

Effect of the Timing of Thyroxine Intake on Thyroid Stimulating Hormone Levels in Ramadan

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ABSTRACT

Aims: To compare pre and post Ramadan thyroid stimulating hormone (TSH) levels and to correlate the effect of timing of levothyroxine intake with TSH levels and to correlate lipid profile with TSH.

Study design: Cohort study

Place and duration of study: Department of Endocrinology of Lady Reading Hospital (LRH) Peshawar in Holy month of Ramadan, 11th April to 25th June 2019.

Methods: Pre Ramadan blood samples were taken within 3 weeks before Ramadan and post Ramadan samples within 2 weeks after Eid-ul-Fitar from 44 patients. A fasting blood sample of 3ml withdrawn in plain tube and serum was used to measure TSH by electrochemoluminescence (ELCIA) method by machine e411 Roche Company.

Results: The mean Pre Ramadan TSH was 2.85 ± 1.34 m IU/L. The Post Ramadan TSH increased to 3.84 ± 2.46 m IU/L. and the difference was significant ($p=0.014$). Pre-Ramadan TSH levels was documented in normal range of 36 patients, while 8 patients showed high TSH levels and post Ramadan TSH levels were increased in 20 patients. Increase levels of TSH were seen in case of intake of thyroxine less than 30 minutes before taking of food in sahour. The serum cholesterol levels showed the positive correlation with TSH levels.

Conclusion: There is an increase in TSH in participants taking thyroxine less than 30 minutes before sehari with sehari or post sehari and there is a positive correlation between TSH levels and lipid parameters.

Keyword: Thyroxin, Thyroid stimulating hormone, Fasting, Effectiveness

INTRODUCTION

Hypothyroidism a common metabolic disorder results from an under activity of thyroid gland.¹ This disease occurs mostly due to lack of iodine in water and its key features are; decreased mental activity, diminished metabolism and retardation of development and growth.² Hypothyroidism is evident with decreased level of thyroid hormone and elevated thyroid stimulating hormone (TSH).³ According to a local study the frequency of hypothyroidism was 3.83% in Charsadda district, 3.17% in Nowshera, 3% in Mardan. This study also revealed that incidence of hypothyroidism was more in these three district as compared to Peshawar⁴.

Levothyroxine a drug treatment of hypothyroidism is generally recommended to be taken empty stomach half hour before food for maximum efficiency.⁵ In the holy month of Ramadan Muslims all over the world observe 29 to 30 days of fasting.⁶ During this fast, Muslims are abstain from drinking and eating food from dawn (sahour) to sunset (iftar). As The absorption of thyroxine declines from 80% in the fasting condition to 60% in the fed condition^{7,8}. It is difficult to manage its intake during Ramadan. During the month of Ramadan the usual practice in our culture is that patients take levothyroxine at sahour time with some water and wait 30 minutes before eating their food or take it after aftari. The L-thyroxine is challenging to take during fast on empty stomach before one hour of iftar because intake of water, food and even tablet will break the fast. Likewise, taking L-thyroxine is also not manageable before one hour

of sahour as most of the people prefer to sleep at night and they wake up for sahour.⁹ To date, there is lack of sufficient evidence which can guide us about the best time of intake of levothyroxine in Ramadan. So the present cohort study was aimed to reveal the changes in TSH level on the timing of Levothyroxine intake in Ramadan.

MATERIALS AND METHODS

This was a cohort study done in Endocrinology Unit of Lady Reading Hospital (LRH) Peshawar and samples were analyzed in the laboratories of (LRH), Peshawar. The study was conducted in the month of Ramadan, 11th April to 25th June 2019. Pre Ramadan blood samples were taken within 3 weeks before Ramadan and post Ramadan samples were taken within 2 weeks after Eid-ul-Fitar. A total of 44 participants of hypothyroidism were enrolled Post Ramadan samples were taken from those 44 patients who fasted for at least 20 days in the month.

The patients of hypothyroidism visiting Endocrinology Unit of LRH were informed about research and those who were willing to participate were included in the study. Patients taking dopamine, steroids, lithium, antipsychotic drugs and those patients who were admitted for severe illness and having sick euthyroid were also excluded from the study. Pregnant and lactating females were also not included. Patient's pre and post Ramadan weight were noted and blood pressure (B.P) was recorded at resting position by auscultatory method. Both pre and post Ramadan 3ml fasting blood sample was collected from participants in plain tube and serum was used to measure TSH by electrochemoluminescence (ELCIA) method by machine e411 Roche Company. Serum triglycerides and

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total cholesterol was also measured from the sample. The normal range of serum TSH was taken as 0.4 to 4.2 mIU/L⁹.

SPSS-20 was used to analyze the data and to measure the mean, standard deviation and the frequencies of different parameters. The mean values of Pre and Post Ramadan TSH and weight were compared using paired T test. Pearson correlation was done to correlate the quantitative variables. Stratification of timing of thyroxine intake and TSH levels were compared using chi-square test. A value of $p < 0.05$ was considered significant.

RESULTS

Mean age of the participants was 32.68 ± 10.58 years. The mean systolic BP was 122.50 ± 11.93 mm of Hg, mean diastolic BP was 79.09 ± 6.73 mm of Hg. The mean Pre Ramadan TSH was 2.85 ± 1.34 mIU/L. The Post Ramadan TSH increased to 3.84 ± 2.46 mIU/L. and the difference was significant ($p = 0.014$). Pre Ramadan weight was 67.77 ± 8.91 kg and Post Ramadan weight was 68.05 ± 8.78 kg with a mean difference of weight 0.27 ± 1.364 ($P = 0.109$) which was insignificant (Table 1).

