Effects of Ramadan Fasting on Fetal Health: A Systematic Review.

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Abstract

Background Ramadan fasting (RF) is mandatory for all healthy Muslims in the ninth month of Islamic calendar. Pregnant women are exempt from fasting but many willfully practise it. There are concerns that fasting during pregnancy is harmful to the fetus but there are no firm recommendations regarding its safety. Objectives To provide a systematic review on the effects of RF on fetal health. Search Strategy We conducted literature search for peer-reviewed articles through Ovid MEDLINE, PubMed, SCOPUS, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) until 31 December 2021. Selection Criteria All case-control and observational cohort studies that reported on fetal outcomes of pregnant women who underwent RF for at least 1 day at any point of time during pregnancy are included. Data Collection and Analysis Two researchers independently reviewed the eligibility of all studies. A third researcher resolved any conflict between researchers. Findings are extracted from eligible papers and presented as narratives. Main Results 18 articles are included based on eligibility criteria, with a total sample size of 3,213,070. There are studies demonstrating negative associations between RF and neonatal weight, amniotic fluid index, preterm birth and growth parameters mainly during second and third trimesters, but those evidences are not strongly supported. Conclusion There is limited data to elucidate the relationship between RF and fetal health, hence the need for more studies to provide better understanding. Funding None. Keywords Ramadan fasting, pregnant women, fetal outcomes.

Introduction

Fasting is the willful abstinence of food, water, or both. It is practised globally for therapeutic, religious, political or cultural reasons.[1] It can be broadly categorized into complete or partial fasting, intermittent fasting, and fasting based on duration.[2]

Ramadan is a month of prayer, community, reflection, and fasting for Muslims, which falls on the ninth month of the Islamic calendar.[3,4] Abstaining from sinful behaviors and RF are believed to cleanse the soul, divert the heart from worldly activities and instil self-discipline.[4] RF is a form of intermittent fasting lasting from sunrise to sunset, but unlike intermittent fasting where consuming zero-calorie fluids is allowed, RF is more intense, entailing total abstention from food and water.[4] There is a major shift from normal eating habits to exclusively nocturnal eating.[5] It is non-mandatory for those who are ill, elderly, travelling, menstruating, breastfeeding, and pregnant. However, they are compelled to substitute missed days.[3] Ideally, fasting during pregnancy is not advised, but there are some who still practise it during Ramadan.[6]

As the oldest and most commonly employed method to evaluate fetal well-being, maternal awareness of fetal movements is reliable and done without medical equipment.[7] It is linked with improved perinatal outcomes, as concerned mothers present themselves for assessment once reduced fetal movement is detected. At least 10

fetal movements in 12 hours is considered normal.[8]Nevertheless, a decrease in fetal activity during Ramadan appears less uncommon. Studies have hypothesized that nutritional deficit may contribute to reduced fetal movements to conserve energy as it compensates for lack of nutrient transfer across the placenta.[9]

There are concerns that RF during pregnancy may cause adverse maternal or neonatal outcomes. For this review, we centred around fetal health rather than maternal health. To date, there is insufficient evidence linking RF and pregnancy. Existing evidence do not show significant association.[10,11] Considering that normal fetal movement is highly specific and objective measurement of fetal viability, it is reasonable to include fetal movement as an outcome measure.

Before suggesting that RF during pregnancy is safe, it is important to have conclusive data that allows health professionals to provide firm recommendations. Consequently, we conducted this systematic review to gain clearer insights into the effects of RF on fetal health.

Methodology

The systematic review is structured according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 protocol and checklist.[12] The protocol of this review has been registered with the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42021254301).

2.1 Search strategy

We searched the following electronic database sources for relevant articles according to the search strategy: Ovid MEDLINE, PubMed, SCOPUS, EMBASE and CENTRAL for peer-reviewed articles published until 31st December 2021. The following combination of Medical Subject Heading (MeSH) terms and keywords was used: ('fasting' or 'intermittent fasting' or 'diet restriction' or 'Ramadan' or 'Muslim' or 'Islam') and ('fetal movement' or 'fetal wellbeing' or 'fetal development' or 'biophysical profile') and ('pregnancy' or 'pregnant women' or 'expectant mother'). Search was restricted to 'human studies' and English language where possible. The searches conducted in all e-databases are provided as Supplementary Table S1.

2.2 Study selection

The article selection process was facilitated using Covidence software.[13] The articles obtained from the database searches were imported to Covidence, where duplicated records were deleted. A two-stage screening process was utilized in our study selection process. At the first screening stage, titles and abstracts were screened according to inclusion and exclusion criteria. Potential articles were included, and studies that cannot be excluded based on title/abstract underwent the second stage of screening. Full texts were retrieved and again screened in the second stage according to inclusion and exclusion criteria.

