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The Comparison of Serum Levels of IGF1 before and After Fasting in Healthy Adults

Bita Saifi[1], Nastaran Dousti Majd[2], Mojtaba Meshkat[3]*, Arian Amali[4]

1. Assistant Professor, Department of Basic Science, Faculty of Medicine, Mashhad Medical Sciences, Islamic Azad University, Mashhad, Iran.
2. General Practitioner, Department of Medical Sciences, Faculty Of Medicine , Mashhad Medical Sciences, Islamic Azad University, Mashhad, Iran.
3. Assistant Professor, Department of Community Medicine, Faculty Of Medicine, Mashhad Medical Sciences, Islamic Azad University, Mashhad, Iran.
4. Student Research Committee, Paramedical Department, Islamic Azad University, Mashhad Branch, Mashhad, Iran.

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ABSTRACT

Introduction: Ramadan is the ninth month of the lunar year, in which Muslims avoid eating and drinking from sunrise to sunset. Insulin-like growth factor 1 (IGF1) is a small peptide circulating in the blood. IGF1 is essential in regulating proliferation, differentiation, apoptosis, and transformation. Studies have shown that a slight increase in IGF1 levels increases the risk of prostate, breast, colon, and lung cancer. This study evaluated the effects of fasting with regular consumption patterns and food avoidance on serum IGF1 concentration in healthy subjects before and after fasting.

Methods: A total of 40 healthy adults aged 18-55 years who fasted for about 16 hours a day and at least 20-25 days in Ramadan were included. The first sample was collected one week before Ramadan, and the second was obtained at the end of Ramadan. After taking 2cc of whole venous blood, sera were isolated, and IGF1 concentration was calculated by quantitative ELISA method using a DiaMetra kit.

Results: There were 40 participants in the study, 31 of whom were female, and nine were male. The mean IGF1 before and after fasting were 198.6 ± 77.9 and 146.3 ± 44.5 ng/ml, respectively, with a 52 ng/ml difference.

Conclusion: Based on the results, fasting reduces the level of IGF1, indicating the benefits of fasting because of limiting the harmful effects of a risk factor for some diseases.

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Introduction

Ramadan is the ninth lunar month, in which Muslims avoid eating and drinking from sunrise to sunset. The length of the fasting period depends on its coincidence with each season of the solar year. Fasting means avoiding eating and drinking from sunrise to sunset (1, 2). Generally, calorie intake is decreased daily during Ramadan, and research has shown that fasting can reduce cholesterol, triglyceride, and LDL and enhance HDL levels (3).

IGF1 (Insulin Growth Factor 1) is a polypeptide hormone that comprises 70 amino acids like cholesterol as a type of cytokine, and its homolog has 60 and 50% structural similarity with IGF2 and Insulin, respectively. This substance is an anabolic hormone produced in response to the growth hormone, mainly in the liver and peripheral tissues such as the growth plates (4). IGF1 is often used as an indicator of growth hormone deficiency for assessing the efficacy of growth hormone replacement therapy (4).

In addition, IGF1 plays a pivotal role in regulating replication, differentiation, apoptosis, and transformation, working in an endocrine, autocrine, and paracrine manner (5). Studies have revealed that a slight increase in IGF1 levels is associated with a more significant prostate, breast, colon, and lung cancer risk. Studies have indicated that the expression of the IGF1 gene has increased in breast cancer patients compared to healthy individuals (6, 7).

The metabolic and endocrine effects of fasting in adults have been the subject of much research. The levels of IGFs are not affected by short-term food deprivation (36 hours), but long-term food deprivation (7 days) decreases serum levels of IGF1 (8, 9).

"Insulin-like" to absorb glucose in adipose and muscle cells with both IGF1 and IGF2, showing 50% homology with insulin. Research has shown

* *Corresponding author:* Mojtaba Meshkat, Department of Community Medicine, Faculty Of Medicine, Mashhad Medical Sciences, Islamic Azad University, Mashhad, Iran. Tel: +989155112899, Email: m.meshkat@sbmu.ac.ir.

that growth hormone binds to its transmembrane receptor, initiating a signaling cascade that contributes to the transcriptional regulation of IGF-1 and relevant genes (10).

