



Can Monocyte/HDL Ratio Be Used in the Follow-Up of Patients with Acromegaly?

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ABSTRACT

Objective: Insulin-like growth factor-1 (IGF-1) level was used in the follow-up of acromegaly patients. The aim of this study is to investigate the relationship between pre- and postoperative IGF-1 levels and monocyte/high-density lipoprotein (HDL) ratio, which is a novel inflammatory marker, in patients diagnosed with acromegaly.

Material and Methods: Thirty-two acromegaly patients (17 males and 15 females) were included in this retrospective study. Demographic characteristics of the patients and their laboratory data before and six months after the operation were scanned from their files.

Results: While preoperative IGF-1 level was 515.8 ± 197.0 ng/ml, postoperative IGF-1 level was 121.1 ± 89.4 ng/ml. While preoperative MHR was 13.9 ± 4.33 μ l/mg/dl, it was calculated as 9.52 ± 4.43 μ l/mg/dl postoperatively. There was a significant difference in pre- and postoperative IGF-1 levels and monocyte/HDL ratio ($p=0.006$ and $p<0.001$, respectively). A positive relationship was found between the pre- and post-operative monocyte/HDL ratio and IGF-1 levels. ($p<0.001$ vs $\beta=0.727$ and $p=0.001$ vs $\beta=0.540$, respectively).

Conclusion: IGF-1 level is correlated with the monocyte/HDL ratio. In addition to IGF-1 level, monocyte/HDL ratio may also be directive during the follow-up of patients with acromegaly and especially for complications that may develop. Prospective and randomized studies with large patient groups are needed to give more detailed results.

Keywords: Acromegaly, IGF-1, monocyte/HDL ratio

ÖZ

Akromegali Hastasının Takibinde Monosit/HDL Oranı Kullanılabilir mi?

Giriş: Akromegali hastalarının takibinde insülin benzeri büyüme faktörü-1 (IGF-1) düzeyi kullanılmaktadır. Bu çalışmanın amacı; akromegali tanısı almış hastaların operasyon öncesi ve sonrası IGF-1 düzeyleri ile yeni enflamasyon belirteci olan monosit/high-density lipoprotein (HDL) oranının ilişkisini araştırmaktır.

Gereç ve Yöntemler: Retrospektif olarak yapılan bu çalışmaya 32 akromegali hastası (17 erkek ve 15 kadın) alındı. Hastaların demografik özellikleri ve operasyon öncesi ile operasyondan altı ay sonrası laboratuvar verileri dosyalarından tarandı.

Bulgular: IGF-1 düzeyi operasyon öncesi 515.8 ± 197.0 ng/ml iken operasyon sonrası 121.1 ± 89.4 ng/ml, monosit/HDL oranı ise operasyon öncesi 13.9 ± 4.33 μ l/mg/dl iken operasyon sonrası 9.52 ± 4.43 μ l/mg/dl olarak hesaplandı. Operasyon öncesi ve sonrası IGF-1 düzeyi ve monosit/HDL oranı açısından anlamlı bir fark vardı (sırasıyla $p=0.006$, $p<0.001$). Operasyon öncesi ve sonrası monosit/HDL oranı ile IGF-1 düzeyi arasında pozitif ilişki olduğu tespit edildi (sırasıyla $p<0.001$ vs $\beta=0.727$, $p=0.001$ vs $\beta=0.540$).

Sonuç: IGF-1 düzeyi ile monosit/HDL oranı ilişkilidir. Akromegali hastalarının takibi sırasında ve özellikle gelişebilecek komplikasyonlar açısından IGF-1 düzeyi yanında monosit/HDL oranında yol gösterici olabilir. Daha detaylı sonuç vermek için geniş hasta gruplarıyla prospektif ve randomize çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Akromegali, IGF-1, monosit/HDL oranı

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INTRODUCTION

Acromegaly develops as a result of excessive secretion of growth hormone (GH). GH and Insulin-like growth factor-1 (IGF-1) cause metabolic changes in patients with acromegaly (1). Endothelial dysfunction and microvascular involvement have been demonstrated in patients with acromegaly (2).