All case-control studies and observational cohorts (prospective or retrospective) that reported on fetal movements of pregnant women who underwent RF for at least 1 day at any point of time during pregnancy are included. For the purpose of this review, fasting is defined as RF which is an Islamic rule that requires Muslims to have total abstinence from food and water from sunrise to sunset for a consecutive period of 29-30 days.[14] On the other hand, fetal movement is defined as the fluttering movements of a fetus perceived by a pregnant woman at around 20 weeks of pregnancy, which indicates the fetus's growth in size and strength.[15]

Grey literature, conference proceedings, theses, reviews, non-peer-reviewed monographs, books, book chapters, study protocols, case studies, and cross-sectional studies were excluded. We excluded studies conducted in vitro or in vivo, single-armed or cohort studies with no comparator group, and studies where fasting duration during Ramadan is less than a day.

Two researchers independently reviewed, discussed, and agreed upon the eligibility of all studies. A third researcher resolved any conflict in the agreement between the researchers. We did a manual search of the reference lists of the included articles for other relevant studies not found in the database search.

2.3 Data extraction and synthesis

Eligible papers are categorized in a Google sheet to provide clarity. The study origin, the mean age of participants, study setting, trimester, type of fasting, outcome reported, and most important findings are extracted from the final eligible papers. As this is a qualitative synthesis, the findings are presented as narratives, including tables and figures to aid in data presentation where appropriate.

2.4 Quality assessment

Two researchers conducted quality assessment for the quantitative studies using the Newcastle-Ottawa Scale (NOS)[16]checklist independently. Similar to the screening process, a third researcher acted as a conflict resolver.

Results

3.1 Study selection and characteristics

We identified 1,366 records through electronic database searches and 8 records through manual searching. A total of 216 duplicate records were removed, and subsequently, the titles and abstracts of 1,158 records were screened for inclusion. The full texts of 44 articles were reviewed for eligibility, and finally, 18 studies were included in the review (Supplementary Table S2). The study selection process is summarized in a PRISMA 2020 flow diagram (Figure 1).

[insert Figure 1]

The majority of the studies were conducted in Turkey (33.3%), followed by Iran (16.7%), Canada (11.1%) and Saudi Arabia (11.1%) (Table 1). Sixteen studies were published within the last decade. Two-thirds of the studies were of cohort designs (prospective or retrospective), and all involved RF. Most of the studies were conducted across all trimesters (38.9%) or in the second and third trimesters (27.8%). A total of 3,213,070 samples were reported collectively in the included studies, with mostly the mean maternal age ranging from 27 and 30 years (50.0%).

[insert Table 1]

According to NOS, the median quality score was 5 (range: 4-6) for case-control studies and 7 (range: 6-9) for cohorts (Table 2). Overall, eleven studies (61.1%) scored 7 and above, indicating high quality, while the other seven (38.9%) scored 4–6, indicating intermediate quality.

3.2 Effect of fasting on neonatal outcomes.

Table 3 presents the summary of outcomes that were reported by the studies included in this review. Thirteen studies (72.2%) reported the effect of fasting on neonatal weight, followed by six studies (33.3%) on amniotic fluid index. Five studies (27.8%) reported on biparietal diameter, estimated fetal body weight, head circumference and fetal femur length, while gestational age at delivery, preterm birth/delivery and length were reported by four studies (22.2%). Fewer studies reported other outcomes like abdominal circumference, biophysical profile, APGAR score and stillbirth.

[insert Table 3]

3.3 Neonatal weight

Only one study found a significant association between maternal fasting and neonatal weight.[21] The authors reported significantly lower birth weight in neonates of Ramadan-fasted women during the second and third trimesters than the control group (3094±467g vs.202±473 g; P=0.024). Savitri et al.'s study[22] among women who fasted in their first trimester showed a potential reduction in the birthweight of newborns than of non-fasting mothers. However, the results were insignificant (-198 g, 95 % CI -447–51, P=0.12).[22]

3.4 Amniotic fluid index (AFI)

The results on AFI were not statistically significant in all but two studies.[24,26] Karateke et al.,[25]which presented AFI findings for both second and third trimesters fasting respectively, determined a significant reduction in AFI for second trimester fasting only (11.4(9.8-14.1)cm vs 16.2(12.6-18.3)cm, P=0.02). Seckin and colleagues[23] noted a significant decrease in AFI in the fasting group for third trimester fasting (20.1±11.2cm vs11.5±6.4cm,P<0.001). They concluded that maternal fasting reduced the interval for development of oligohydramnios.

