changes experienced by pregnant women during Ramadan.

Table 1. Studies addressing the practice of Ramadan fasting by pregnant women

Reference country	Study design population characteristics	Outcome measures	Results/Conclusion
1- Mubeen et al., 2012 [17] Pakistan	Cross-sectional study using questionnaire 353 experienced pregnancy during Ramadan at least once.	Incidence of fasting , duration of fasting, and belief / knowledge, and food intake	12.5% did not fast. 87.5% fasted during their pregnancies. 42.5% fasted for the whole month. 24% broke their fast with risk. 88% believed that fasting during pregnancy is "obligatory". Association between gravida and education with fasting (P=0.03). Among those who did not fast, 36 (81.8%) thought about repaying fast after pregnancy was over, whereas 8 (18%) respondents did not. 59% perceived no harm. 16% thought weakness is caused by lack of nutrition. Hunger/thirst (26.5%) and weakness (25%) were the most frequent side effects. Severe vomiting (8.8%) and taking medication (25.7%) nullify the fast. 48.7% admitted that fasting is difficult. 48.7% increased food intake
2- Jooseph et al., 2004 [18] Singapore	Retrospective study of 182 Muslim women who were pregnant and received antenatal care using mailed questionnaire	Incidence of fasting Duration of fasting, belief / knowledge, and food intake	13% did not fast. 87% fasted at least one day. 57% fasted >20 days. 1 – 10 ds: 13%, 11 – 20 ds:17%. Multigravida fast (97%)> Primigravida (60%). 13% did not fast. 30% were adversely affected and 17% women broke fast. 67% felt that fasting is obligatory. 16% perceived harm to own self, 16% to fetus, 11% to both, and 79% perceived no harmf. 52% found fasting difficult. 21% eat more during Souhor, 25% eat more during Iftar, and 12% eat more during both.
3- Makki 2002 [19] Yemen.	Cross-sectional study of 4343 pregnant women	Incidence of fasting	90.3% were fasting for 20 or more days during their last pregnancy, and 5.4% were fasting for 10-19 days. 1.6% were fasting between 1 and 9 days.
4- Robinson & Raisler 2005 [20] US	Cross-sectional study 32 women who had or had not fasted during their most recent pregnancy participated in tape-recorded focus groups.	Incidence of fasting, belief and practice	28 of 32 women chose to fast. 25 out of 30 had been pregnant during Ramadan within the previous 2 years and fasted. 16 fasted for a full month. Immigrant women fasted more days than US women. (60%–90% vs. 30–50%)30 believed that fasting during pregnancy is safe. All participants agreed that a woman should not fast if it would hurt her or the baby. 19 women discussed fasting at a prenatal visit. 13 initiated discussion with their doctor. 5 women experienced their doctor as judgmental. 6 women mentioned that their HCP had given them advice

Reference country	Study design population characteristics	Outcome measures	Results/Conclusion
5- Ziaee et al., 2010 [2] Iran	Historical cohort: 189 pregnant women: NFG, 1–10 days fasting, 11–20 days fasting, and 21–30 days fasting .	Incidence of fasting, duration of fasting, and food intake	65.1% were fasting, and 31.7% were on full fasting. Average fasting days: 13 days. According to Iftar and Souhor meals: appropriate (2 complete meals), moderate (1 complete meal), or poor (no complete meal): 52% had appropriate, 39.9% had moderate, and 8.1% had poor nutritional habits.
6- Bander 2005 [21] Iraq	Cross-sectional study of 225 pregnant women either fasted for the whole Ramadan or consented to biochemical investigation after an overnight fast, aged 18-35 years, healthy, in 22–28 weeks of gestation, non- smokers and not-receiving any medication	Incidence of fasting BMI changes and biochemical changes	114 out of 225 were fasting with a prevalence of 50.66%, For other results, see Table 2.
7-Salleh 1989 [22] Malaysia	Cross-sectional study of 605 pregnant women	Incidence of fasting and weight gain	477 out of 605 was fasting during pregnancy with a prevalence of 78.84% No significant weight gain.
8- Kiziltan et al., 2005. [23] Turkish	Case control study of 98 pregnant women: 49 RFG vs. 49 NFG.	Weight gain Diet composition Energy intake Biochemistry	Micronutrient deficiency in both groups Compared with NFG, RFG showed lower weight gain and energy intake, higher % of protein and CHO, and higher FBG, HDLc, and TG with lower urea, TC, LDL, and total protein and albumin

CHO: Carbohydrates, RFG: Ramadan fasting group, NFG: Non-fasting group.