Table 1: Demographic and laboratory values of the participants (n=44)

Variable	Mean \pm SD	P value
Age (years)	32.68 \pm 10.58	0.014
Systolic B.P (mmHg)	122.50 \pm 11.93	
Diastolic B.P (mmHg)	79.09 \pm 6.73	
Pre Ramadan TSH (mIU/L)	2.85 \pm 1.34	
Post Ramadan TSH (mIU/L)	3.84 \pm 2.46.	0.109
Pre Ramadan weight (kg)	67.77 \pm 8.91	
Post Ramadan weight (kg)	68.05 \pm 8.78	

Table 2: Pre and Post Ramadan TSH values (n=44)

Variable	No.	P value
Pre Ramadan TSH (m IU/L)		
≤ 4.2	36	0.001
> 4.2	8	
Post Ramadan TSH (m IU/L)		
≤ 4.2	24	0.001
> 4.2	20	

Table 3: Stratification of timing of thyroxine intake with Post and Pre Ramadan TSH difference (n=44)

TSH difference	≥ 30 mins before sehari (n=18)	< 30 mins before sehari (n=12)	Post or with sehari (n=14)	p-value
Increased ≥ 2 mIU/L	-	9	11	> 0.001
Increased < 2 mIU/L	1	3	3	
Decreased ≥ 2 mIU/L	13	-	-	
Decreased < 2 mIU/L	4	-	-	

Table 4: Correlation of parameters with TSH (n=44)

Variable	TSH correlation(r)	p-value
Total cholesterol	$r = 0.52$	$P = 0.001$
Triglyceride	$r = 0.25$	$P = 0.037$

Thirty six had Pre Ramadan TSH in normal range while only 8 had high TSH levels. Post Ramadan TSH was increased from the normal range in 20 participants (Table 2).

There was an increase in value of TSH in all participants taking thyroxine less than 30 mins before sehari with sehari or post sehari while there was a drop in TSH value in all those participants who took thyroxine more than 30 minutes before sehari (Table 3).

A positive correlation of TSH with total cholesterol ($r = 0.52$, p value was 0.001) was seen. The correlation of TSH with triglyceride was also significant ($r = 0.25$, p value = 0.037) [Table 4].

DISCUSSION

In the present study we have reported that Ramadan fasting influence TSH levels as the post Ramadan TSH was increased in our study and the difference in TSH level was also significant in our case. A similar cohort study conducted in Karachi reported that TSH levels were significantly increased in participants after Ramadan in a earlier mentioned study the mean weight change was 0.22kg similar to our study. In this study 8 participants had TSH > 4 which increased to 28 participants with more than 4 m IU/L TSH ($p = 0.28$) there was a significant difference in pre and post Ramadan TSH levels 2.37 ± 1.35 m IU/L.⁸ Kaissi et al¹⁰ reported a significant increase in plasma TSH post-Ramadan which was similar to the findings of the present study.

In the present study, we had almost same statistics, out of 44 participants 8 had Pre Ramadan TSH more than 4.2 m IU/L which increased to 22 participants having Post Ramadan TSH more than 4.2 m IU/L. The present study also reports that TSH was within normal range of those participants who had at least of 30mins interval between meal and the drug. Another study reported that as a result of Ramadan fasting there is a change in gastric motility and circadian rhythm due to which there is an alteration in the metabolism of thyroxine in the body. so it was proposed that drug should be taken atleast 30 minutes before sehari or taken bed time to show its maximum effects¹¹. The present study also reports that TSH concentration can be kept in normal ranges if the drug meal interval is more than 30 minutes before sehari.

It is advocated that maximum effect of thyroxine is achieved if it is taken an hour before sehari as absorption of this drug is 80% if taken 60 minutes before a meal and it drops by 60% if taken after meal¹².

Dellal et al¹³ checked thyroid profile a few weeks before Ramadan in hypothyroid patients and then the subjects were divided into two groups with one taking thyroxine before sleep and group two taking it 30 minutes before sehari. TSH was increased in both groups after Ramadan with significant increase in group two. So they concluded that taking levothyroxine in late evening i.e. before sleep resulted in more stable thyroid hormones compared to pre-sehari intake. The interaction of TSH level and meal intake during Ramadan was checked by another study in which the participants were instructed to take thyroxine two hrs after dinner. This study concluded that bed time thyroxine intake is beneficial in maintaining TSH

levels but the meal and drug interval should be kept at least two hours¹⁴ Zaboon et al⁹ compared TSH levels in three groups i.e pre-iftar, post-iftar and pre suhoor group and observed no statistical difference in groups. The results have contradiction with the timings of L-thyroxine intake in Ramadan. Some studies preferred intake of L-thyroxine at bed time^{15,16}, while other studies supported intake of L-thyroxine at early morning fasting.¹² Yet, few other studies found no difference in metabolism of L-thyroxine related to timings.¹⁷ The optimum intake timing of L-thyroxine consumption is still undetermined in Ramadan. Thyroid hormones also regulate body metabolism and has a strong influence on lipid and carbohydrate metabolism. Many studies report increased level of cholesterol and triglyceride in hypothyroidism and a positive association between these parameters and TSH¹⁸⁻²⁰.

CONCLUSION

There is an increase in TSH in participants taking thyroxine less than 30 mins before sehari with sehari or post sehari and there is a positive correlation between TSH levels and lipid parameters.

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