Despite showing no significant difference in AFI increase between fasting and non-fasting groups, Sakar et al.'s[32]demonstrated a significantly lower increase in AFI of fasting group, potentially due to higher incidence of dehydration among fasting group, attributed by longer daytime above 17 hours and high temperatures between 36°C to 43°C.

3.5 Increase in biparietal diameter (BPD)

Only one study showed a significant association between both variables.[32] Sakar and colleagues[32]noted that increase in BPD was significantly different from initial measurements between fasting and non-fasting groups (9.69±3.07mm vs10.74±1.99mm,P=0.041) for pregnant women in their second and third trimesters. Other than Sakar et al.,[32] all four remaining studies reported insignificant findings. Except for Dikensoy et al.,[29,30] three other studies demonstrated that increase in BPD was greater in non-fasting control groups.[23,25,31]

3.6 Increase in estimated fetal body weight (EFBW)

Findings correlating the increase in EFBW and fasting were not significant in all articles (P>0.05). In Karateke's[25] and Sakar's[32] studies, there were expected greater increases in EFBW in non-fasting groups, compared to the fasting groups.[25,32] However, the inverse was true for the three remaining studies.[23,29,30,31]

3.7 Increase in fetal femur length (FL)

Only one study showed a significant association between fasting and increase in fetal FL. Sakar et al.'s[32] study showed a significantly more significant increase in fetal FL in the non-fasting control group than with second and third trimesters fasting (9.98±1.86mm vs8.57±2.56mm, P=0.002). As for the remaining articles with insignificant findings, three studies[23,29,30,31] noted that the increase in fetal FL was lesser in the control groups than in the study groups, unlike in Karateke et al.,[25] which reported a larger increase in fetal FL in the non-fasting control group.

3.8 Gestational age at delivery

Only Alwasel's study[19] found a significant association between RF and gestational age at delivery. The author reported that girls whose mothers were in their second trimester of pregnancy during the fasting month endured a shorter gestation period than girls who were not in utero during Ramadan (39.4weeks vs39.8weeks,P=0.04). The differences in gestational age at delivery for other trimesters and boys in general, were not statistically significant.

In two other studies,[21,23] mothers who fasted during pregnancy also experienced a shorter gestational period than pregnant mothers who did not fast. Contrarily, one study[26]noted that pregnant women fasted during their third trimester had a longer gestational age at delivery than their non-fasting counterparts.

3.9 Increase in length, head circumference (HC), and abdominal circumference (AC)

In Sakar and colleagues's study[32], second and third trimesters' fasting had significant increase on HC in the control group than study group (39.12±7.42cm vs 35.12±12.22cm, P=0.046). However, the other articles[6,19,28] showed no significant between fasting and an increase in HC. Alwasel et al.[19] also noted boys' HC in utero were generally larger than girls' during fasting.

Only one study[19] showed the length of boys whose mothers were in their second trimesters of pregnancy was significantly greater than boys who were not in utero during Ramadan (52.3cm vs 51.1cm, P=0.005). However, no significant association was found between fasting and babies' height in three other studies.[6,27,28]

All three articles reporting on AC indicated insignificant association between fasting and increased AC.[23,31,32] The increase in AC was greater in the non-fasting groups in Moradia et al.[31] and Sakar et al.[32]

3.10 Preterm Birth

According to Tith et al.,[33] the risk of preterm birth is significantly increased when participants fasted during second-trimester. Arabic-speaking women who fasted between weeks 15 and 21 of gestation and weeks 22 and 27 had 1.33 (95% CI:1.06-1.68) and 1.53 (95% CI:1.21-1.93) times the risk of very preterm birth, respectively than non-fasting group. When both parents had Arabic mother tongue and spoke the language at home, RF in weeks 15 to 21 was linked to 1.38 times the risk of very preterm birth (95% CI:1.03-1.85) and 1.65 times in weeks 22 to 27 (95% CI:1.23-2.21). If compared to non-Arabic speakers who were pregnant in the same period, the risk reduced to 1.25 (95% CI:1.02-1.53) and 1.33 (95% CI:1.08-1.63) times respectively.

Petherick et al.[24] and Hossain et al.[28] showed no association between RF and the risk of preterm birth, even after adjusting for covariables. Awwad and colleagues[21] noted that despite having higher incidence of preterm birth in the fasting group, the difference was insignificant.

3.11 Biophysical Profile (BPP)

All study results showed no significant difference between fasting pregnant women and non-fasting pregnant women.[26,29,30]In one study,[29,30] there was an average score of 7.8 in the fasting group, compared to 7.0 in the control group. However, the difference was statistically insignificant.