A simple synthesis of data (Fig. 1) revealed that the total number of healthy pregnant women included in this review was 3828, where 85.57% experienced fasting during their pregnancies, 76.26% fasted the whole month or ≥ 20 days, 80.9% perceived fasting as obligatory, 63.1% perceived no harm in fasting during pregnancy, and 17.6% broke their fast because of harm during pregnancy. Fig. 2 shows the summary of the 2 studies [17,18] that addressed the reasons for non-fasting among pregnant women during Ramadan. The most common causes were in order: pregnancy (25%), coexisting medical problems (20.6%), symptoms (16.2%), daily commitments (16.2%), and personal and family reasons (13.2%). However, the least common cause was their belief that fasting is not compulsory (8.8%).

3.2 Effect of Ramadan Fasting on Maternal Health

In addition to 2 related studies [22,23] shown in Table 1, 13 studies [21,24-35] (Table 2) addressed the effect of Ramadan fasting on maternal health as the primary or the secondary outcome variables. They were 4 full text and 9 abstracts, 6 case controls [24,25,27,28,29,35], 1 cross-sectional [31], and 6 prospective cohort studies [21,26,30,33,34]. They were performed in different countries (Gambia [24], Iraq [21], UK [25], Lebanon [26], Turkey [27,28,29,34], Iran [30,32,33,35], and UAE [31]) (Table 2). All were controlled studies (fasting versus non-fasting groups) except 2 studies [30,33]. Most studies [24,25,27,28,29,30,33,34] were of a small sample size (less than 100). Studies addressed glucose homeostasis during Ramadan

differently with different outcomes and different results ranging from accelerated starvation with evident low blood glucose and elevated beta-hydroxybutyrate [21,24,25,29,33], especially in late pregnancy [24], to ketosis and ketonemia [26,29]. Hyoglycemia (defined as serum levels <3.33 mmol/l.) was recorded in one study [26], whereas hyperglycemia (defined as serum levels >6.7 mmol/l) or gestational diabetes (defined by ADA criteria) were recorded in 2 studies [31,32]. Five studies [22,23,26,30,35] stressed on failure of maternal weight gain. Two studies addressed rise in non-esterified fatty acid with [25] and without [24] rise in triglycerides. Another reported low LDL/HDL

ratio [28]. One study addressed oxidative stress [34], and another [35] addressed blood pressure changes. Hormonal changes were reported differently in 2 studies. One study addressed elevated serum cortisol [28], and another reported significant changes in female hormones and leptin [30] during fasting. Three studies [17,18,26] addressed the common symptoms of Ramadan fasting in pregnancy (Fig. 3). In total, common symptoms were hunger or thirst (16.82%), nausea or vomiting (7.47%), giddiness or dizziness (6.66%), weakness or fatigue (17.01%), and fever or headache (2.72%).

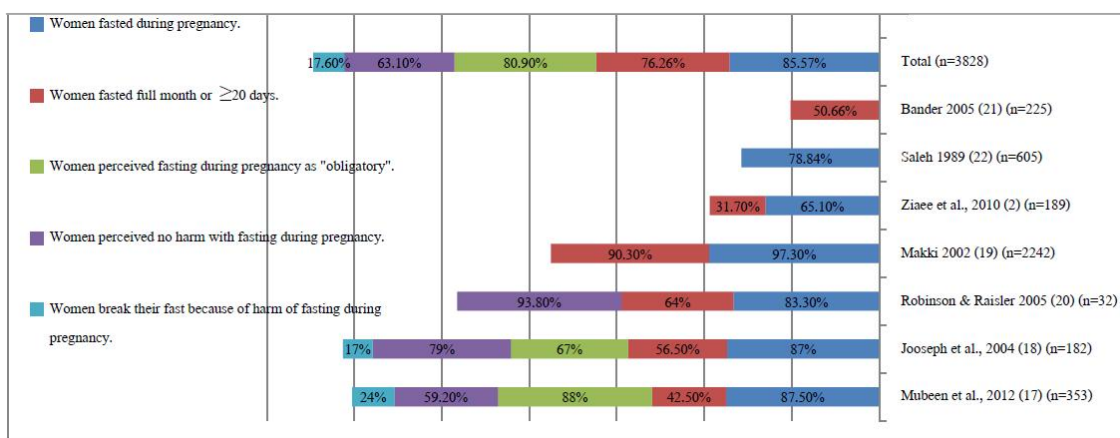


Fig. 1. Summary figure of the 6 studies addressing the practice of Ramadan fasting among pregnant women

