



# Thyroxine Replacement Therapy during Ramadan Fasting: A Narrative Review

Asma Aljaberi<sup>1,2</sup> Reem Alamoudi<sup>3,4,5</sup> Tamer M. Elsherbiny<sup>6</sup> Khadija Hafidh<sup>7,8</sup>  
Syed Abbas Raza<sup>9</sup> Salem A. Beshyah<sup>8</sup>

<sup>1</sup>Department of Endocrinology, Tawam Hospital, Al Ain, United Arab Emirates

<sup>2</sup>Internal Medicine Department, College of Medicine and Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates

<sup>3</sup>College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, Jeddah, Saudi Arabia

<sup>4</sup>King Abdullah International Medical Research Center, Jeddah, Saudi Arabia

<sup>5</sup>Department of Medicine, King Abdulaziz Medical City, Jeddah, Ministry of National Guard-Health Affairs, Jeddah, Saudi Arabia

<sup>6</sup>Endocrinology Unit, Alexandria Faculty of Medicine, Alexandria University, Khartoum Square, Azarita, Alexandria, Egypt

**Address for correspondence** Salem A. Beshyah, MB, DIC, PhD, MRCP, Department of Medicine, Dubai Medical College, Dubai, United Arab Emirates (e-mail: beshyah@yahoo.com).

<sup>7</sup>Diabetes Unit, Department of Internal Medicine, Dubai Academic Health Corporation, Dubai, United Arab Emirates

<sup>8</sup>Department of Medicine, Dubai Medical College, Dubai, United Arab Emirates

<sup>9</sup>Shaukat Khanum Cancer Hospital and Research Center, Lahore, Pakistan

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## Abstract

**Introduction** Ramadan fasting-induced changes in eating and sleeping patterns pose a risk of influencing thyroid hormone levels. There is a recognition of the potential impact of fasting and feasting on levothyroxine (L-T4) absorption.

**Materials and Methods** A narrative, nonsystematic literature review from two major medical online databases (PubMed and Google Scholar) from their inception to the search day (February 22, 2024). A relevant combined search term was used. The retrieved literature is narrated in a concise account.

**Results** There is a relationship between metabolism and thyroid-stimulating hormone (TSH). This relationship contributes to transient metabolic disturbances that influence the pharmacodynamics and pharmacokinetics of various drugs, adding complexity to the management of hypothyroidism during Ramadan fasting. Several observational studies have studied the changes in thyroid function levels during unmodified L-T4 regimens. Experimental trials explored the impact on body weight, well-being, and thyroid functions when the timing of L-T4 administration changes. Findings are far from homogeneous due to different study protocols. A recent meta-analysis demonstrated a significant post-Ramadan increase in TSH levels among euthyroid patients. L-T4 timing points, encompassing pre-Iftar, post-Iftar, and pre-Suhoor, are associated with elevated TSH levels after Ramadan fasting. The emphasis on individualized L-T4 regimens during Ramadan fasting is underscored, with recommendations for patients to refrain from food for at least 3 hours before and 30 minutes

## Keywords

- ▶ Ramadan fasting
- ▶ thyroid
- ▶ hypothyroid
- ▶ levothyroxine
- ▶ food-drug interaction

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after L-T4 intake to ensure optimal compliance by most experts. The association between adherence to L-T4 during Ramadan fasting and maintaining euthyroid status is highlighted, encouraging patients to follow prescribed regimens diligently. Modified dosing frequencies, such as weekly regimens, exhibit promising results, especially in patients grappling with compliance issues. Proactive consultations with physicians before Ramadan are needed to review the latest thyroid function test and make possible dose adjustments.

**Conclusion** Managing hypothyroidism during Ramadan necessitates an understanding of medication timing, food-drug interactions, and prior regimens. Adherence, facilitated by flexibility, plays a critical role in achieving euthyroid status.

## Introduction

During Ramadan, Muslims worldwide abstain from food and fluid intake from dawn to sunset for 29 to 30 days. The two main meals are taken just before dawn (*Suhoor*) and after sunset (*Iftar*). This prolonged fasting causes several minor metabolic and hormonal changes in the body, which rarely cause any problems for a healthy individual. However, concerns may arise in certain chronic diseases, and thus, patients are advised to consult their physicians before planning to fast.<sup>1</sup>

Hypothyroidism (HypoT) is a common endocrine disorder.<sup>2</sup> Several studies have demonstrated that optimal and more consistent levothyroxine (L-T4) absorption occurs under fasting conditions.<sup>3</sup> Nonfasting administration of L-T4 has been criticized for being associated with higher and more variable serum thyroid-stimulating hormone (TSH) concentrations.<sup>4</sup>

During Ramadan fasting (RF), patients may find taking L-T4 on an empty stomach challenging since the first evening meal is commonly associated with family gatherings and other social activities. Several early reviews on the thyroid during RF were published when the evidence was limited. Several opinion-based pieces were published long ago, mostly based on extrapolating other fasting scenarios to RF.<sup>5–8</sup> For instance, Beshyah et al, while discussing the management of common endocrine conditions other than diabetes mellitus during RF, suggested that L-T4 should be taken on an empty (or near-empty) stomach and not followed by food for 0.5 to 1 hour, according to the patient's lifestyle.<sup>5</sup> Similarly, Raza et al advised that during Ramadan, patients with thyroid diseases usually do not need treatment adjustments and can quickly and safely avoid any health hazards.<sup>6</sup> Patients with HypoT taking thyroxine can take their tablets on an empty stomach at bedtime instead of half an hour before Suhoor. The difference between taking it on an empty stomach or taking it in bed was not significant. Also, Azizi concluded that changes in serum thyroid hormones and, therefore, TSH concentrations during Islamic fasting are minimal and do not alter the health of fasted individuals.<sup>7</sup> In addition, RF per se does not cause any need for a change in the dosage of L-T4 in hypothyroid patients. However, other factors that require a change in L-T4 dose, particularly the distance between the ingestion of medication and the last and/or next meals, should be considered. Also, Hameed and Raza reiterated

that patients with thyroid diseases do not normally need medication adjustment and can fast safely.<sup>8</sup> On the other hand, hypothyroid patients are prescribed thyroxine tablets, which should be taken on an empty stomach at bedtime or half an hour before *Suhoor*.

However, more data on various questions were generated recently. Therefore, we aimed to produce an updated literature review incorporating all the newer data and suggesting some evidence-based clinical practice guidelines.

## Materials and Methods

We searched two online databases (PubMed [National Library of Medicine] and Google Scholar). The combined search term [(Ramadan) AND (Thyroxine OR Thyroid OR Hypothyroid OR Hypothyroidism OR Thyroxine OR "Thyroxine replacement")] was used to identify the relevant records from their inception to the search day (February 22, 2024). Fifty-five and 434 records were identified in the PubMed and Google Scholar databases, respectively. Records were retrieved, pooled to remove duplicates, and examined for relevance. Only full-text articles in English regarding RF and thyroid replacement as a core content were included. These resulting articles were examined and the relevant articles were included in this review. This is a narrative, nonsystematic review of the literature, and thus, no statistical analysis was conducted on the data contained in the original articles, and detailed numerical presentations were avoided. All types of manuscripts were included in the search.

## Results

The research questions addressed by or from original studies and opinion pieces on the interplay between RF and thyroid function (TF) and thyroxine hormone replacement therapy are summarized in ►Table 1. These will be discussed briefly below.