3.12 APGAR Score

Hossain and colleague's study[28] demonstrated that 5-min APGAR score was significantly higher in the fasting group than non-fasting group (9.00±0.01 vs 8.92±0.53, p=0.044). While the study showed a similar trend for 1-min Apgar score, the difference was not significant. In Abd-Allah Rezk et al.'s study[26], the 5-min APGAR score for non-fasting group had an average of 8.52±1.1, while the fasting group had an average of 8.44±1.2. Similarly, in Karatake et al. 's study,[25] there was insignificant difference between the two groups for both 1-min and 5-min APGAR scores.

3.13 Stillbirth

In both adjusted and unadjusted models, RF during first and second trimesters was not associated with risk of early and late stillbirths when compared to no exposure. Nevertheless, when the data was further classified according to causes of death, Bernier and colleagues[34] found that Ramadan exposure between weeks 15 to 21 of pregnancy increased the risk of early stillbirth due to congenital anomaly by 3.96 times (95% CI1.35-11.57). However, this reported findings has not been adjusted for covariates.

3.14 Other outcomes

Seckin et al.[23] reported that a significantly higher number of participants with normal initial AFI subsequently developed oligohydramnios (20/82 vs 6/87,P=0.03) in the fasting group. Naderi et al.[17] reported insignificant difference in the rate of fundal height increment between fasting and non-fasting groups. In Alwasel et al.'s study,[19] there was no significant association between fasting and chest circumference regardless of baby's gender and fasting trimester. In Abd-Allah Rezk et al.'s study,[26] the difference in reactivity of the non-stress test between fasting and non-fasting groups was insignificant.

Discussion

4.1 Main Findings

Our study demonstrated few significant findings. RF negatively affected neonatal weight,[21] AFI,[23,25]gestational age at delivery,[19] preterm birth[33] and changes in growth parameters except abdominal circumference.[19,32]

We found three other reviews[11,35,36] that looked into the effects of RF during pregnancy on perinatal outcomes. Glazier and colleagues[11] had reported similar outcomes, specifically preterm birth and birth weight. They found that RF did not significantly affect the frequency of preterm delivery (OR 0.99,95% CI 0.72-1.37), birth weight (SMD 0.03, 95% CI 0.00-0.05) and proportion of low-birth-weight babies (OR 1.05,95% CI 0.87-1.26), irrespective of pregnancy trimesters. Oosterwijk et al.[35] and Noshili et al.[36] included data on fetal growth indices and birth indices. Both reviews inferred that RF has some associations with fetal growth indices and birth indices but predominantly found in lower quality studies. Certain included articles[23,25,32]described lower AFI in the fasting group during second or third trimester of pregnancy, and BPD, HC and FL[32] were significantly affected by fasting ($p<0.05$). Only one high quality study mentioned that mean birth weight was significantly lower in exposed neonates (108g, $p=0.024$). Apart from that, differences in birth indices were statistically insignificant.

4.2 Interpretation

Our findings are consistent with data gathered by the three systematic reviews,[11,35,36] with little supporting evidence that RF has some associations with poor fetal health. This is because we discovered that evidence linking RF and changes in certain fetal outcomes only appeared in one of many articles examining them. Notably, there is a trend that all significant changes occurred especially when pregnant women fasted during second or third trimesters. This could be an important reference point for future studies whereby fasting during second and third trimesters of pregnancy may result in higher risks of poor fetal outcomes.

4.3 Strengths and Limitations

Maternal ethnicity and height were not adjusted for in all the articles. Certain ethnicities are known to have above average height and maternal height is a strong predictor of offspring nutritional status. Stulp and colleagues[37] mentioned that taller parents have heavier newborns. Birth weight was found to be both independently and positively affected by maternal and paternal height, with a 66% stronger effect ascribed to maternal influence. Inversely, a research done in Brazil[38] showed that adult stature reflects nutritional status and health processes throughout life. Earlier research demonstrated that short stature is likely due to combined genetic and environmental effects, such as nutritional stresses in early stages of life.[39] Short mothers with poorer quality of life are likely to provide insufficient nutrients to fetuses during pregnancy, resulting in small-for-gestational-age (SGA) babies.[39] Similarly, mothers who were SGA at birth are at greater risks of giving birth to SGA offspring.[39]

Our original intent of this study was to investigate the effects of RF on fetal movements because it is one of the easiest ways to monitor fetal growth and activity. Decreased fetal movement may be the first sign of an underlying pathology and warrants further assessment. We had to modify the primary objective of this study because there was not enough data for further analysis. We only found two out of eighteen included articles that reported fetal movement as an outcome of measurement in the form of non-stress tests.