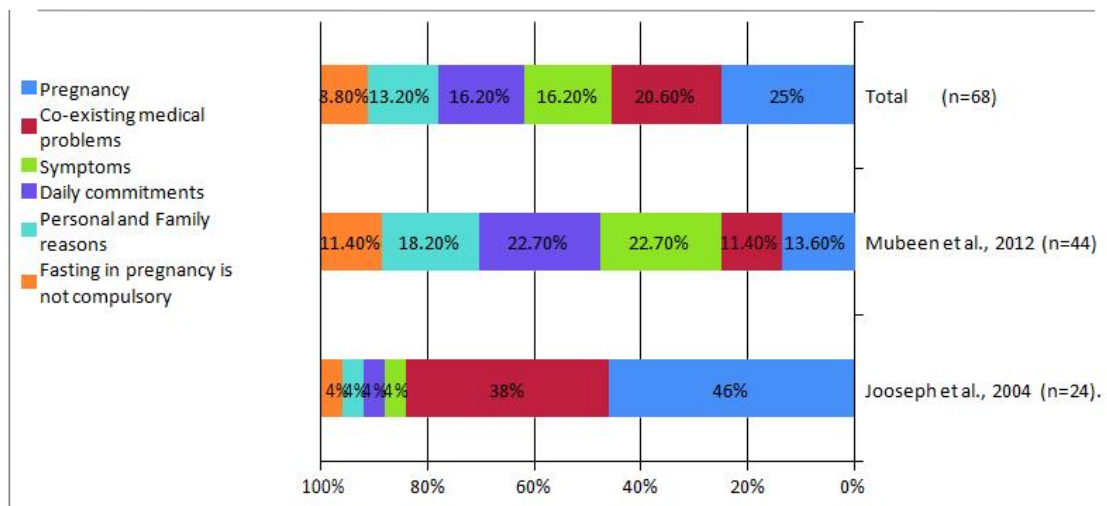


Fig. 2. Summary figure of the 2 studies addressing the reasons for non-fasting during Ramadan among pregnant women

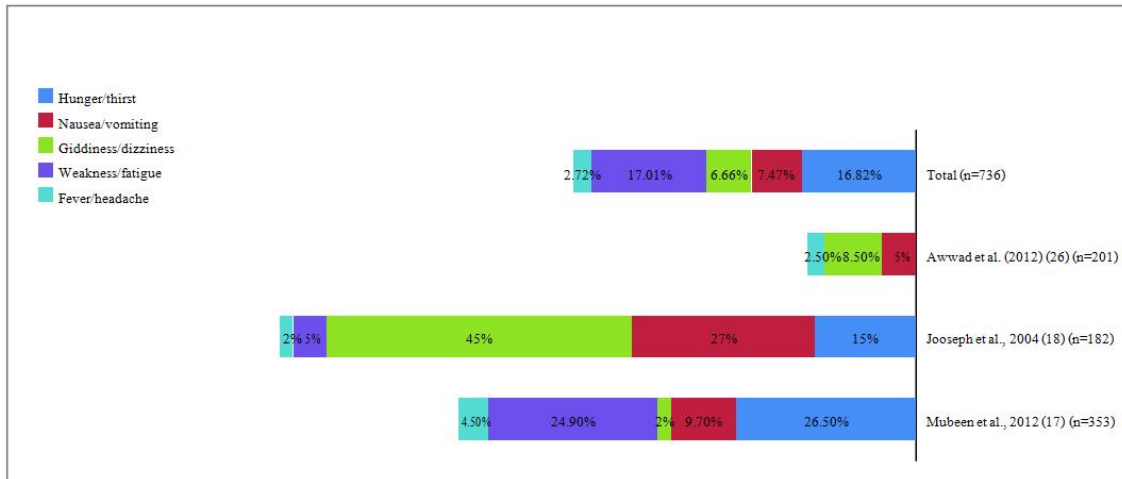


Fig. 3. Summary figure of the common symptoms during Ramadan fasting in pregnancy