Monocytes and macrophages are cells involved in the synthesis and release of pro-inflammatory and pro-oxidant cytokines (3). Monocyte activation and differentiation into lipid-laden macrophages is important at the onset of atherosclerotic lesions (4). It is known that high density lipoprotein cholesterol (HDL) protects the endothelium from the harmful effects of low density lipoprotein cholesterol (LDL) and inhibits the oxidation of LDL cholesterol. Thus, HDL acts as an anti-inflammatory and antioxidant (5,6). Monocyte/HDL ratio (MHR) has emerged as a novel marker of inflammation and oxidative stress and is closely related to the presence and prognosis of some cardiovascular diseases (7-9).

MHR may be an important predictor of disease activity in patients with acromegaly. The relationship between IGF-1 level and MHR in patients with acromegaly is unknown. The aim of this study was to investigate the relationship between pre- and postoperative IGF-1 levels and MHR, a novel inflammatory marker, in patients diagnosed with acromegaly.

MATERIALS and METHODS

This study was conducted by retrospectively examining the records of patients diagnosed with acromegaly between 2014 and 2020 in Internal Medicine and Endocrinology Clinics of Adana City Training and Research Hospital. Study protocol was approved by the institutional ethics committee. The patients were divided into two groups according to their treatment status as pre- and post-treatment groups. Patients with malignancy, rheumatic disease, thyroid dysfunction, hyperlipidemia, hematological, liver, renal, cardiac and pulmonary diseases were excluded from the study. Thus, the demographic characteristics and pre- and post-treatment laboratory data of a total of 32 operated acromegaly patients were analyzed. IGF-1 level and MHR were recorded from the laboratory data. Post-treatment

IGF-1 change (Δ -IGF-1) was accepted as pre-treatment IGF-1 - post-treatment IGF-1, and post-treatment MHR change (Δ -MHR), was accepted as pre-treatment MHR - post-treatment MHR.

Statistical Analysis

All analyses were performed using SPSS 22.0 (Chicago, IL, USA) statistical software package. Variables were divided into two groups as categorical and continuous variables. Whether the distribution of continuous variables was normal was evaluated using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean \pm SD. Categorical variables were specified with numbers and percentages. Paired sample t test was used to compare laboratory variables obtained pre- and post-treatment. Statistical details between the groups are indicated in the tables. Pearson's and Spearman's correlation method was used to determine the correlation between pre- and post-treatment IGF-1 and MHR levels and post-treatment Δ -IGF-1 and Δ -MHR. Linear regression analysis was conducted in case of statistical significance. Statistical significance was accepted as $p < 0.05$.

RESULTS

None of the 32 operated patients diagnosed with acromegaly included in the study were on medication for acromegaly and all of them were in remission. Seventeen (53.1%) of the patients were males, 15 (46.8%) of the patients were females. The mean age of the patients was 59.2 ± 10.3 . Twenty-two of the patients (68.7%) had type II diabetes mellitus and 17 (53.1%) had hypertension. While preoperative IGF-1 level was 515.8 ± 197.0 ng/ml, postoperative IGF-1 level was 121.1 ± 89.4 ng/ml. While preoperative MHR was 13.9 ± 4.33 μ l/mg/dl, it was calculated as 9.52 ± 4.43 μ l/mg/dl postoperatively. There was a significant difference in pre- and postoperative IGF-1 level and MHR. ($p = 0.006$ and $p < 0.001$, respectively) (Table 1). A positive relationship was found between pre- and post-operative MHR and IGF-1 level ($p < 0.001$ vs $\beta = 0.727$ and $p = 0.001$ vs $\beta = 0.540$, respectively) (Table 2 and 3) (Figures 1 and 2). No relationship was found between post-treatment Δ -IGF-1 and Δ -MHR (Table 4).