Another limitation identified is that most studies are performed in the Middle East, and less so in Western

and Asian countries. Dietary patterns and cultures differ across countries. It may be a confounding factor that has not been accounted for during this study. For instance, Middle Easterners usually consume healthy Mediterranean diet which mainly consists of whole foods including vegetables, fruits, whole wheat, legumes, nuts, seafood and spices. Red meat, dairy and processed food are typically in smaller amounts than a standard Western diet. Depending on the types of food pregnant mothers eat while breaking fast during Ramadan, there will be a difference in nutritional components, which inadvertently affects fetal growth parameters. For this systematic review, we could not find any article that was based in the Asian community, therefore it is difficult to translate any evidence into practical recommendations that are aimed towards Asian lifestyle.

Furthermore, only articles published in the English language and involved human studies are included. There could be articles not published in the English language related to our topic but are omitted. Some articles demonstrated potential health effects of fasting through animal models. Therefore, they were not included in this study. For example, Alkhalefah et al.[40] reported intermittent fasting in pregnant Wistar rats induces fetal growth restriction and down-regulated placental amino acid transport. For these reasons, the number of articles included in our review was narrowed down, which could contribute to lower strength of evidence.

Although some individual studies have associated RF with potential health impacts, we could not perform a meta-analysis to calculate an overall effect due to limitations of data available. While some outcomes could not be presented as mean and standard deviation, most are not available from included studies. Correspondingly, we could not determine the effect size and heterogeneity of each outcome.

There are two studies[36,41] referenced in this review that looked at long-term consequences of individuals exposed to RF in utero, including physical traits and cognitive effects. As our study mainly focuses on short-term or immediate outcomes, those data are excluded, but they could always be considered for future research questions.

Conclusion

This systematic review found that there is insufficient data to associate RF with poor fetal outcomes.

5.1 Implications for Research

While there are negative associations between RF and fetal health, the findings appeared to be inconsistent across studies. Our review highlighted the importance of having further prospective research and outcome-specific retrospective observational studies that take into account multiple confounding factors to provide a more definitive evidence. We are hoping that this systematic review could be used as a guide for future pilot studies across different regions to look at the effects of RF on fetal health, to provide reassurance and advice to pregnant mothers who wish to safely practise fasting and avoid any adverse outcomes.

5.2 Implications for Practice

This systematic review provides recommendation to health professionals and pregnant women on the safety of RF during pregnancy.

Acknowledgement

None.

Author Contribution

The study was formulated by AKWO, ALY and AJHF. AR carried out the literature search. ALY and AJHF screened through and selected eligible studies. Differences in opinion were sorted out by AKWO. AKWO and ALY extracted data and carried out the data analysis. AKWO and AJHF performed quality assessment for all included studies. VJTA supervised the data analysis and write-up of study. All authors were involved in interpretation of data and revised the article critically.

Conflict of Interests

None declared.

Ethical Approval

None.

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Table S1: Search strategies

OVID Medline

#	**Searches**	**Results**
1	Fasting.mp. or exp Fasting/	112134
2	Intermittent fasting.mp. or exp Fasting/	35880
3	Fast*.mp.	467768
4	Intermittent fast*.mp.	496
5	Ramadan.mp.	1013
6	Muslim.mp. or exp Islam/	7294
7	exp Caloric Restriction/ or diet restriction.mp.	6771
8	1 or 2 or 3 or 4 or 5 or 6 or 7	480057
9	F?etal movement.mp. or exp Fetal Movement/	2218
10	F?etal development.mp. or exp Fetal Development/	118977
11	F?etal wellbeing.mp.	301
12	Biophysical profile.mp.	539
13	9 or 10 or 11 or 12	119846
14	exp Pregnancy/ or pregnancy.mp.	956844
15	Pregnant wom#n.mp.	95333
16	Expectant mother.mp.	197
17	14 or 15 or 16	963080
18	8 and 13 and 17	1228
19	Limit 18 to (human and English language and yr=1883-2021)	833

Note: As searched on 14th March 2022

PubMed

#	**Searches**
1	((((((fasting[Title/Abstract]) OR (intermittent fasting[Title/Abstract])) OR (ramadan[Title/Abstract])) OR (islam[Tit
2	((pregnancy[Title/Abstract]) OR (pregnant women[Title/Abstract])) OR (expectant mother[Title/Abstract])