4. DISCUSSION

In the light of available research, the majority of pregnant women showed great religious interest and enthusiasm to observe Ramadan fasting, even though some of them did not fully recognize their right to be exempted by the Islamic Law. Evidence for accelerated starvation due to Ramadan fasting during a healthy pregnancy is available, but there is still no definite evidence that it can adversely affect maternal health. In this review, 8 studies [2,17-23] addressed the practice and perception of Ramadan fasting and 15 studies [21-35] reported on the metabolic effects of Ramadan fasting on maternal health in healthy pregnant women. First, the results of this review strongly support the belief that Ramadan fasting is valued by pregnant Muslim women. We can speculate that the high incidence of fasting by pregnant women (85.57%) may be due to their belief that fasting is obligatory (80.9%) and associated with no harm (63.1%). Although a substantial number had observed fasting during pregnancy even for the whole month (76.26%), only 17.6% of the pregnant women broke their fast because of harm during pregnancy (Fig. 1). In Islam, pregnant women are allowed not to observe fasting if they are worried about risking the health of their fetus or themselves. About half of the studied women considered fasting during pregnancy difficult [17,18], whereas non-fasting due to pregnancy was reported in only 25% of cases (Fig. 2). This could be reflected in how they perceive the rule for fasting in pregnancy or how their healthcare staff failed to provide them with relevant information. Other reported causes of non-fasting included coexisting medical

problems (20.6%), symptoms (16.2%), daily commitments (16.2%), and personal and family reasons (13.2%) and the least common cause was their belief that fasting is not compulsory (8.8%) (Fig. 2). The ethnic diversity of perception and practice among pregnant women was reported in only one small study from the United States [20]. Studies that addressed the lifestyle changes during Ramadan fasting were very deficient and inconclusive with no available study addressing the expected changes in the physical activity or the sleeping hours during fasting and their impact on maternal health. This is very limiting, as during the month of Ramadan it is expected that modifications of the rhythm of life with disturbances of the cycle of sleep, eating pattern, and meal frequency could strongly influence different aspects of pregnant women's health [36].

Second, overall, results of the studies on the metabolic effects of Ramadan fasting in healthy pregnant women [21-35] (Tables 2) give enough evidence that accelerated starvation, especially in late pregnancy [24], exists during fasting day hours with evident low blood glucose, elevated beta-hydroxybutyrate [21,24,25,29,33], ketosis, and ketonemia [26,29]. These results were evident when comparing levels in fasting pregnant women with non-fasting [21,24-29], non-pregnant [24], or lactating women [24] or even with their own levels measured before and after breaking fast [33]. One study [25] showed that at the end of the fast day all fasted pregnant women showed abnormal biochemistry with a significant fall in glucose, insulin, lactate, and carnitine, and a rise in triglyceride, non-esterified