### What is the Impact of Food Intake and Fasting on Levothyroxine Absorption?

It is well established that an acidic environment in the stomach promotes L-T4 absorption, mostly in the jejunum and ileum. Absorption of oral L-T4 is approximately 75 to 80%

**Table 1** The research questions addressed by or resulted from original studies and opinion pieces on the interplay between Ramadan fasting, thyroid function, and thyroxine hormone replacement therapy

1. What is the impact of food intake and fasting on thyroid hormone homeostasis?
2. What is the impact of RF on L-T4 replacement therapy?
3. What is the best time to take L-T4 during RF?
4. Is routine change in L-T4 dose required during RF?
5. Can L-T4 be given less often than daily to enhance compliance with timing?
6. Are changes in thyroid hormone levels clinically meaningful?
7. Are certain groups of patients more vulnerable than others?
8. Is routine monitoring of thyroid function tests required after Ramadan over and above the usual clinical need?

Abbreviations: L-T4, levothyroxine; RF, Ramadan fasting.

in the fasting state, with a decrement in absorption if the L-T4 tablet is given in a nonfasting state.<sup>9</sup> Absorption is as low as 59 to 68% when nonfasting, compared to 78 to 80% when fasting.<sup>9</sup> Thus, when giving L-T4 intravenously, if necessary in a hospitalized patient, approximately 75% of the oral outpatient dose can be used. Some foods and beverages reported as culprits in reducing L-T4 absorption include fiber, soybeans, coffee, and grapefruit.<sup>9</sup>

The impaired absorption associated with food and drinks may be overcome by changing the time of the L-T4 administration, or a higher dose of L-T4 may be administered to compensate for the effect of the decreased absorption. Vitamin C, on the other hand, can improve L-T4 absorption.<sup>10,11</sup> Another important factor that may reduce exposure to thyroxine intake is the time of day “diurnal variation”; taking L-T4 at bedtime (3 hours after the evening meal) has been shown to increase free thyroxine (fT4) and reduce TSH blood levels, proposing the move of administration timing from morning to evening.<sup>10,11</sup>

### What is the Impact of Ramadan Fasting on Thyroid Hormone Homeostasis?

► **Table 2** summarizes the setting, main findings of the reviewed studies, and their implications for L-T4 management during Ramadan. RF may affect some laboratory findings. Fedail et al measured fasting serum thyroxine and triiodothyronine (T3) in a group of 24 Muslims at the beginning and end of Ramadan.<sup>12</sup> There was a small but significant rise in thyroxine, but no significant change was observed in T3. Although unlikely to affect normal people, these changes may be substantial in patients. Sulimani measured plasma total T4, TSH, fT4, and free T3 (fT3) levels in 28 healthy male subjects before and at the end of RF.<sup>13</sup> The effect of short-term food deprivation between dawn and sunset was also investigated. There were no significant differences between the morning and evening values in

the TF tests (TFTs) for all comparisons. In addition, there was no substantial change in the results of the TFTs done before and at the end of RF. The values for plasma T4, T3, fT4, and TSH before and after RF were not significantly different for all comparisons. Also, Sajid et al compared TFTs in 46 individuals before, during, and after RF.<sup>14</sup> The results showed a significant gradual rise in TSH throughout the fasting month, reaching a maximum on the 26th day of fasting, although the mean levels remained within normal limits. TSH increased linearly in relation to the number of fasting days. Pre-Ramadan levels were reattained after 5 months, well after the end of Ramadan. There was no significant change in T3 and T4 levels. Bogdan et al measured serum concentrations of several hormones, including TSH and thyroid hormones, around the clock at six 4-hour intervals before and on the 23rd day of Ramadan.<sup>15</sup> Time series were analyzed using repeated measures. Serum TSH rhythm was blunted over the test period in the form of decreased midnight and increased afternoon values. These data suggest fasting, modifications in sleep schedule, and psychological and social habits during Ramadan induce changes in the rhythmic pattern of many hormonal variables, including thyroid hormones. Bahrayni et al evaluated the changes in TSH, fT4, and T3 serum levels and body composition in 58 premenarche girls (9–13 years old) through Ramadan.<sup>16</sup> Thirty-one fasted and 27 did not fast. RF induces a significant decrease in body mass index and weight in the fasted group, while a substantial increase was observed in the nonfasted group. Although T3 decreased significantly by fasting, it remained in the normal range. Hence, T4 decreased and TSH increased slightly in both groups. So, despite a significant reduction of T3 in the fasting group, variation in thyroid hormone levels remained within the normal range during RF.

The differences in the reported results from studies summarized earlier may be due to different fasting hours (16 vs. 14.5 hours), different locations with different atmospheric temperatures (Khartoum and Bristol vs. Pakistan), different demographics of included subjects (males vs. females), and different post-Ramadan follow-up time points.

During Ramadan, patients often find it difficult to administer L-T4 on an empty stomach since they may not wake up so early, so in this article, the suggestion has been given to take it at bedtime. Karoli et al studied the impact of bedtime L-T4 on TSH levels in fasting patients with HypoT in a prospective observational study.<sup>17</sup> They found 29/47 patients showed higher TSH values ( $\geq 2$  mIU/L) while 18/47 patients had a 2-mIU/L variations in TSH than their pre-Ramadan assessment. The meal-L-T4 interval and concomitant illnesses were significantly different in the two groups. The variation in TSH has a significant correlation with meal-L-T4 interval. They suggested that bedtime doses can be appropriate for HypoT patients during RF or at other times, as long as there is an interval of a minimum of 2 hours since the last meal is maintained. They called for frequent and close monitoring to keep TSH in the narrow range, such as pregnant, the elderly, and those who have osteoporosis. El-Kaissi et al examined patients who had TFTs available within 3 months pre-Ramadan and 2 months post-Ramadan.<sup>18</sup> They

**Table 2** A summary of the setting, main findings, and the implications for levothyroxine management during Ramadan

Study [reference]	Population/Setting	Key findings	Implications for levothyroxine management
Fedail et al (1982) <sup>12</sup>	24 Muslims during Ramadan	No significant change in triiodothyronine levels.	Minimal impact of RF on thyroid function in healthy individuals
Sulimani (1988) <sup>13</sup>	Healthy male subjects	No significant changes in TSH, T4, fT4, and fT3 levels pre- and post-RF	Stability of thyroid function during RF in healthy males
Sajid et al (1991) <sup>14</sup>	46 individuals during Ramadan 1989	A gradual rise in TSH during fasting; normal levels resumed post-Ramadan. No significant changes in T3 and T4 levels	Transient, noncritical TSH elevation during RF without long-term impact
Bogdan et al (2001) <sup>15</sup>	Hormone levels during Ramadan	Daytime fasting altered the rhythmic pattern of TSH and other hormones	Highlights the effect of RF and lifestyle changes on hormonal rhythms
Bahrayni et al (2013) <sup>16</sup>	Premenarche girls	Decrease in T3 but within normal range; slight increase in TSH	RF can affect body composition and thyroid function in young females
Karoli et al (2013) <sup>17</sup>	Hypothyroid patients during Ramadan in a prospective observational study	Impact of bedtime L-T4 on TSH levels in fasting patients with HypoT	They suggested that bedtime doses can be appropriate for HypoT patients during Ramadan
El-Kaissi et al (2020) <sup>18</sup>	L-T4-treated hypothyroid patients	Significant post-Ramadan increase in plasma TSH, independent of L-T4 administration timing	Emphasizes the need for possible adjustments in the L-T4 regimen during RF
Dellal et al (2020) <sup>19</sup>	Hypothyroid patients during Ramadan	Insignificant changes in TSH between L-T4 administration times (late evening vs. pre-Suhoor)	Indicates the need for individual assessment of optimal L-T4 timing during RF
Alkaf et al (2022) <sup>20</sup>	Hypothyroid patients on L-T4	Significant increase in TSH post-Ramadan; changes in TF more pronounced in those with higher baseline TSH	Highlights the importance of baseline TSH monitoring and potential adjustments pre-RF
Elsherbiny (2023) <sup>21</sup>	Hypothyroid patients during Ramadan	Increase in post-Ramadan TSH; better control in adherent patients	Stresses adherence to prescribed L-T4 regimen and pre-Ramadan thyroid assessment