GF1 (Growth Factor 1) is a primary intermediate for the effects of growth hormone (11) and binds to IGF1R on the surface of cells in various tissues (12).

Previous research has shown that IGF1Rs are upregulated in most cancerous cells. There is no concentration of IGFs in specific tissues, but they are present in high quantities throughout the body. The concentration of these hormones in the body increases almost one thousandfold more than most peptide hormones. Although the presence of these hormones in tissues is lower, it is still more than what is needed for maximal stimulation of cells. IGFBPs significantly slow their clearance, enabling the maintenance of such high levels of IGFs (10).

Sanjari et al. examined 132 individuals who had fasted for at least 25 days in Ramadan and demonstrated no statistical significance about IGF1 fluctuations ($p=0.46$). The mean serum levels of LDL were significantly reduced, with a weak correlation observed between serum levels of IGF1 and LDL fluctuations (1).

Bouhlel et al. evaluated the effects of fasting on different factors in the body of nine male rugby players. The subjects had considerable weight loss ($p<0.001$), yet glucose, growth hormone, IGF1, and IGFBP3 levels did not go through any significant changes (13).

Fontana et al. (2008) assessed the long-term effects of calorie and protein restriction on serum levels of IGF1 in humans at Washington University. Unlike rodents, severe calorie restriction could not alter the serum levels of IGF1 without malnutrition. A considerable reduction was observed in the resistance to insulin and leptin hormone (leptin is an essential indicator of the amount of energy stored in adipose tissues) (14).

Another research was conducted based on the possibility that more extended periods of calorie restriction are required to reduce serum levels of IGF1 in humans. In this study, serum concentration of IGF1 was compared among two groups; one group of 28 vegetarians with a daily protein consumption of 0.76 g/kg of the body through 5 years, and another group of 28 with a high daily protein intake of 1.73 g/kg of the body. Finally, the serum levels of IGF1 were considerably lower among the group of vegetarians compared with the other group. However, both groups had a similarly significant decrease in serum levels of fasting insulin and CRP (C-Reactive Protein). The high consumption of proteins inhibits the reduction of serum IGF1. As a result, another study demonstrated the effects of protein consumption on the serum levels of IGF1. For this purpose, six volunteers participated in this study to reduce their protein intake from 1.67±0.1 g/kg of the body to 0.95±0.1 g/kg for three weeks. This short-term reduction in protein consumption resulted in a 25% decrease in IGF1 serum levels (from 194±34 ng/ml to 152±41 ng/ml) in all 6 participants. Therefore, high protein intake inhibited the reduction of IGF1. Studies have shown that long-term calorie restriction does not remove free and total IGF serum levels in healthy individuals with high protein intake. Moreover, protein consumption more effectively regulates IGF1 concentration than calorie intake (14).

Luigi et al. experimented with assessing the 2-year effects of a 25% reduction in calorie intake on the levels of IGF1, IGFBP, and cortisol circulating in the blood. Unless protein consumption is also decreased, calorie restriction does not increase serum cortisol levels or reduce serum IGF1 and IGF1:IGFBP-3 levels. Constant and considerable increase in the serum concentration of IGFBP1 and the decrease in IGF1:IGFBP1 was observed in the group with calorie restriction compared with the control group. Serum levels of IGFBP3 in the group with calorie restriction considerably decreased in 12 months, yet the same was not observed in 24 months. No significant difference was reported between the test and control groups regarding IGF1 and IGF1:IGFBP3 levels in the 12- and 24-month periods. Research regarding the mechanisms of aging and cancer has demonstrated that IGF1 plays a role in the biology of aging and the pathogenesis of several malignant tumors (e.g., colon, prostate, breast, and ovary), affecting cancer through this mechanism. Previous studies have shown that decreasing daily protein intake from 1.6 to 0.95 g/kg of the body is vital for reducing the serum concentration of IGF1. In addition, protein intake restriction significantly inhibits prostate and breast tumor growth in animal models by reducing serum IGF1 levels without dependency on calorie consumption. The results of this

massive random clinical trial showed that long-term calorie restriction does not reduce IGF1 serum levels but decreases the bioavailability of IGF1 and considerably increases IGFBP1 in youths, middle-aged, or slightly obese individuals. Restricting food consumption reduces the harmful effects of aging and positively affects longevity. The calorie restriction and indirect reduction of nutritional substances like proteins are unknown among these positive effects (15). Other studies also have indicated that fasting has a significant effect on IGF1 and weight loss (16, 17)