Table 2. Studies involving the effect of Ramadan fasting on maternal health

Reference, Country	Design population characteristics	Outcome measure	Results
1-Prentice et al., 1983 [24]. Gambia	Case control (n=42) 22 pregnant, 10 lactating, and 10 non- pregnant, non- lactating women.	Serum glucose, free fatty acid, triglyceride, beta-hydroxybutyrate, alanine, insulin, glucagon, and T3 levels measured during Ramadan day (0700 & 1900 h) and outside Ramadan (overnight- fasted values)	Ramadan-fasted (1900 h) glucose values (At time of Iftar) from women in late pregnancy were significantly lower than the 2 groups and were 15% lower than overnight-fasted values outside Ramadan. Higher fasted free fatty acid and beta- hydroxy butyrate and lower alanine values in late than in early pregnancy.
2-Bandar 2005 [21]. Iraq	Cross-sectional study 225 pregnant, 114 RFG, and 111 non NFG	BMI, glucose, insulin, lactate, and hydroxybutyrate were collected on 2 nd , 4 th , and 28 th days of Ramadan, between 12.00 and 13.00 hours, after a fast of 10–14 hours	Plasma glucose was lower in RFG (4.2 ± 0.68) than in the NFG (4.5 ± 0.5); P<0.001. Plasma glucose was highest on the 2 nd day of Ramadan fasting and declined throughout the 14 th day and 28 th days of fasting (p< 0.001). Similarly, plasma insulin and lactate levels were significantly decreased throughout the fasting Ramadan, with the decline being greatest during the last 14 days (101.05 ±19.0 pmol/L, 0.73 ± 0.3 mmol/L, for insulin and lactate in the 2 nd days Vs 90.0 ± 20.0 pmol/L, 81.3 ± 17pmol/L and 0.64 ± 0.5 mmol/L, 0.5 ± 0.6 at 14 th and 28 th days, respectively). By the 28 th day of Ramadan, the serum hydroxybutyrate levels were significantly increased (p <0.001) in the RFG.
3-Malhotra et al., 1989 [25]. UK	Case control study RFG: 11 fasting mothers who were Pakistani or Bangladeshi by 28–37 weeks with normal pregnancy. Overnight fasting (ONF) group: 11 non- fasting mothers included in the larger study of glucose metabolism were Pakistani or Bangladeshi, at 29 weeks of normal pregnancy	Serum glucose, insulin, lactate and carnitine, TG, NEFA, and 3- hydroxy-butyrate RFG: 2 samples: (1) at the antenatal clinic in the morning (10.50–11.45 hours), after a fast of 8-14 h timed from Souhor, the last meal before sunrise; (b) at home in the evening (18.25–20.03 hours), after a fast of 15–22 h and before the first meal after sunset. One sample was taken from the ONF mothers at 09.00–10.00 hours at the antenatal clinic after a fast of 9–14 h	At the end of the Ramadan fast day, all pregnant women in RFG showed abnormal biochemical values with a significant fall in glucose, insulin, lactate, and carnitine, and a rise in triglyceride, non-esterified fatty acid and 3-hydroxybutyrate compared with ONF.
4-Awwad et al. (2012) [26].	A prospective cohort study of 402 Pregnant women at	Secondary endpoints: % of women with confirmed	The likelihood of hypoglycemia was similar between the RFG and NFG both at the beginning and at the end of

Lebanon.	20–34 weeks of gestation: 201 RFG vs. 201 NFG	hypoglycaemia, ketosis, and ketonuria.	Ramadan. Compared with NFG, RFG had higher ketosis and ketonuria, lower mean increase in maternal weight at the end of the fasting month (1.6 ± 2.2 kg vs. 2.3 ± 2.0 kg; $P = 0.001$), and higher frequency of vomiting ($P = 0.011$), diarrhoea ($P = 0.004$) and dizziness ($P = 0.001$).
5-Hizli et al., 2012 [27]. Turkey	Case control study of 56 RFG vs 54 NFG: pregnancies of ≥ 28 week gestation who had fasted for at least 10 consecutive days during Ramadan.	Maternal lipid levels, BG, and ketonuria	Compared with NFG, RFG had lower VLDL, TG and higher ketonuria. No statistical difference was found between the groups from fetal perspectives.
6-Dikensoy et al., 2009 [28]. Turkey	Case control study. RFG: 36 healthy women with uncomplicated pregnancies of ≥ 20 weeks. NFG: 29 matched group	Maternal serum cortisol, lipid evaluated before and after Ramadan	No significant difference was found between the two groups for the fetal age, maternal weight gain. In RFG, serum cortisol on day 20 was significantly higher than the initial levels obtained at 1 week before Ramadan ($p < 0.05$). In RFG, total cholesterol and triglyceride levels increased insignificantly during Ramadan but significantly increased compared with NFG. LDL, and VLDL levels and showed a non-significant decrease at the end of the Ramadan. HDL levels showed a slight increase, but LDL/HDL ratios were significantly decreased in the fasting group ($p < 0.05$).
7-Dikensoy et al., 2008 [29]. Turkey	Case control RFG:36 healthy women with uncomplicated pregnancies of ≥ 20 weeks NFG: 29 matched group	Maternal levels of 3- hydroxy- butyrate, glucose, and ketonuria.	The mean duration of fasting in the study group was 18 ± 2.1 days. The mean maternal glucose level was significantly lower in RFG than in NFG ($P = 0.003$). No statistically significant differences were found between the two groups in 3-hydroxy-butyrate. No statistically significant differences were found between the two groups in the comparisons of other parameters.
8-Khoshdel et al., 2014 [30]. Iran	Cross-sectional study of 30 fasting pregnant women.	FSH, LH, oestrogen, progesterone, and leptin were measured in 1st, 2nd, and 4th week of Ramadan and in 2nd week post-Ramadan	The weight and BMI did not change A significant change in FSH, oestrogen, progesterone, and leptin was observed ($p < 0.05$). Leptin decreased significantly at 2 weeks after Ramadan.
9-Elkotby et al., 2014 [31]. UAE	Cross-sectional study: 150 (76 during Ramadan and 74 after Ramadan), with uncomplicated pregnancies at a gestational age between	RFG: Glucose level during fasting and 1- hour postprandial glucose level after fasting NFG: FBG, 1h after main meal, at bed.	The two groups of pregnant women had similar physiological parameters. Using the oral glucose tolerance test, the mean random blood glucose level after 1 hour of breaking the fast was significantly higher ($p = 0.002$) in RFG