Abbreviations: fT4, free thyroxine; HypoT, hypothyroidism; L-T4, levothyroxine; RF, Ramadan fasting; TF, thyroid function; TSH, thyroid-stimulating hormone.

documented the adherence to L-T4, eating patterns, and L-T4 administration about meal times during RF. Pre- and post-Ramadan TFTs in 112 patients (89 females) with a mean age of 44.7 years. The mean TSH within 2 months post-Ramadan was higher than before Ramadan (BR) (3.072 vs. 1.809 mIU/L). After RF, 32.1% of the patients had a plasma TSH outside of the normal reference range. Older patients and males were more likely to have an increased plasma TSH post-Ramadan. There was no relationship between the time of L-T4 administration and the change in TSH level. Dellal et al evaluated the changes in TFTs during Ramadan and compared late evening and pre-Suhoor use of L-T4 in patients with HypoT.<sup>19</sup> Patients on L-T4 treatment who had normal TFTs were recruited for the study in the last week BR. Patients were offered to take L-T4 at 10.30 to 11.00 p.m. before sleep or between 01:30 and 03:00 a.m. at least 30 minutes pre-Suhoor. There were mostly females (85.5%). The mean basal

TSH was 2.02  $\mu$ IU/mL and insignificantly increased at the end of Ramadan (2.18  $\mu$ IU/mL). fT3 decreased while fT4 increased. Eighteen patients preferred to take L-T4 in the late evening, and 44 preferred to take it at pre-Suhoor. There were insignificant increases in TSH in both groups. At the end of Ramadan, TSH increased by 63.9%, decreased by 36.1%, and did not change in one patient. The authors considered the increase in TSH was not significant after Ramadan. While there was an insignificant increase in median TSH, about one-third of patients had lower TSH. Furthermore, Alkaf et al examined RF's short- and long-term impact on TF in patients with primary HypoT on L-T4.<sup>20</sup> TFTs in patients with primary HypoT were retrospectively analyzed in 481 patients within 3 months BR, 1 to 2 weeks (PR1), and 3 to 6 months (PR2) post-Ramadan. Controlled TF was defined as TSH between 0.45 and 4.5 IU/L. Inadequate control was defined as TSH > 4.5 IU/L. The median TSH level increased significantly

from BR to PR1 levels ( $p < 0.001$ ). This was accompanied by a fall in  $ft_4$  and  $ft_3$  at PR1 ( $p < 0.001$ ). About a quarter of patients with previously controlled TFTs at BR had deterioration in TFTs at PR1. Sixty-one percent of patients with previously uncontrolled TFTs at BR remained uncontrolled at PR1. Baseline TSH was significantly associated with loss of thyroid control in Ramadan. TSH,  $ft_4$ , and  $ft_3$  levels returned to normal at PR2. The authors concluded that RF can negatively affect the TFTs of patients on L-T4 replacement. Albeit modestly and transitory in most patients, a significant minority exhibits more pronounced and clinically relevant changes. Finally, Elsherbiny prospectively studied the impact of fasting in a relatively large cohort.<sup>21</sup> Patients choose one of three L-T4 regimens during Ramadan. Regimen 1: 60 minutes before *Iftar*, regimen 2: 3 to 4 hours after *Iftar*, 60 minutes before *Suhoor*, and regimen 3: before the start of the next fast, 3 to 4 hours after the early *Suhoor*. The study included 292 adequately replaced hypothyroid patients. Most patients were adherent (85.3%). The mean post-Ramadan TSH was significantly higher than pre-Ramadan. Most patients were still euthyroid post-Ramadan (79.8%). Post-Ramadan TSH significantly correlated to pre-Ramadan TSH ( $p < 0.001$ ). Post-Ramadan TSH was considerably higher in nonadherent patients than in adherent patients. The authors concluded that post-Ramadan TSH and euthyroidism are related to adherence and pre-Ramadan TSH.

### What is the Optimal Timing of Levothyroxine Intake during Ramadan?

A number of studies focused on determining the optimal time for administration of L-T4 during Ramadan (–Tables 2–4). Hossain et al examined the effects of evening versus morning L-T4 dosing on serum TSH and  $ft_4$  levels, along with secondary analysis of lipid profiles.<sup>22</sup> They randomized 147 patients (73 in group A, evening dose; 72 in group B, morning dose). Fifty-eight patients in group A and 57 in group B were considered for statistical evaluation. There was no statistical difference in the achievement of euthyroidism and improvement of thyroid profile between the two groups. Changes in total cholesterol, triglyceride values, low-density lipoprotein (LDL), very LDL, and high-density lipoprotein were not significantly different between the groups. The authors concluded that taking L-T4 at bedtime improved thyroid hormone levels. Serum lipid levels showed no significant changes with bedtime versus morning intake. Also, Dabbous et al explored the impact of two different dosing times of L-T4 during Ramadan on TSH levels, compliance, and convenience in a randomized, open-label, prospective trial.<sup>23</sup> The study enrolled adult patients with primary HypoT and stable TSH levels over the previous 6 months who planned to fast during Ramadan. All patients were randomly assigned to two groups. In group A ( $n = 50$ ), patients took L-T4 30 minutes before breaking the fast at sunset (*Iftar*), and in group B ( $n = 46$ ), patients took it 30 minutes before an early morning meal before sunrise (*Suhoor*). After Ramadan, TSH levels increased in groups A and group B, and there was no difference between the two groups. Compliance with intake instructions was reported in 41.6% of group A and 35.7% of

group B patients. In both groups, 95% of patients said taking the medication at the assigned time was convenient. Choosing an optimal time for L-T4 intake during the month of Ramadan remains a challenge. The study did not establish a definitive optimal timing or dosage for L-T4 administration during Ramadan to effectively manage HypoT. Zaboony et al investigated the optimal timing for L-T4 intake during Ramadan in a prospective study involving 50 patients with primary HypoT over 3 months, including both fasting and prefasting periods.<sup>24</sup> The patients were divided into three groups with different times of L-T4 intake. The participants were divided into three groups based on L-T4 administration times: pre-*Iftar* (L-T4 at *Iftar* time with a 30-minute delay before eating), post-*Iftar* (L-T4 2 hours after *Iftar*), and pre-*Suhoor* (L-T4 1 hour before *Suhoor*, after fasting for 2 hours). When TSH levels were compared BR and after Ramadan, there were no significant differences within or among all the study groups. Moreover, the frequencies of the TSH control after Ramadan showed no significant differences within each of the study groups ( $p = 0.18, 0.75, 1.0$  for pre-*Suhoor*, pre-*Iftar*, and post-*Iftar*, respectively). Similarly, comparison among the study groups showed no significant differences regardless of whether the patients had controlled or uncontrolled TSH BR ( $p = 0.75$  and  $0.67$ , respectively). In the patients with controlled TSH BR, 8 out of 10 (pre-*Suhoor*), 8 out of 12 (pre-*Iftar*), and 4 out of 6 (post-*Iftar*) maintained their control after Ramadan. While in the patients with uncontrolled TSH BR, 7 out of 10 (pre-*Suhoor*), 6 out of 8 (pre-*Iftar*), and 2 out of 4 (post-*Iftar*) achieved controlled TSH after Ramadan. The authors concluded that no significant differences in TSH control were observed in patients taking L-T4 at pre-*Iftar*, post-*Iftar*, or pre-*Suhoor* time in Ramadan.