3	(((fetal movement[Title/Abstract] OR (fetal wellbeing[Title/Abstract])) OR (fetal wellbeing[Title/Abstract])) OR (bio
4	(((((((fasting[Title/Abstract]) OR (intermittent fasting[Title/Abstract])) OR (ramadan[Title/Abstract])) OR (islam[T
5	(((((((fasting[Title/Abstract]) OR (intermittent fasting[Title/Abstract])) OR (ramadan[Title/Abstract])) OR (islam[T
6	(((((((fasting[Title/Abstract]) OR (intermittent fasting[Title/Abstract])) OR (ramadan[Title/Abstract])) OR (islam[T
7	(((((((fasting[Title/Abstract]) OR (intermittent fasting[Title/Abstract])) OR (ramadan[Title/Abstract])) OR (islam[T

Note: As searched on 14th March 2022

SCOPUS

#	**Searches**
1	TITLE-ABS-KEY (fast*) OR TITLE-ABS-KEY (intermittent AND fast*) OR TITLE-ABS-KEY (ramadan) OR TITL
2	TITLE-ABS-KEY (f?etal AND movement) OR TITLE-ABS-KEY (f?etal AND development) OR TITLE-ABS-KEY (
3	TITLE-ABS-KEY (pregnan*) OR TITLE-ABS-KEY (pregnant AND wom?n) OR TITLE-ABS-KEY (expectant AND
4	(TITLE-ABS-KEY (fast*) OR TITLE-ABS-KEY (intermittent AND fast*) OR TITLE-ABS-KEY (ramadan) OR TIT
5	(TITLE-ABS-KEY (fast*) OR TITLE-ABS-KEY (intermittent AND fast*) OR TITLE-ABS-KEY (ramadan) OR TIT

Note: As searched on 14th March 2022

EMBASE

#	**Searches**	**Results**
1	fasting.mp. or exp Fasting/	181781
2	intermittent fasting.mp. or exp Fasting/	13506
3	fast*.mp.	761185
4	intermittent fast*.mp.	1081
5	ramadan.mp.	2036
6	muslim.mp. or exp Islam/	7056
7	exp Caloric Restriction/ or diet restriction.mp.	120636
8	1 or 2 or 3 or 4 or 5 or 6 or 7	810513
9	f?etal movement.mp. or exp Fetal Movement/	4286
10	f?etal development.mp. or exp Fetal Development/	36827
11	f?etal wellbeing.mp.	670
12	biophysical profile.mp.	978
13	9 or 10 or 11 or 12	41644
14	exp Pregnancy/ or pregnancy.mp.	1038028
15	pregnant wom#n.mp.	170987
16	expectant mother.mp.	949
17	14 or 15 or 16	1074954
18	8 and 13 and 17	527
19	limit 18 to (human and english language and yr="1883-2021")	326

Note: As searched on 14th March 2022

Cochrane Central Register of Controlled Trials

#	**Searches**	**Results**
1	fasting.mp. or exp Fasting/	35015
2	intermittent fasting.mp. or exp Fasting/	3331
3	fast*.mp.	66732

4	intermittent fast*.mp.	166
5	ramadan.mp.	185
6	muslim.mp. or exp Islam/	292
7	exp Caloric Restriction/ or diet restriction.mp.	6914
8	1 or 2 or 3 or 4 or 5 or 6 or 7	68566
9	f?etal movement.mp. or exp Fetal Movement/	167
10	f?etal development.mp. or exp Fetal Development/	3013
11	f?etal wellbeing.mp.	75
12	biophysical profile.mp.	81
13	9 or 10 or 11 or 12	3240
14	exp Pregnancy/ or pregnancy.mp.	60667
15	pregnant wom#n.mp.	14950
16	expectant mother.mp.	54
17	14 or 15 or 16	64243
18	8 and 13 and 17	72
19	limit 18 to (human and english language and yr="1883-2021")	66

Note: As searched on 14th March 2022

Table S2: Summary of included studies (n=18)

Study / Country	**Study design**	**N**	**Trimester**	**Mean maternal age (y)**	**Type of fasting**	**Main finding**
Naderi (2004) *Iran*	Case-control	101	Second and third	Case = 28.3 (5.5) Control = 28.8 (5.7)	Ramadan fasting	No significant difference in fundal height increase in 5 performed examinations, and mean BW between study groups.
Dikensoy (2008, 2009) *Turkey*	Prospective cohort	65	Second and third	Fasting = 24.0 (5.3) Control = 26.0 (4.2)	Ramadan fasting	No difference in increase in BPD, FL, EFBW, and fetal BPP and AFI between the groups. Fetal BPP and AFI were within normal ranges in both groups.