	20 and 36 weeks. NFG: measured outside Ramadan		than in NFG, and this was not affected by the number of fasting days. In 50% of patients after Ramadan and 70.5% during Ramadan, this value was abnormal (>6.7 mmol/l).
10-Mirghani et al., 2006 [32]. Iran	Prospective study of 168 RFG vs.156 NFG.	Pregnancy outcome	Compared with NFG, RFG had higher incidence of gestational diabetes in RFG vs. NFG (p = 0.001), induction of labor (15.5% vs.7.1%) (p = 0.004), and cesarean section (p = 0.01).
11-Mirghani et al., 2004 [33]. Iran.	Cross-sectional study: 63 healthy fasting pregnant women with singleton uncomplicated pregnancies of ≥ 30 weeks' gestation.	Maternal blood glucose level during and after fasting.	Maternal glucose level during fasting was significantly lower than after breakfast. There was a significant association between maternal glucose levels and number of days fasted.
12-Ozturk et al., 2011 [34]. Turkey.	Prospective controlled study: 42 RFG and 30 NFG pregnant women (2 nd trimester) fasting days ≥ 10 or ≥ 15 days	Antioxidant (TAS, TOS, and OSI) levels maternal age, gestational age, parity, birth weight, or weight gain)	No significant differences between both groups except in TAS was significantly higher (P = 0.027) in the ≥ 10 fasting days group compared to NFG.
13- Naderi et al., 2004 [35]. Iran.	Case control study on 51 fasting and 50 non-fasting pregnant women	Mothers' weight increase and Mothers' blood pressure changes	No significant difference between the 2 groups with regard to mothers' weight increase, mothers' blood pressure

RFG: Ramadan fasting group, NFG: non-fasting group, TG: triglycerides, NEFA: non- esterified free fatty acids, BG: blood glucose, VLDL: very low denisty lipoprotein, LDL: low denisty lipoprotein, HDL: high density lipoprotein.

fatty acid, and 3-hydroxybutyrate compared with non-fasting pregnant women. Another study [33] reported significant correlations between the number of fasted days and the glucose level and suggested a cumulative effect of glucose level during maternal Ramadan fasting. The levels to which blood glucose drops during fasting were not defined in different studies, and it seems that it was a matter of relative hypoglycemia. However, hypoglycemia defined as <3.33 mmol/l was reported in one study [26]. The severity of hypoglycemia was not reported and it might be difficult to define due to the diversity of the length of fasting time according to the geographical position of the country or the season in which the month of Ramadan falls. There were no data which supported that hypoglycemia or reduced caloric intake caused the women's symptoms during fasting such as hunger, giddiness or dizziness, weakness or fatigue, and headache (Fig. 3). Accelerated starvation was first defined in 1982 by Metzger and his coworkers [37], who found that pregnant women skipping breakfast already after nocturnal fasting experienced signs of starvation in contrast to non-pregnant women. In addition, starvation signs became faster during the day with performing physical activity while fasting [38]. Human and animal studies showed that acute starvation in pregnant women results in decreased blood glucose but within a normal range [39], and fetal energy was well maintained by multiple compensatory mechanisms [40]. Consequent to caloric restriction, many studies [22,23,26,30,35] reported on the failure of maternal weight gain during the month of Ramadan. Unfortunately, the clinical significance of such findings was not addressed in any study. While fasting, hypoglycemia was reported in fasting pregnant women [21,24,25,29,33] as well as in non-pregnant Muslims during Ramadan [41]; postprandial blood glucose measurement was ignored in almost all studies. This is important, because pregnancy itself is known as a state of increased insulin resistance and insulin secretion and of reduced hepatic insulin extraction that may lead to lower fasting glucose but higher postprandial glucose and insulin levels in healthy pregnant women compared with non-pregnant women [42]. In this review, 2 studies [31,32] were the first to report on hyperglycemia [31] and increased incidence of gestational diabetes [32] during Ramadan fasting. More studies are needed to clarify the response of postprandial blood glucose to fasting in pregnant women, especially in Muslim