El-Kaissi et al attempted to find the best time to instruct patients to take L-T4 during Ramadan to minimize changes in TFTs during this period.<sup>25</sup> In a randomized prospective study, HypoT patients were instructed to take L-T4 at one of three times: 30 minutes before *Iftar* (group 1), 3 hours after *Iftar* (group 2), or 30 minutes before *Suhoor* (group 3). TFTs were performed 3 months BR and 6 weeks post-Ramadan. Data from patients with at least one blood test BR or after Ramadan were analyzed using mixed-effects regression models. Plasma TSH levels were available at one or more time points for 148 patients, group 1 ( $n = 50$ ), group 2 ( $n = 46$ ), and group 3 ( $n = 52$ ). A significant within-patient increase in plasma TSH was seen in patients at the 25th percentile pre-Ramadan in groups 2 and 3 ( $p$ -values  $< 0.001$ ) but not in group 1. A significant within-patient decrease in plasma TSH was found in patients at the 75th percentile in group 1 only. No significant within-patient changes were found for patients at the 50th percentile pre-Ramadan, though descriptively, increases in plasma TSH were observed for groups 2 and 3. In contrast, a decrease was observed in group 1. The authors suggest that taking L-T4 at *Iftar* 30 minutes before the *Iftar* meal minimizes unfavorable changes in plasma TSH post-Ramadan. In contrast, taking L-T4 3 hours post-*Iftar* or 30 minutes before *Suhoor* led to a greater rise in post-Ramadan TSH. Ghaffar et al investigated

**Table 3** Demonstration of the importance of individualizing levothyroxine administration timing during Ramadan based on patient preference and lifestyle, as the impact on thyroid function seems minimally affected by the specific timing of intake

Reference	Study design	L-T4 intake timing	Key findings	Recommendations for levothyroxine management
Hossain et al (2018) <sup>22</sup>	Randomized comparison	Evening vs. morning doses	No significant difference in achieving euthyroidism or improvement in thyroid profile between groups	Bedtime L-T4 can be as effective as morning intake; patient preference can guide timing
Dabbous et al (2019) <sup>23</sup>	Open-label, randomized, prospective	Pre-Iftar vs. pre-Suhoor	No significant difference in TSH levels or compliance between timings	The timing of L-T4 intake should be chosen based on individual convenience and adherence
Zaboon et al (2020) <sup>24</sup>	Prospective study	Pre-Iftar, post-Iftar, pre-Suhoor	No significant differences in TSH control post-Ramadan among the different timings	L-T4 intake timing during Ramadan may not significantly affect TSH control; patient preference should be considered
El-Kaissi et al (2021) <sup>25</sup>	Randomized prospective	Before Iftar, after Iftar, before Suhoor	Minimal unfavorable changes in plasma TSH when L-T4 is taken 30 minutes before Iftar	L-T4 intake just before Iftar minimizes negative effects on thyroid function tests post-Ramadan
Ghaffar et al (2021) <sup>26</sup>	Cohort study	Varied timing around meals	Increased TSH in participants taking L-T4 less than 30 minutes before food at Suhoor	Taking L-T4 at least 30 minutes before food may prevent undesirable TSH elevations
Al-Qahtani et al (2022) <sup>27</sup>	Randomized controlled trial	30 minutes pre-Iftar, 3 hours post-Iftar, 1 hour pre-Suhoor	No significant TSH change in the pre-Iftar group; significant increases in post-Iftar and pre-Suhoor groups	Pre-Iftar timing of L-T4 intake is optimal during Ramadan for those who underwent thyroidectomy
Mahzari et al (2023) <sup>28</sup>	Randomized trial	30 minutes before iftar, 3–4 hours after Iftar	No significant effect on TSH or fT4 levels by timing; increased TSH levels post-Ramadan	Timing flexibility is suggested: either 30 minutes before Iftar or 3–4 hours after Iftar, depending on the patient's lifestyle
Alamoudi et al (2023) <sup>29</sup>	Multicenter randomized controlled trial	Pre-Iftar vs. pre-Suhoor	No significant change or difference in thyroid profile between the two regimens post-Ramadan	Both pre-Iftar and pre-Suhoor timings are effective and can be chosen based on patient preference

Abbreviations: fT4, free thyroxine; L-T4, levothyroxine; TSH, thyroid-stimulating hormone.

the relationship between the timing of L-T4 intake, TSH levels, and lipid profiles in a cohort study of 44 patients.<sup>26</sup> The post-Ramadan TSH increased significantly. Pre-Ramadan TSH levels were in the normal range in 36 patients, while 8 patients showed high TSH levels, and post-Ramadan TSH levels were increased in 20 patients. Increased levels of TSH were seen in the case of intake of thyroxine less than 30 minutes before taking food in *Suhoor*. Serum cholesterol levels showed a positive correlation with TSH levels. Al-Qahtani et al conducted a parallel, double-blind, randomized controlled trial (RCT) to evaluate the impact of L-T4 timing on TSH levels in patients who had undergone total thyroidectomy and fasted  $\geq 20$  days of Ramadan.<sup>27</sup> Patients had stable TF for 6 months before the study period and fasted  $\geq 20$  days of Ramadan. Participants were in three groups: group A, 30 minutes pre-Iftar ( $n=31$ ); group B, 3 hours post-Iftar ( $n=34$ ); or group C, 1 hour pre-Suhoor ( $n=22$ ). The changes in TSH and fT4 levels 2 weeks BR and after Ramadan were

compared. Factors associated with a change in TSH levels were examined through multivariable analysis. The TSH levels significantly increased in group B ( $p=0.003$ ) and group C ( $p=0.011$ ) but not in group A ( $p=0.158$ ). The change in fT4 levels was comparable among the groups. Multivariable linear regression identified age, weight gain, and non-adherence to L-T4 as significant predictors of TSH level changes, suggesting optimal timing for intake might be pre-Iftar to stabilize TSH levels during Ramadan. Similarly, Mahzari et al also investigated the impact of different administration times of L-T4 on TSH and fT4 levels before and after RF.<sup>28</sup> Patients were randomized to three groups during Ramadan: group 1, 30 minutes before the *Iftar* meal; group 2, 3 to 4 hours after the Iftar meal, with no food taken for at least 1 hour after the meal; and group 3, were not given specific instructions for taking L-T4 during Ramadan. TFTs were performed 2 weeks before and 2 weeks after Ramadan. Compliance was lower in patients taking L-T4 3 to 4 hours