Table 1. Comparison of pre- and post-operative IGF-1 and MHR data

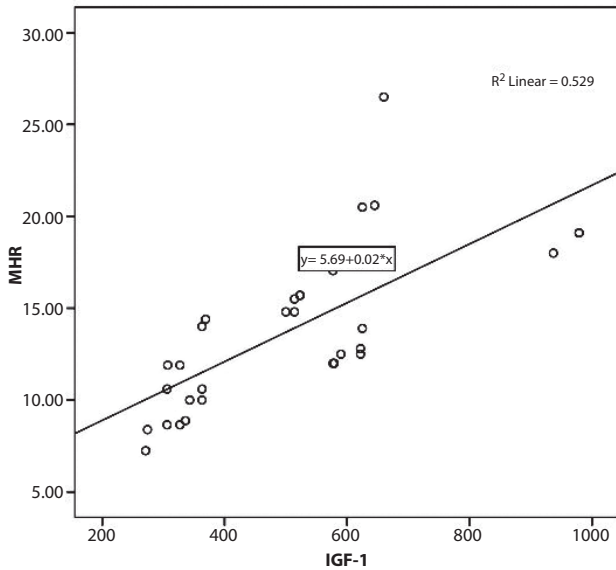
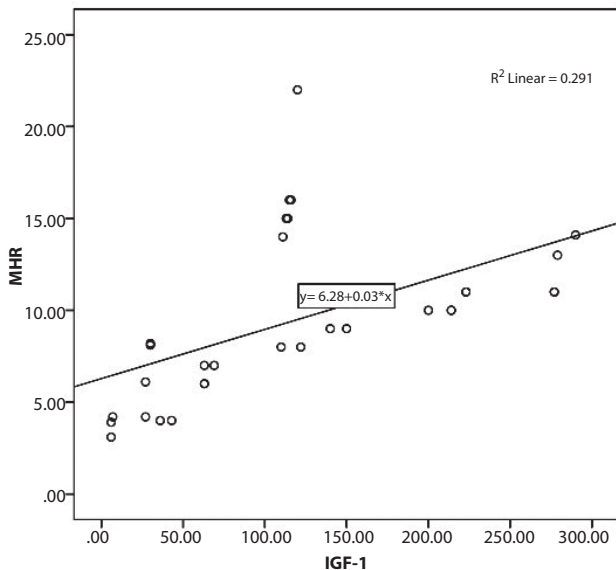
	Pre-operative n= 32	Post-operative n= 32	p
IGF-1 (ng/ml)	515.8 ± 197.0	121.1 ± 89.4	0.006
MHR (μ L/mg/dl)	13.9 ± 4.33	9.52 ± 4.43	<0.001

IGF-1: Insulin-like growth factor-1, MHR: Monocyte/high-density lipoprotein ratio.

Table 2. Correlation and regression analysis between patients' pre-treatment IGF-1 level and MHR

Univariate analyze			Multivariate analyze	
Variable	p	r	p	β
MHR ($\mu\text{l}/\text{mg}/\text{dl}$)	<0.001	0.837	<0.001	0.727

IGF-1: Insulin-like growth factor-1, MHR: Monocyte/high-density lipoprotein ratio.
 $*R^2_{\text{Adjusted}} = 0.529$

**Figure 1.** The relation between patients' pre-treatment IGF-1 level and MHR.**Figure 2.** The relation between patients' pre-treatment IGF-1 level and MHR.**Table 3.** Correlation and regression analysis between patients' post-treatment IGF-1 level and MHR

Univariate analyze			Multivariate analyze	
Variable	p	r	p	β
MHR ($\mu\text{l}/\text{mg}/\text{dl}$)	<0.001	0.716	0.001	0.540

IGF-1: Insulin-like growth factor-1, MHR: Monocyte/high-density lipoprotein ratio.
 $*R^2_{\text{Adjusted}} = 0.291$

Table 4. Correlation analysis between post-treatment Δ -IGF-1 and Δ -MHR

Univariate analyze		
Variable	p	r
Δ -MHR ($\mu\text{l}/\text{mg}/\text{dl}$)	<0.402	0.153

Δ -IGF-1: Pre-treatment IGF-1 – post-treatment IGF-1, Δ -MHR: Pre-treatment MHR – post-treatment MHR.