Methods

This longitudinal study included 40 healthy adults aged 18 to 55 who participated. The sample size was determined based on mean serum levels of IGF1 in the survey of Fontana et al., which was 194±34 ng/ml before and 152±41 ng/ml after the survey, with a confidence interval and statistical power of 99% using the following formula:

$$n = 2 \times \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2 \sigma_P^2}{(\mu_1 - \mu_2)^2}, \sigma_p^2 = \sigma_1^2 + \sigma_2^2 - 2\rho\sigma_1\sigma_2$$

Individuals with any kind of metabolic disease, such as diabetes, hyperlipidemia, and pregnancy, were excluded. The ethics committee approved this research project for biomedical research in the Islamic Azad University School of Medicine with the IR ethics code.IAU.MSHD.REC.1396.69.

1- Demographic information and the desired parameters of the study were gathered after providing the patients with a full explanation of the research purpose and obtaining their consent.

2- Information regarding height, weight, BMI (kg/m^2), and IGF1 was collected after providing the patients with a full explanation of the purpose of the research and obtaining their consent.

Only individuals who would fast for about 16 hours a day for at least 20-25 days were included.

Initial sampling was carried out a week before Ramadan, and secondary sampling was conducted at the end of Ramadan. First, 2cc of venous blood was drawn from the subjects. Then, samples were centrifuged, and their serum was separated. Afterward, the IGF1 serum concentration was calculated by the ELISA method using DiaMetra kits (Normal range: 28-237 ng/ml). All expenses were covered by the researchers.

The data was normality assessed using the Lilliefors test, and parameters were evaluated by the Wilcoxon signed-rank test and Student's t-test. The statistical analysis was conducted using SPSS software version 18, and a p-value of less than 5% was considered significant.

Table 1. The distribution of weight loss among healthy adults with regular fasting in Ramadan

Weight Loss (kg)	Frequency	Percentage
1≥	6	15
2	20	50
3≤	14	35
Total	*40*	*100*

Table 2. The distribution of IGF (ng/ml) in healthy adults with regular fasting in Ramadan compared among different ranges of age, BMI, and among genders

Variable		Before	After	Within P	Change %	Between P
Age	<30 Years	288.8±81.8	165.0±42.0	0.0001[W]	24. 8±11.9	0.517[t]
	≤ 30 Years	153.4±43.4	118.3±32.1	0.0001[T]	22.4±10.5	
Gender	Female	189.9±74.9	141.1±41.9	0.0001[W]	23.6±10.5	0.840[t]
	Male	228.6±85.2	164.2±50.8	0.004[t]	24.5±14.3	
BMI	Normal	204.4±77.6	149.1±38.2	0.0001[W]	23.8±10.6	0.992[t]
	Overweight	185.1±80.3	139.7±57.9	0.002[t]	23.7±13.3	

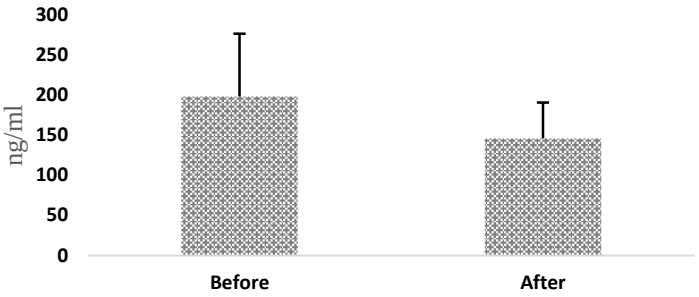

Figure 1. The distribution of IGF (ng/ml) among healthy adults with regular fasting in Ramadan

Results

This study evaluated 40 volunteers aged 22 to 48 with a mean age of 31.5±8.1. The participants' mean weight was 68.9 kg, and the mean BMI was 24.7±3.2 kg/m^2. The fasting days ranged between 20-28 days, with a mean of 22.9±2.6. About 50% of the subjects lost almost 2 kg of weight (Table 1).