**Table 4** The key findings and implications of each study related to alternative dosing regimens of levothyroxine

Study reference	Study design	Regimen	Patient compliance (%)	Post-RF TSH (mIU/L)	Euthyroid post-RF (%)	Key findings
Elsherbiny (2022) <sup>30</sup>	Pilot study	Twice or thrice weekly vs. daily	Group 1: 90.9, group 2: 88.5	Group 1: 1.9, group 2: 2.0	Group 1: 81.8, group 2: 82.3	There were no significant differences in adherence, TSH levels, or thyroid status between twice/thrice weekly and daily dosing
Elsherbiny (2023) <sup>31</sup>	Expanded study	Twice or thrice weekly vs. daily	TTW: 96.5, SDT: 89.0	Similar rates between groups	TTW: 91.2, SDT: 94.5	Similar adherence and euthyroid rates; the TTW group preferred regimen 1 significantly more
Zakaria and Shahar (2022) <sup>32</sup>	Randomized trial	Weekly vs. daily	Not specified	Weekly: stable, daily: significant increment	Weekly: 100, daily: not specified	Patients prefer weekly dosing; no significant safety issues, and weekly dosing may prevent TSH elevation

Abbreviations: RF, Ramadan fasting; SDT, standard daily dosing; TSH, thyroid-stimulating hormone; TTW, twice or thrice weekly.

after Iftar. In addition, most patients who had not received a specific recommendation took L-T4 30 minutes before *Iftar*. There was a significant increase in TSH ( $p = 0.006$ ) and fT4 ( $p = 0.044$ ) levels after Ramadan. In multivariate analysis, the cause of HypoT and L-T4 dose significantly affected fT4 levels. The timing of L-T4 intake during Ramadan did not significantly affect TSH or fT4 levels. This led to the conclusion that timing flexibility could be accommodated for L-T4 intake during Ramadan, allowing either 30 minutes before or 3 to 4 hours after Iftar, based on patient preference. Alamoudi et al conducted a multicenter, open-label, RCT to evaluate the effects of different L-T4 administration times during Ramadan on thyroid profiles and patient satisfaction in individuals with primary HypoT. Patients were recruited from three centers in three cities in Kingdom of Saudi Arabia.<sup>29</sup> TSH and fT4 were measured 2 weeks BR and 4 to 6 weeks after Ramadan. Three hundred three patients were randomized: 156 to take the L-T4 dose at sunset with sips of water at the time of Iftar and wait 30 to 60 minutes to eat the main Iftar meal (pre-Iftar), and 147 to take the L-T4 dose just before the start of fasting (pre-*Suhoor*) regardless of their last meal intake. The mean weekly L-T4 dose in the pre-Iftar versus pre-*Suhoor* group was 753 versus 733 mcg,  $p = 0.001$ , and the pre-Ramadan thyroid profile was similar. Post-Ramadan TSH increased and T4 decreased. The estimated difference within the group means post-Ramadan was  $-0.41$  mIU/L,  $p = 0.43$  for TSH, and  $0.32$  pmol/L,  $p = 0.24$  for fT4. The generalized linear model repeated the measure of the analysis of variance, which showed no significant difference over time in TSH or fT4 within or between groups. Patient compliance and satisfaction with the regimens were similar between groups. Consequently, the study concluded that either regimen could be equally effective and selected based on patient preferences, as neither significantly impacted the thyroid profile during the fasting period of Ramadan.

#### What are the Alternative Levothyroxine Regimens that Can be Used during Ramadan?

Elsherbiny examined the effect of twice or thrice weekly (TTW) versus standard daily L-T4 dosing during Ramadan on adherence, post-Ramadan TSH, and thyroid status.<sup>30</sup> The study included two groups; group 1 included 11 patients assigned to take L-T4 twice or thrice a week, and group 2 included 113 patients assigned to take L-T4 daily. Patients chose between three L-T4 regimens: regimen 1: 60 minutes before Iftar; regimen 2: 60 minutes before *Suhoor*, on an empty stomach for 3 to 4 hours; and regimen 3: before the next fast, on an empty stomach for 3 to 4 hours. Thyroid status was assessed before and within 6 weeks after Ramadan. Only euthyroid patients were included. No significant differences were observed between the two groups regarding adherence, post-Ramadan TSH, or post-Ramadan thyroid status. Note that 90.9% in group 1 and 88.5% in group 2 were adherent. Post-Ramadan TSH in group 1 was 1.9 mIU/L, in group 2 was 2 mIU/L ( $p = 0.809$ ). Note that 81.8% in group 1 and 82.3% in group 2 were euthyroid post-Ramadan ( $p = 0.209$ ). In this pilot study, taking L-T4 TTW during

Ramadan achieved similar adherence and metabolic control to standard daily L-T4, making it an easier option for hypothyroid patients wishing to observe RF. The study was expanded later.<sup>31</sup> The study included two groups: the TTW group included patients assigned to take L-T4 twice or thrice a week, and the standard daily dosing (SDT) group included patients assigned to take L-T4 daily. Patients freely chose between three L-T4 regimens: before Iftar, Suhoor, or the next fast. Thyroid status was assessed before and within 6 weeks after Ramadan. Only euthyroid patients were included. The TTW group included 57 patients, while the SDT group included 91 patients. Pre-Ramadan TSH in the TTW group was higher compared to the SDT group ( $p = 0.003$ ). Similar adherence rates were observed in both groups, 96.5% in the TTW group versus 89% in the SDT group. Similar rates of post-Ramadan euthyroidism were also found in both groups, 91.2% in the TTW group versus 94.5% in the SDT group. TTW group preferred regimen 1 significantly more than the SDT group ( $p = 0.001$ ). The authors concluded that TTW L-T4 results in similarly high adherence rates (96.5%) and post-Ramadan euthyroidism (91.2%) compared to daily L-T4 during RF.

Additionally, Zakaria and Shahar compared the efficacy, safety, and patient preference of weekly versus daily dosing of L-T4 in Ramadan in a pilot randomized open-label controlled trial among HypoT patients during Ramadan.<sup>32</sup> Patients were randomized into weekly and daily arms. The weekly arm took  $7 \times$  their usual L-T4 dose at least 30 minutes pre-Suhoor once a week, while the daily arm took their usual daily dose at least 2 hours after the last meal before bed. Thyroid hormones, lipid profile, cardiac parameters, and cognitive and psychological function were assessed at baseline and week 4. Cardiac reassessment was done within 24 hours after weekly dosing in week 2. Eighteen patients were randomized into weekly and daily arms. The majority (66.7%) were hypothyroid secondary to radioiodine therapy. At the end of the study, there were no significant changes in thyroid hormone levels for the weekly arm. However, a substantial increment of TSH was observed in the daily arm ( $p = 0.011$ ). In terms of toxicities, there were no hyperthyroid or cardiac toxicities observed despite the significant increment of fT4 within 24 hours of weekly dosing ( $p = 0.011$ ). All patients were euthyroid and had no side effects. The majority (83.3%) of patients preferred weekly dosing during Ramadan. The authors concluded that weekly L-T4 dosing during Ramadan appeared safe, efficient, and preferred.