Alwasel et al (2010) *Saudi Arabia*	Retrospective cohort	7083	First, second and third	29.5	Ramadan fasting	No difference in birth weight between babies in utero and not in the utero during Ramadan regardless of the trimester and gender. No difference in other outcomes (BW, HC, CC), between babies in utero and not in utero during Ramadan, regardless gender.
Ziaee (2010) *Iran*	Retrospective cohort	189	First, second and third	25.9	Ramadan fasting	No significant increase in risk of low BW with fasting in the first trimester. No significant differences between BW, length, HC and number of days on fasting.

Alwasel (2011) *Saudi Arabia*	Retrospective cohort	967	First, second and third	Boys = 29.3 (6.1) Girls = 29.5 (5.9)	Ramadan fasting	Babies who were boys and were in the second trimester of gestation during Ramadan were significantly longer at birth than babies that were not in utero during Ramadan and baby girls. Girls who were in their second trimester of gestation during Ramadan had significantly shorter gestation periods.
Moradia (2011) *Iran*	Case-control	52	Second and third	Fasting = 28.3 (5.5) Non-fasting = 28.3 (5.5)	Ramadan fasting	No significant difference between fasting and non-fasting groups in terms of increase in BPD, FL, AC, fetal weight (fetal weight gain, increase in gestational age related to BPD, FL and AC, and changes in AFI.
Ozturk (2011) *Turkey*	Prospective cohort	72	Second	Fasting = 30.1 Control = 29.5	Ramadan fasting	No significant difference in birth weight between study groups.

Awwad (2012) *Lebanon*	Prospective cohort	402	Second and third	Fasting = 29.7 (5.2) Control = 30.0 (5.4)	Ramadan fasting	Neonates of fasted women had lower BW than controls. No significantly different in preterm delivery rates, small for gestational age, and gestational age at delivery.
Petherick (2014) *United Kingdom*	Prospective cohort	300	First, second and third	Fasted = 27.6 (4.7) None = 29.0 (5.4)	Ramadan fasting	No significant association between fasting, preterm birth and low BW before and after adjustment for other covariables

Savitri (2014) *Netherlands*	Prospective cohort	130	First, second and third	Fasting < half a month = 28.9 (4.9) Fasting > half a month = 28.9 (4.7) Non-fasting = 29.3 (4.2)	Ramadan fasting	Significantly lower BW of new-borns of women who fasted in the first trimester than non-fasting women, after adjustment for covariates. No differences in BW found in the second or third trimester. Lowest BW in new-borns of women who fasted more than half a month, but no significant interaction suggesting the opposing effects of fasting per trimester of exposure.

Seckin (2014) *Turkey*	Prospective cohort	169	Third	Fasting = 24.0 (4.2) Non-fasting = 26.1 (5.9)	Ramadan fasting	Significantly greater mean BW and change in AFI in fasting women compared to non-fasting group. The number of patients who initially had a normal amniotic fluid measurement and subsequently developed oligohydramnios was significantly higher in the religious fasting group than in the non-fasting group. No significant differences in changes in BPD, AC, FL, fetal weight gain, changes in age-BPD, age-FL, age-AC, and mean gestational age at delivery between groups.

Karateke (2015) *Turkey*	Prospective cohort	240	First, second and third	26.2 (3.7)	Ramadan fasting	Lower AFI in fasting than without fasting among pregnant women in the second trimester. No significant differences between the groups in terms of increase of fetal BPD, increase of fetal femur length, increase of fetal EFBW, AFI in first and third trimesters, newborn BW, rate of low BW, and Apgar score.

Sakar (2015) *Turkey*	Case-control	166	Second and third	Fasting = 26.8 (5.2) Non-fasting = 28.4 (5.0)	Ramadan fasting	Significant difference in increase in BPD, HC, FL, increase in gestational age related to HC and FL between groups. Increase in AFI was significant in the non-fasting group only. No significant differences in increase in AC, gestational age related to BPD, AC and fetal weight gain between groups.
Abd-Allah Rezk et al (2016) *Egypt*	Case-control	450	Third	Fasting = 23.2 (4.3) Non-fasting = 23.0 (4.0)	Ramadan fasting	No significant differences in reactivity of NST, modified biophysical scores, gestational age at delivery, neonatal weight, 5-min Apgar scores and admission to neonatal intensive care unit. Short-term maternal fasting has no deleterious effect on fetal well-being parameters or neonatal outcome.