The mean IGF1 was 198.6±77.9 ng/ml before fasting, and it was 146.3±44.5 ng/ml with a 52.3 ng/ml difference and statistical significance after fasting (p=0.0001).

Furthermore, 29 participants (72%) had normal IGF1 levels at the beginning of the study, which was observed in 36 participants at the end (90%).

Mean serum IGF1 levels in individuals ≤30 were 228.8±81.8 ng/ml before and 165±42.0 ng/ml after Ramadan. Further, mean serum IGF1 levels in subjects ≥30 were 153.4±43.4 ng/ml before and 118.3±32.1 after Ramadan. These findings were both statistically significant (p<0.05). No statistical significance was observed when the two age groups were compared. The mean IGF1 levels in women were 189.9±74.9 ng/ml before and 141.1±41.9 ng/ml after Ramadan. The mean IGF1 levels in men were 228.6±85.2 ng/ml before and 164.2±50.8 ng/ml after Ramadan. The findings in both genders were statistically significant (p<0.05), but no such significance was observed when the two groups were compared. The mean serum IGF1 levels in individuals with a normal BMI before and after Ramadan were 204.4±77.6 and 149.1±38.2 ng/ml, respectively. The same variable in overweight individuals before and after Ramadan was 185.1±80.3 and 139.7±57.9 ng/ml, respectively. The findings in both groups had statistical significance (p<0.05), but no such significance was found when the two groups were compared. IGF1 levels before fasting were considered dependent variables in linear Model fitting, and IGF1 levels were considered independent variables after fasting, age, gender, and BMI. The age, gender, and BMI variables did not considerably affect IGF1 levels (p>0.05).

Discussion

The results revealed that the mean IGF1 levels were reduced from 198.6±77.9 ng/ml before Ramadan to 146.3±44.5 at the end of Ramadan, with a difference of 52.3 ng/ml and a statistical significance (p=0.0001). Sanjari et al. collected three different blood samples. The first sample was taken one week before Ramadan (after 12 hours of fasting from the night before), and the second and third samples were collected on the 24th and 28th day of Ramadan (both 2 hours before sunset). Based on the results, IGF1 levels were reduced, but unlike the present study, the findings were not statistically significant, which can be due to shorter fasting periods each day. The fasting hours on each day of the Sanjari were around 12 hours, but this variable was around 16 hours in the present study (1). Furthermore, Bouhlel et al. demonstrated that glucose, growth hormone, IGF1, and IGFBP3 rates did not considerably change after fasting compared to their rates before fasting. These results could be achieved due to the low number of their participants (9 rugby players) in comparison to the sample size of the present study (40 individuals) (13).

Previous research has also indicated that reducing protein consumption can decrease IGF1 serum levels (6). In the present, the subjects were asked to lower their protein intake, which could have contributed to the reduction of IGF1 levels at the end of the study. Levine et al. investigated the effects of low protein intake on IGF1, cancer, and overall mortality in a population aged 50≤ years. Based on protein share in total calorie intake, subjects were

divided into three groups: one group with high protein intake (20%≤), another with medium protein intake (10-19%), and a group with low protein intake (10%≥). Inadequate protein consumption reduced IGF1 levels and cancer-related mortality rates in the 50 to 65-year-old population, and that medium and high protein intake increased the chances of cancer and death (15).

No correlation was reported between serum IGF1 levels and BMI, and the same was found in Sanjari's study (1). Moreover, the difference in IGF1 rates before and after Ramadan was higher in the subjects aged 30≥ years compared to subjects aged 30≤ years. However, no significant correlation was found between age and IGF1 levels, possibly due to the small sample size. The difference in IGF1 levels before and after Ramadan in men was more significant than in women, which could be attributed to the higher number of days that men can adhere to fasting regulations. However, no statistical significance was found between gender and IGF1 levels, possibly because of our study's more significant number of women. No other research has investigated the correlation between age and IGF1, as well as gender and IGF1.