### How Levothyroxine Dose May be Adjusted during Ramadan?

Hadjzadeh et al<sup>33</sup> was the first to suggest an increase in the daily dose of L-T4 for hypothyroid patients during RF from the beginning of the month till 2 to 3 weeks after the end of the fasting month by 25 to 50  $\mu\text{g}$ . They founded their suggestion on their own clinical experience with their patients, and they implemented this practice with their patients. Also, Or Koca et al<sup>34</sup> compared the values of HypoT patients obtained through TFTs BR and after Ramadan. Ninety-seven patients,

ranging from 18 to 65 years old, who were followed with a diagnosis of HypoT, fasted during Ramadan, and had no change of their L-T4 dose for at least 6 months were included in the study. Patients' median serum TSH level before fasting was 2.19 mIU/L, while the median serum TSH after fasting was 2.73 mIU/L. Serum TSH values after Ramadan increased significantly compared to those BR ( $p = 0.004$ ). This study demonstrated a significant increase in serum TSH levels after Ramadan but no significant change in serum fT4 levels in fasting HypoT patients. They suggested a small increase in L-T4 dose BR in some HypoT4 patients wishing to fast. Several factors need to be evaluated. For instance, first, who should have this increase? This was addressed by Alkaf et al,<sup>20</sup> who suggested that an increase in L-T4 dose may be applied only to those with pre-Ramadan TSH in the highest quartile. Second, what is the increase in amount? Should it be a fixed dose increase in the range of 25 to 50 mcg, or should it be a percentage of the pre-Ramadan dose, which would be more logical because the L-T4 dose range is usually wide from as low as 25 mcg and up to 200 mcg per day? Third, what is the time range for this dose increase? Should the patients return to the pre-Ramadan dose at the end of the month, or should it be extended 2 to 3 weeks after Ramadan as originally suggested by Hadjzadeh et al?<sup>33</sup> Some of these questions still need to be answered when such a study is conducted and its results reported. The majority of Ramadan studies, regardless of the timing tested, have consistently shown a rise in TSH post-Ramadan compared to pre-Ramadan. However, it remained within the normal acceptable range. L-T4 dose was not changed in these studies. Given the lack of significant differences between regimens, patient preference and convenience should be a determining factor, and choosing the most appropriate time should be individualized. On the other hand, despite the consistent findings in studies, there has been an elevation in TSH that remains within an acceptable range and returns to pre-Ramadan level shortly after, suggesting no strong need to make changes unless the patient is on a specific suppressive dose like thyroid cancer patients; dose adjustment would not be needed.

### Special Issues on Ramadan-Thyroid Interplay

#### Quality Of Life

Sheikh et al<sup>35</sup> aimed to determine the change in TSH level and quality of life (QoL) BR and after Ramadan in patients with primary HypoT. This prospective cohort study included 64 adult patients on stable doses of L-T4 who fasted for at least 20 days during Ramadan. TSH levels were recorded 6 weeks BR. Post-Ramadan TSH was tested within 1 to 2 weeks after *Eid-ul-Fitr*. The mean difference (MD) between TSH pre- and post-Ramadan was 2.32 mIU/L ( $p < 0.001$ ). However, the difference in TSH was not significantly different between those who were compliant with meals and L-T4 interval versus those who were not (compliant, 2.04 mIU/L; noncompliant, 3.15 mIU/L). Overall, an increase in QoL scores in the domains of physical health, psychological health, and social relationships was observed after Ramadan. The authors concluded that change in TSH was not affected by the timing



of L-T4 intake and interval from meal, and there was no correlation between change in TSH scores and any of the QoL domain scores.

### Maternal and Fetal Health

Pakdel et al<sup>36</sup> evaluated the impact of RF on the levels of thyroid hormones in fasting women with HypoT and L-T4 intake. Serum levels of fT4 and TSH were measured in 36 women with HypoT aged 12 to 56 years who fasted during Ramadan. Three blood samples were collected 3 days before, on day 27 of Ramadan, and 2 months after Ramadan. In addition, the levels of hemoglobin and hematocrit (HCT) were measured during and after Ramadan. The serum level of fT4 significantly decreased during Ramadan compared to BR ( $p < 0.05$ ). However, no significant difference was observed in the serum fT4 level BR and after Ramadan.

On the other hand, the TSH was higher during Ramadan than BR, although the difference was not considered significant (in the normal range). TSH level was reduced after Ramadan compared to during Ramadan, while no significant difference was noted in the TSH level at the three measurement times. In addition, hemoglobin and HCT decreased significantly after Ramadan compared to during Ramadan. The authors concluded that fasting during Ramadan could reduce the serum levels of fT4 in women with HypoT. However, only a slight increase was observed in the TSH levels, which was not considered significant. Further investigation is required regarding the changes caused by fasting during Ramadan in the levels of hemoglobin and HCT.

### Physicians' and Patients' Perceptions

Two different studies explored the physicians' and patients' perceptions regarding the impact of RF on L-T4 replacement therapy. Oudghiri et al<sup>37</sup> investigated the effect of fasting on thyroid hormone balance in patients with HypoT on L-T4 therapy in a prospective study in Morocco during Ramadan. They included 65 patients with HypoT who fast and take L-T4 with a normal TSH level BR. Treatment adherence was good in 82.1%, moderate in 12.5%, and poor in 5.4% of the patients. After Ramadan, 80% of patients remained euthyroidism, while 9% were overreplaced, and 10% were underreplaced. The authors underscored the importance of treatment adherence and abiding by the recommended interval between the meal and L-T4 intake to maintain euthyroidism. Beshyah et al<sup>39</sup> studied patients' and professionals' perspectives on thyroid replacement during RF. An online survey of 218 physicians explored their perceptions and practices, and an interview of 172 HypT4 patients documented their practices and sources of information. Patients' median age was 46 (17–90) years; they had HypoT for 5 years and took a median thyroxine dose of 100 µg daily. Over half of the patients (50.3%) recalled that their physician advised them to take their thyroxine during RF. About 59.9% of the patients took thyroxine with Iftar, 23.8% with Suhoor, and 16.3% at different times. Concerning the physicians' survey, the majority (58.4%) were senior physicians and 46.1% were endocrinologists represented. Over half (52.3%) thought RF was not

clinically relevant in most patients on L-T4 replacement. However, 27.5% thought RF affects L-T4 replacement therapy in a clinically relevant manner. About 77.1% of respondents reported giving advice routinely to all patients on L-T4 replacement during RF. Respondents ( $N = 164$ ) were divided between recommending taking the L-T4 with Iftar, *Suhoor*, or other times. Most respondents (73.9%) do not repeat measurements of thyroid hormone levels after RF unless needed during their scheduled clinic visit. In those patients where TFTs were available before and after RF, serum TSH and serum fT4 did not show a specific pattern in the group as a whole and with subgroups.

The reviewed literature reported several factors that determine post-Ramadan TSH and thyroid status. Adherence and pre-Ramadan TSH were the most consistent among the reviewed factors. Adherence was reported to affect post-Ramadan TSH, pre-Ramadan TSH, and the L-T4 regimen. Age was reported twice. Male sex was reported only. **Fig. 1** shows the general trend of association between adherence rates and euthyroid rates.