Sakar (2016) *Turkey*	Case-control	338	Third	Fasting = 28.0 (5.8) Non-fasting = 27.6 (5.5)	Ramadan fasting	No significant differences in mean BW, height and HC between groups.
Tith (2019) *Canada*	Retrospective cohort	3123508	First, second and third	NA	Ramadan fasting	Ramadan fasting in week 15-21 and 22-27 of gestation were associated with greater risk of very preterm birth.
Bernier (2021) *Canada*	Retrospective cohort	78623	First and second	35.0	Ramadan fasting	Ramadan fasting has no significant association with the risk of early or late stillbirth overall.
Hossain (2021) *Pakistan*	Prospective cohort	215	Third	Fasted = 26.54 (4.82) Not fasted = 26.84 (5.06)	Ramadan fasting	5-min Apgar scores are significantly higher in the fasted group than the non-fasted group. However, there is no significant difference in rate of preterm delivery and anthropometric measurements between both groups

Table 1: Summary characteristics of the included studies (n=18)

		N=18
Country	Turkey	6 (33.3)
	Iran	3 (16.7)
	Canada	2 (11.1)
	Saudi Arabia	2 (11.1)
	Egypt	1 (5.6)

	Lebanon	1 (5.6)
	Pakistan	1 (5.6)
	United Kingdom	1 (5.6)
	Netherlands	1 (5.6)
Year	Earlier than 2005	1 (5.6)
	2005-2009	1 (5.6)
	2010-2015	11 (61.1)
	2016-2020	4 (22.2)
	2021-2022	1 (5.6)
Study design	Case-control	6 (33.3)
	Prospective cohort	7 (38.9)
	Retrospective cohort	5 (27.8)
Type of fasting	Ramadan fasting	16 (100.0)
Number of samples		3,213,070
Trimester	Second only	1 (5.6)
	Third only	4 (22.2)
	First, second and third	7 (38.9)
	First and second	1 (5.6)
	Second and third	5 (27.8)
Mean maternal age (years)*	<25	3 (16.7)
	25-27	4 (22.2)
	27-30	9 (50.0)
	35	1 (5.6)
	Not available	1 (5.6)

Table 2: Quality assessment of the included studies (n=18)

Case-control studies	**Case-control studies**	**Case-co**
Study	**Study**	**Selectio**
		Adequate case definition	**Case re**
Naderi (2004)	Naderi (2004)	
Moraida (2011)	Moraida (2011)	
Sakar (2015)	Sakar (2015)	
Abd-Allah Rezk (2016)	Abd-Allah Rezk (2016)	
Sakar (2016)	Sakar (2016)	
Cohort studies	**Cohort studies**	**Cohort**
Study	**Study**	**Selectio**
		Exposed cohort representativeness	**Non-exp**
Dikensoy (2008), Dikensoy (2009)	Dikensoy (2008), Dikensoy (2009)	
Alwasel (2010)	Alwasel (2010)	
Ziaee (2010)	Ziaee (2010)	
Alwasel (2011)	Alwasel (2011)	
Ozturk (2011)	Ozturk (2011)	
Awwad (2012)	Awwad (2012)	
Patherick (2014)	Patherick (2014)	
Savitri (2014)	Savitri (2014)	
Seckin (2014)	Seckin (2014)	
Karateke (2015)	Karateke (2015)	
Tith (2019)	Tith (2019)	
Bernier (2021)	Bernier (2021)	
Hossain (2021)	Hossain (2021)	

Table 3: Summary of outcomes reported in the studies (n=18)

Study	Neonatal weight	AF I	Increase in BPD	Increase in EFBW/ FWG	Increase in fetal FL	HC	Gestational age at delivery	Length/ height	Preterm birth/ delivery	Increase in AC	5-min APGAR score	BPP	Still
Naderi (2004)													
Dikensoy (2008, 2009)													
Alwasel (2010)													
Ziaee (2010)													
Alwasel (2011)													
Moradia (2011)													
Ozturk (2011)													
Awwad (2012)													
Savitri (2014)													
Seckin (2014)													
Petherick (2014)													
Karateke (2015)													
Sakar (2015)													
Abd-Allah Rezk (2016)													
Sakar (2016)													
Tith (2019)													
Bernier (2021)													
Hossain (2021)													
TOTAL	**13**	**6**	**5**	**5**	**5**	**5**	**4**	**4**	**4**	**3**	**3**	**2**	**1**

AFI=amniotic fluid index, BPD=fetal biparietal diameter, BPP=fetal biophysical profile, EFBW=estimated fetal body weight, FWG=Fetal weight gain, FL= femur length, HC=head circumference, AC=abdominal

circumference, =positive association, =no association, =negative association.

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`Figure 1.docx` available at https://authorea.com/users/521743/articles/594533-effects-of-ramadan-fasting-on-fetal-health-a-systematic-review