countries with a high incidence of gestational diabetes. Very few studies provided some evidence of negative impact of fasting on serum levels of lipids [24,25,28]. On the other hand, no significant effects of fasting on oxidative stress [34] or blood pressure [35] were detected. Hormonal changes were reported differently in 2 studies. One study addressed elevated serum cortisol [28], whereas another reported significant changes in female hormones and leptin [30] during fasting. However, again, the clinical significance of such changes was not well studied. Not enough studies about the risk of insufficient fluid intake, the prevalence of urinary tract infection, or the increased risk of hyperemesis gravidarum were reported in pregnant women during Ramadan fasting.

5. LIMITATIONS

The major limitation of the included studies was their low statistical power with too small sample sizes to detect significant effects, which ranged from 30 to 4343 pregnant women with the majority having less than 100 observations. Moreover, most study designs were case and control design, which does not provide causal evidence of fasting. Some covariables were missed in some studies such as different stages of pregnancy, bad obstetric history, age, parity and health concerns of mothers, socioeconomic level, duration of fasting, and seasonal variation. For example, in one study [25], Ramadan fast hours lasted up to 22 hours which exceeds normal overnight fast, or the duration of Ramadan fast experienced in the geographical proximity of the equator. This prolonged fasting may have different biochemical and clinical implications. Other limitations included absence of identification of ethnic background of the respondents in some studies, absence of validity of any of the used questionnaires, absence of risk assessment of clinical harm as odd ratios or relative risk, and, finally, reliability of results could not be assessed precisely due to a deficiency in data presentation even in full text papers. Review methods were limited by unavailability of some articles such as one study in French and one article reported on possibility of increased hyperemesis gravidarum during Ramadan [43], and others reported on accelerated starvation [44,45]. Since this review is the first trial to collect evidence for expert opinion, we included all published work on this subject, even those that were old or of a small sample size. We could not compare our work with any previous systematic reviews or with the

South Asian consensus statement on women's health and Ramadan [46], because the later was based mainly on expert opinion besides a few studies.

6. CONCLUSION

This review offered strong and consistent evidence for a positive attitude of pregnant Muslim women to Ramadan fasting, whereas there was inconsistent evidence of an association between accelerated starvation due to fasting and untoward maternal health. Some of the pregnant women did not fully recognize their right to be exempted by the Islamic Law. Most healthy pregnant women can fast safely without much complaints but they are exposed to metabolic changes of accelerated starvation that could explain most of their symptoms during fasting. There is simply not enough evidence to arrive at a definite conclusion pertaining to safety of Ramadan fasting in pregnancy, especially because we need also to review evidence for safety of fetal development and fetal outcomes with fasting. Despite the possibility that the weight of the available evidence is in favor of safety of fasting in terms of women perspectives, generalization of this conclusion may not be possible and still decisions for fasting during pregnancy should be individualized. Although results of this review demonstrated clearly the high incidence of fasting among pregnant Muslim women and the phenomena of accelerated starvation, there are major research gaps in other areas of practice and the impact of metabolic and hormonal changes on fasting. Lifestyle changes are particularly the most defective area in reporting. Some indications pointed to impaired glucose tolerance and hormonal alteration, including cortisol and leptin, but more specifications of their magnitude and their clinical significance are needed.

7. RECOMMENDATION

Additional research in the areas of lifestyle and metabolic changes during Ramadan fasting in pregnant women is needed to provide missing information. Due to the magnitude of the women who are expected to fast during Ramadan, there is a need for careful management of fasting during pregnancy in parallel with Islamic teachings. Empowering health professionals through generating standard guidelines would be the next step. These guidelines should specify with certainty the conditions under which

a woman can fast or keep on fasting, delineate the best way of monitoring, and managing lifestyle changes during fasting. Therefore, to obtain stronger evidence, we need to increase the power of studies by including more numbers, using more precise measurement of the actual effect of fasting using well-designed clinical trials that could provide causal evidence of Ramadan fasting

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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