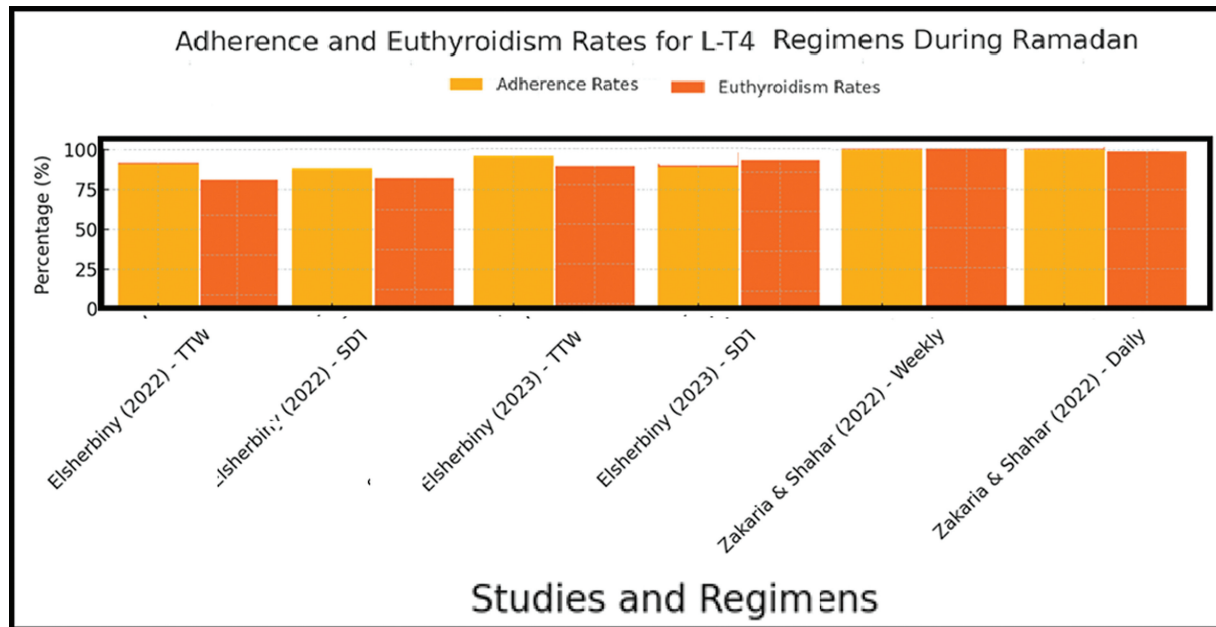
### Unsettled Question and Limitations

A couple of recent systematic reviews and meta-analyses attempted to put the published work in perspective. The earlier study by Hadjzadeh et al<sup>33</sup> searched PubMed and Google Scholar databases using keywords such as Ramadan, fasting, HypoT, and food restriction. Four animal and seven human studies were included in this article. The more recent Belal et al<sup>40</sup> searched eight databases for RCTs and observational studies investigating the effect of RF on TFs in HypoT individuals taking L-T4. Relevant data was extracted and analyzed. MD and standard deviation were used to evaluate the continuous data. Risk ratios with a 95% confidence interval were used for outcomes constituting dichotomous data. National Institutes of Health tools were used to assess the risk of bias. Fourteen studies met their inclusion criteria, 3 RCTs and 11 observational studies, all designed as pre-post studies.

The available literature has several noteworthy limitations. The comprehensive overview of existing literature may only cover some existing studies due to the selective search and inclusion criteria focused on specific databases and terms. Some relevant studies, particularly those not indexed in the selected databases or published in languages other than English, might have yet to be included. This approach limits the generalizability of the findings and might introduce selection bias.

### Practical Implications and Suggested Management Guidelines

Based on currently available data, **Table 5** outlines the practical management of HypoT during Ramadan fasting. Managing HypoT during Ramadan necessitates a nuanced understanding of medication timing, metabolic interactions, and individualized regimens. Adherence plays a critical role in maintaining euthyroid status, and weekly dosing frequencies introduce promising alternatives. Preventive measures, including proactive consultations and open communication, are essential for optimizing thyroid control during RF.



**Fig. 1** The general trend of association between adherence rates and euthyroid rates.

**Table 5** Proposed practical management of hypothyroidism during Ramadan

Stages	Themes	Guidance
Before Ramadan	TFT and L-T4 dose	Check the latest TFT on record and optimize the dose before the RF
	Education	Reiterate the advice on the possible (best) timing of doses The freedom to choose between different timings according to patient preference is key to better adherence The possibility of using pre-Iftar for some days and pre-Suhoor for some days according to social commitments during Ramadan may also lead to better adherence
During Ramadan	Dose	Use the same pre-Ramadan dose, and suggest once, twice, or thrice weekly L-T4 dosing for well-educated and motivated patients, especially those expressing dissatisfaction from altered daily routines during past fasting experiences
	Timing	Pre-Iftar: Observing the food-medication 30-minute interval needed between L-T4 and food
		Pre-Suhoor: To observe the food-medication 30-minute interval needed between L-T4 and food, this entails waking up around 45 minutes before
	Pre-Fajr: May be used for the minority (5%) of patients who skip <i>Suhoor</i>	
After Ramadan	Reflect on patients' experiences and outcomes	Correlating between nonadherence and post-Ramadan hypothyroidism may reinforce adherence in subsequent fasting years
	Dose	Refrain from titrating the L-T4 dose using TSH measured within the first 6 weeks post-Ramadan. Titrate the dose if clinically indicated using TSH determined at least 2 or more months after Ramadan
	Timing	Return to the same plans observed before Ramadan
	Monitoring	Remeasure TSH and T4 only if indicated clinically

Abbreviations: L-T4, levothyroxine; RF, Ramadan fasting; TFT, thyroid function test; TSH, thyroid-stimulating hormone.

## Conclusion

Patients with HypoT need to continue taking L-T4 replacement during RF. The conventional timing of L-T4 intake in relation to food intake may be burdensome. Conventionally, L-T4 should be taken with some amount of water at least half an hour before breakfast on an empty stomach to prevent drug interaction and increase intestinal absorption. Variability of L-T4 absorption may be further reduced if we keep the pattern of food intake in reference to L-T4 intake consistent with the timing of food as then absorption is consistent. During RF, respecting the interval between the intake of L-T4 and meals can be difficult and may impact thyroid hormone balance. A literature review suggested that the changes seen in the earlier observational studies seemed minimal and may not be clinically relevant. The sample sizes and timing of measurements may have been flexible, and most professional opinions worked from general principles rather than with evidence. However, more recent studies addressed specific questions about the best timing. The findings of these studies are not uniformly concordant, and confusion still needs to be resolved.

The inhomogeneous nature of the available literature calls for more RCTs to solidify the recommendations provided by the mentioned studies. For instance, an RCT looking at the different formulations of L-T4, such as liquid or soft gel capsules, and comparing them to tablets in terms of absorption may be needed once these new formulations become more widely available in Muslim-majority regions. Also, other RCTs look at the impact of the dietary influence of regular food on nonfasting days versus high carbs (Ramadan-type food) on L-T4 absorption. Furthermore, different RCTs may examine Ramadan-induced changes in certain subgroups like older adults, young adults, or even children or the impact of the interplay between HypoT and other common chronic disease medications during the fasting state.

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S.A.B. proposed the study, performed the literature searches, and drafted the manuscript. All authors reviewed the document for intellectual content and approved its final version.

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No ethical approval is required.

### Disclaimer

To the best of our abilities, we presented our perception of the published work in good faith. Original authors cannot be held responsible for any misrepresentation.

### Conflict of Interest

None declared.