Conclusion

Based on the results, fasting for about 16 hours a day and reducing protein intake could decrease IGF1 levels. Furthermore, IGF1 is claimed to be a risk factor for cancers like prostate, breast, kidney, and lung, and controlling the level of IGF1 can be potentially beneficial. TakeThe results of this study indicated the potential benefits of fasting on human health.

Conflict of Interest

The authors declare no conflict of interest.

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References

1. Sanjari M, Larijani B, Bradar-Jalili R, Amini MR, Akrami SM. Effects of ramadan fasting on insulin-like growth factor-1 and low-density lipoprotein in healthy adults. Feyz Journal of Kashan University of Medical Sciences. 2005;9(3):30-3.

2. Tawfiqi H .Familiarity with major religions. 18, editor. Tehran: Samt; 2019. 344 p.

3. Adlouni A, Ghalim N, Benslimane A, Lecerf JM, Saïle R. Fasting during Ramadan induces a marked increase in high-density lipoprotein cholesterol and decrease in low-density lipoprotein cholesterol. Annals of Nutrition and Metabolism. 1997;41(4):242-9.

4. Jameson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Loscalzo J. Harrison's principles of internal medicine: McGraw-hill education New York; 2018.

5. Maki RG. Small is beautiful :insulin-like growth factors and their role in growth, development, and cancer. Journal of Clinical Oncology. 2010;28(33):4985.

6. Baserga R, Peruzzi F, Reiss K. The IGF-1 receptor in cancer biology. International Journal of Cancer. 2003;107(6):873-7.

7. Travis RC, Appleby PN, Martin RM, Holly JM, Albanes D, Black A, et al. A meta-analysis of individual participant data reveals an association between circulating levels of IGF-I and prostate cancer risk. Cancer Research. 2016;76(8):2288-300.

8. Aimaretti G ,Colao A, Corneli G, Pivonello R, Maccario M, Morrison K, et al. The study of spontaneous GH secretion after 36-h fasting distinguishes between GH-deficient and normal adults. Clinical Endocrinology. 1999;51(6):771-7.

9. Sävendahl L, Underwood LE. Fasting increases serum total cholesterol, LDL cholesterol and apolipoprotein B in healthy, nonobese humans. The Journal of Nutrition. 1999;129(11):2005-8.

10. Brahmkhatri VP, Prasanna C, Atreya HS. Insulin-like growth factor system in cancer: novel targeted therapies. BioMed Research International. 2015;2015.

11. Yakar S, Rosen CJ, Beamer WG, Ackert-Bicknell CL, Wu Y, Liu J-L, et al. Circulating levels of IGF-1 directly regulate bone growth and density. The Journal of Clinical Investigation. 2002;110(6):771-81.

12. Peruzzi F, Prisco M, Dews M, Salomoni P, Grassilli E, Romano G, et al. Multiple signaling pathways of the insulin-like growth factor 1 receptor in protection from apoptosis. Molecular and Cellular Biology. 1999;19(10):7203-15.

13. Bouhlel E, Zaouali M, Miled A, Tabka Z, Bigard X, Shephard R. Ramadan fasting and the GH/IGF-1 axis of trained men during submaximal exercise. Annals of Nutrition and Metabolism. 2008;52(4):261-6.

14. Fontana L, Weiss EP, Villareal DT, Klein S, Holloszy JO. Long-term effects of calorie or protein restriction on serum IGF-1 and IGFBP-3 concentration in humans. Aging Cell. 2008;7(5):681-7.
15. Levine ME, Suarez JA, Brandhorst S, Balasubramanian P, Cheng C-W, Madia F, et al. Low protein intake is associated with a major reduction in IGF-1, cancer, and overall mortality in the 65 and younger but not older population. Cell Metabolism. 2014;19(3):407-17.
16. Arciero PJ, Arciero KM, Poe M, Mohr AE, Ives SJ, Arciero A, et al. Intermittent Fasting Two Days per Week versus One Day per Week, Matched for Total Energy Intake and Expenditure, Increases Weight Loss in Overweight/Obese Men and Women. 2022.
17. Li C, Xing C, Zhang J, Zhao H, Shi W, He B. Eight-hour time-restricted feeding improves endocrine and metabolic profiles in women with anovulatory polycystic ovary syndrome. Journal of Translational Medicine. 2021;19(1):1-9.