DISCUSSION

The most important finding of our study is that MHR is significantly increased in patients with active acromegaly compared to acromegaly patients in remission. To the best of our knowledge, our study is the first to show MHR level in patients with acromegaly. In addition, in our study, a positive and close relationship was found between MHR and IGF-1 level. The increase in MHR level in patients with active acromegaly and its close relation with IGF-1 suggested that MHR may be used as an important tool during the follow-up of patients with acromegaly and especially in terms of complications that may develop. Therefore, our data provided important information to the literature.

Since there is no study evaluating MHR level in patients with acromegaly in the literature, the data in our study could not be compared with other studies. However, the limited number of studies on MHR in the literature revealed the role of this ratio in predicting inflammation (10). In addition, it has been pointed out that MHR is an independent predictor of increased cardiovascular events in chronic renal failure patients and is associated with a poor prognosis for cardiovascular mortality (11). In addition, it has been shown that MHR is closely related to stent thrombosis in patients who

underwent coronary stent implantation with primary percutaneous intervention (12). In a study by Canpolat et al., it has been observed that having high MHR initially in patients who underwent cryoablation due to atrial fibrillation was associated with the recurrence of atrial fibrillation (13).

It is known that cardiovascular pathologies are associated with GH levels in patients with acromegaly (1). Insulin resistance, diabetes and hyperlipidemia, which are cardiovascular risk factors, are observed at a rate of 15-38% in patients with acromegaly and contribute to cardiovascular diseases (14). In studies, it has been observed that MHR determines adverse cardiovascular events (15,16). In our study, MHR may be associated with vascular and cardiac adverse effects that may be caused by increased inflammation in patients with active acromegaly with high IGF-1 levels.

It is not easy to explain the course of acromegaly with a mechanism that covers all clinical pictures. Considering all physiopathological processes, it is thought that MHR increases especially with tissue damage in patients with active acromegaly.

In our study, it is not clear whether MHR increased secondary to inflammation or cardiovascular involvement in patients with active acromegaly. However, it should be kept in mind that MHR level is elevated in patients with active acromegaly.

Limitations

Our study has several limitations. One of the main limitations of the study is that it is observational, single-centered, and retrospective. In addition, MHR has not been compared with any inflammatory markers such as C-reactive protein, the monocyte count is calculated by automated method from peripheral blood, monocyte subgroups are not measured with flow cytometry and the patients treated could not be followed up for the long term. Although the results of our study were found to be significant, the number of patients was insufficient. In our study, more significant results could be obtained if cardiac markers were evaluated and the duration of the disease was investigated.

CONCLUSION

In conclusion, there is an increase in MHR in patients with active acromegaly compared to acromegaly patients in remission, and there is a positive and close relationship between IGF-1 level and MHR. MHR, which is examined during the follow-up of acromegaly patients, can be an inexpensive and easily accessible parameter that can be used in more detailed screening of cardiovascular diseases. However, large-scale, prospective and randomized studies are needed to obtain clearer results.

Ethics Committee Approval: The study was approved from Cukurova University Faculty of Medicine Clinical Researches Ethic Committee (Date: 01.06.2018, Decision No: 37).

Author Contributions: Concept/Design: EG; Analysis/Interpretation: EG, MZA; Data Acquisition: EG, FA; Writting: EG, FA; Critical Revision: EG, FA; Final Approval: EG, MZA.

Conflict of Interest: There is no conflict of interest.

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