## References

- Beshyah S, Fathalla W, Saleh A. Mini-symposium: Ramadan fasting and the medical patient: an overview for clinicians. *Ibnosina J Med Biomed Sci* 2010;2(05):240–257
- Chaker L, Bianco AC, Jonklaas J, Peeters RP. Hypothyroidism. *Lancet* 2017;390(10101):1550–1562
- Wiesner A, Gajewska D, Paško P. Levothyroxine interactions with food and dietary supplements—a systematic review. *Pharmaceuticals (Basel)* 2021;14(03):206
- Bach-Huynh TG, Nayak B, Loh J, Soldin S, Jonklaas J. Timing of levothyroxine administration affects serum thyrotropin concentration. *J Clin Endocrinol Metab* 2009;94(10):3905–3912
- Beshyah S, Fiad T, Saadi H. Management of common endocrine conditions other than diabetes mellitus during Ramadan fasting. *Ibnosina J Med Biomed Sci* 2012;04(04):137–146
- Raza SA, Ishtiaq O, Unnikrishnan AG, et al. Thyroid diseases and Ramadan. *Indian J Endocrinol Metab* 2012;16(04):522–524
- Azizi F. Islamic fasting and thyroid hormones. *Int J Endocrinol Metab* 2015;13(02):e29248
- Hameed M, Raza SA. Management of thyroid diseases and steroid replacement in Ramadan: a review study. *J Fasting Health* 2016;4(02):70–74
- Lipp HP. Administration and Pharmacokinetics of Levothyroxine. 2021 Mar 12. In: Kahaly GJ, editor. *70 Years of Levothyroxine* [Internet]. Cham (CH): Springer; 2021
- Caron P, Grunenwald S, Persani L, Borson-Chazot F, Leroy R, Duntas L. Factors influencing the levothyroxine dose in the hormone replacement therapy of primary hypothyroidism in adults. *Rev Endocr Metab Disord* 2022;23(03):463–483
- Jonklaas J. Optimal thyroid hormone replacement. *Endocr Rev* 2022;43(02):366–404
- Fedail SS, Murphy D, Salih SY, Bolton CH, Harvey RF. Changes in certain blood constituents during Ramadan. *Am J Clin Nutr* 1982;36(02):350–353
- Sulimani RA. The effects of Ramadan fasting on thyroid functions in healthy male subjects. *Nutr Res* 1988;8(05):549–552
- Sajid KM, Akhtar M, Malik GQ. Ramadan fasting and thyroid hormone profile. *J Pak Med Assoc* 1991;41(09):213–216
- Bogdan A, Bouchareb B, Touitou Y. Ramadan fasting alters endocrine and neuroendocrine circadian patterns. Meal-time as a synchronizer in humans? *Life Sci* 2001;68(14):1607–1615
- Bahrayni S, Vakili R, Nematy M, et al. The effect of Ramadan fasting on thyroid hormones in 9–13 years old pre-menarche girls. *J Fasting Health* 2013;1(02):46–52
- Karoli R, Fatima J, Chandra A, Mishra PP. Levothyroxine replacement and Ramadan fasting. *Indian J Endocrinol Metab* 2013;17(02):318–319
- El-Kaissi S, Dajani R, Lee-St John TJ, et al. Impact of lifestyle changes during Ramadan on thyroid function tests in hypothyroid patients taking levothyroxine. *Endocr Pract* 2020;26(07):748–753
- Dellal FD, Ogmen B, Ozdemir D, et al. Effect of Ramadan fasting on thyroid hormone levels in patients on levothyroxine treatment. *J Coll Physicians Surg Pak* 2020;30(10):1009–1014
- Alkaf B, Siddiqui M, Ali T, et al. Ramadan fasting and changes in thyroid function in hypothyroidism: identifying patients at risk. *Thyroid* 2022;32(04):368–375
- Elshebiny TM. Impact of fasting on thyrotropin and thyroid status during Ramadan in 292 previously well controlled hypothyroid patients. *IFTAR study*. *Endocrine* 2023;79(03):484–490
- Hossain S, Banerjee M, Mondal S, et al. A comparative study on effect of evening versus morning intake of levothyroxine in patients of hypothyroidism. *Thyroid Research and Practice* 2018;15(02):89–93
- Dabbous Z, Alowainati B, Darwish S, et al. A prospective study comparing two-time points of thyroid hormone replacement during the holy month of Ramadan. *Int J Endocrinol* 2019;2019:9843961

- 24 Zaboony IA, Alidrisi HA, Hussein IH, et al. Best time for levothyroxine intake in Ramadan (THYRAM): Basrah experience. *Int J Endocrinol Metab* 2020;18(02):e94325
- 25 El-Kaissi S, AbdelWareth L, Dajani R, et al. Levothyroxine administration during Ramadan: a prospective randomized controlled trial. *Eur Thyroid J* 2021;10(06):455–460
- 26 Ghaffar T, Zulfania, Ahmad I, et al. Effect of the timing of thyroxine intake on thyroid stimulating hormone levels in Ramadan. *PJ M H S* 2021;15(01):46–48
- 27 Al-Qahtani KM, Aldeeri IA, Alshaibi AM, et al. Optimal timing of thyroid hormone replacement during Ramadan fasting: a randomized controlled trial in patients with prior total thyroidectomy. *Thyroid* 2022;32(09):1029–1036
- 28 Mahzari M, Al Remthi F, Ajwah I, et al. Levothyroxine timing during Ramadan: a randomized clinical trial. *Int J Endocrinol* 2023;2023:2565031
- 29 Alamoudi RM, Nawar SM, Alharbi HS, et al. FRI527 timing of thyroxine dose during Ramadan: a randomized controlled trial. *J Endocr Soc* 2023;7(Suppl 1):bvad114.1872
- 30 Elsherbiny TM. Twice or thrice weekly versus daily thyroxine in hypothyroid fasting Ramadan: a pilot study. *Indian J Endocrinol Metab* 2022;26(03):265–268
- 31 Elsherbiny TM. Twice or thrice weekly levothyroxine provides similar rates of adherence and post-Ramadan euthyroidism compared to daily levothyroxine during Ramadan fasting. *Thyroid Res* 2023;16(01):44
- 32 Zakaria NA, Shahar MA. Comparison between weekly vs daily dosing L-thyroxine for the treatment of hypothyroidism in Ramadan – a pilot randomized controlled trial. *Malaysian J Med Health Sci* 2022;18(19):49–54
- 33 Hadjzadeh MA, Pakdel R, Hayatdavoudi P, et al. Hypothyroidism and Ramadan fasting. *J Nutrition Fasting Health* 2014;2(02):80–83
- 34 Or Koca A, Dağdeviren M, Altay M. Should the dose of levothyroxine be changed in hypothyroidism patients fasting during Ramadan? *Turk J Med Sci* 2020;50(04):784–788
- 35 Sheikh A, Mawani M, Mahar SA. Impact of Ramadan fasting on thyroid status and quality of life in patients with primary hypothyroidism: a prospective cohort study from Karachi, Pakistan. *Endocr Pract* 2018;24(10):882–888
- 36 Pakdel R, Mohebbi M, Rezaie N, et al. Ramadan fasting and thyroid hormone levels in women with hypothyroidism. *J Nutrition Fasting Health* 2020;8(01):55–60
- 37 Chaouachi A, Coutts AJ, Wong P, et al. Haematological, inflammatory, and immunological responses in elite judo athletes maintaining high training loads during Ramadan. *Appl Physiol Nutr Metab* 2009;34(05):907–915
- 38 Oudghiri D, Motaib I, Elamari S, et al. Ramadan and hypothyroidism: impact of Ramadan fasting on thyroid status. *Med Clin Res Open Access* 2022;3(01):1–5
- 39 Beshyah SA, Khalil AB, Beshyah AS, et al. Thyroxine replacement therapy during Ramadan fasting: physicians' and patients' perceptions and practices. *J Diab and Endocr Pract* 2023;6(01):17–24
- 40 Belal MM, Youssef AR, Baker H, et al. Effect of Ramadan fasting on thyroid functions in hypothyroid patients taking levothyroxine: a systematic review and meta-analysis. *Ir J Med Sci* 2024;193(02):741–753