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Research Article

Association between Lipid Profile and Glycemic Status in Iraqi patients with Acromegaly Receiving Depot Long-Acting Octreotide

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Abstract

Background: Treatment modalities of acromegaly and disease control impact differently on glucose homeostasis and lipid changes, and consequently on cardiometabolic risk. ***Aim***: To investigate the possible association of lipid profile changes with the glycemic control status in acromegaly patients treated with octreotide LAR. ***Methods***: This cross-sectional study included 52 Iraqi patients with acromegaly treated with octreotide LAR and not using statins. Demographic, anthropometric, and clinical data were collected, as well as the duration of Octreotide LAR administration. The glycemic state was assessed and classified as DM, prediabetes, or normal. Plasma levels of triglycerides, LDL cholesterol, HDL cholesterol, and non-HDL were evaluated using standard methods. ***Results***: Most of the participants presented with low levels of triglycerides, LDL cholesterol, and HDL cholesterol. The lipid profile variables were not significantly correlated with the glycemic control status after treatment with octreotide LAR. ***Conclusion***: Lipid profile parameters were not associated with the different glycemic control status of acromegaly patients treated with octreotide LAR.

Keywords: octreotide LAR, acromegaly, lipid profile, glycemic control

الارتباط بين نسبة الدهون ومستوى جلوكوز الدم في مرضى أكروميجالي العراقيين المعالجين بالأوكتريوتيد طويل المفعول

الخلاصة

الخلفية: أن علاج الأكروميجالي يؤثر بشكل مختلف على توازن الجلوكوز ومستوى الدهون، وبالتالي على مستوى مخاطر أمراض القلب والتمثيل الغذائي. **الهدف**: للتحقق في الارتباط المحتمل للتغيرات في مستوى الدهون مع حالة التحكم في نسبة السكر في دم مرضى الاكروميكالي الذين عولجوا بالاوكتريوتايد طويل المفعول. **الطرائق**: شملت هذه الدراسة المقطعية 52 مريضا عراقيا يعانون من الاوكروميكالي وعولجوا بالاوكتريوتايد طويل المفعول وغير مستخدمين لادوية الستاتين المثبطة للدهون في الدم. تم جمع البيانات الديموغرافية والبشرية والسريرية، فضلا عن مدة استخدام الاوكتريوتايد وتقييم حالة نسبة الكلوكوز في الدم وتصنيفها على انها داء السكري، مرحلة ما قبل السكري او غير مصاب بالسكري. **النتائج**: معظم المشاركين ظهروا بمستويات منخفضة من الدهون الثلاثية، الكولسترول LDL والكوليسترول HDL. لم تكن متغيرات مستوى الدهون مرتبطة بشكل كبير بحالة التحكم في نسبة السكر في الدم بعد العلاج بالأوكتريوتيد طويل المفعول. **الاستنتاج**: لم ترتبط التغيرات في حالة مستوى الدهون بحالة التحكم في نسبة السكر في الدم لمرضى الأكروميكالي الذين عولجوا بالأوكتريوتيد طويل المفعول.

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INTRODUCTION

Acromegaly is a rare condition caused by an increase in IGF-1 levels as a result of excessive GH synthesis. When compared to an age-matched general population, this condition is linked to higher morbidity and death, leading to a higher cardiovascular risk and a worse metabolic profile [1,2]. Acromegaly is complicated by the presence of lipid problems. Anabolic and lipolytic effects of increased GH/IGF-I secretion are well-documented, while hypertriglyceridemia (found in 33-40% of acromegaly patients, three times higher than in the general population) and low HDL cholesterol (found in 39-47%) are the most common lipid profile abnormalities [3,4]. Hypercholesterolemia is also common in the acromegaly population. In contrast, patients with acromegaly have higher levels of circulating lipoprotein-a (Lp-a), Apo A-I, and Apo E, which are implicated in the transfer of triglycerides, cholesterol, and tiny dense LDL particles; in addition to the induction of arterial damage and atherosclerosis [5]. The biochemical regulation of acromegaly has an effect on lipid profile changes as well. Although this did not occur in all individuals with managed illness, a retrospective analysis found an improvement in hypertriglyceridemia and HDL cholesterol levels after normalization of IGF-1/GH levels was achieved with either surgery or pharmacological therapy [6]. Treatment modalities of acromegaly and disease control impact differently on glucose homeostasis and lipid changes, and consequently on cardiometabolic risk. In the class of somatostatin analogs (SSA), pasireotide was shown to significantly influence glucose metabolism [7]. Furthermore, non-diabetic acromegaly patients treated with lanreotide autogel (120 mg/4 weeks) had considerably lower triglycerides and higher HDL cholesterol levels, with no significant changes in total or LDL cholesterol levels [8]. Chen et al. evaluated the pharmacokinetics and safety of pasireotide in healthy Chinese male participants, finding that it decreases serum cholesterol and triglyceride levels in a dose-dependent way [9]. In this sense, the lipid profile has an impact on the visceral adiposity index (VAI), a marker of visceral fat dysfunction that indirectly reflects cardiometabolic risk. VAI appears to be linked to insulin resistance, adipose tissue dysfunction, and cardiometabolic risk in acromegaly, particularly in postmenopausal women [10]. The current study was designed to explore the influence octreotide LAR on the lipid profile of Iraqi patients with acromegaly.

METHODS

Study design

At the Iraqi National Center for Diabetes, Baghdad, 52 adults with acromegaly were enrolled in a cross-sectional observational study. Age, gender, BMI, waist circumference, octreotide treatment duration (independent of dose), GH, IGF1 levels and pituitary tumor size at initial presentation were analyzed from May to October 2018. Diabetes and pre-diabetes, as well as hypertension and the timing of octreotide administration, were also examined. Based on HbA1c and fasting plasma glucose levels, participants were assigned to one of the three glycemic groups: normal, diabetic, or pre-diabetic. Having one or more first-degree relatives with diabetes was regarded as having a positive family history of diabetes (parent, sibling, or offspring). Patients with documented glycemic problems, as well as those taking corticosteroids, beta-blockers, or thiazides, were not allowed to participate in this study.

Ethical consideration

The ethical and scientific committee of the Iraqi Board of Medical Specializations thoroughly evaluated and accepted the research proposal. Before beginning the experiment, the National Center for Diabetes and Endocrinology's health authorities had given their approval for it. As part of the permission process, each patient was given a thorough explanation of the study's goal and assured that any data gathered would only be used for research reasons.

Measurement of biochemical markers

Samples of blood are taken from patients after an overnight fasting period. Part of the sample was utilized for the estimation of HbA1c; the other part was stored in plain tubes for clotting. Centrifuged at 3000 rpm for 10 minutes, the serum was used to measure fasting serum glucose, total cholesterol, HDL cholesterol, and triglycerides in accordance to standard procedures. Using the Friedewald formula, LDL cholesterol (mg/dl) was calculated as LDL cholesterol (total cholesterol - [HDL cholesterol + TG/5]), and non-HDL cholesterol = Total cholesterol - HDL cholesterol.

Statistical analysis

The acquired data was processed and imported into SPSS v24 for statistical analysis. Tables and graphs depicted descriptive statistics. Chi square and Fisher Exact tests were employed to determine the relationship between variables. A *P*-value less than 0.05 was considered significant.

RESULTS

Table 1 demonstrates the demographic and anthropometric characteristics of the patients included in the study. Among the 52 acromegaly patients evaluated, 67.3% were male and 53.8% were under the age of 40, according to the findings of this study. In 59.6% of the cases, the increase in IGF1 was less than twice the usual value (8.5-25.4 nmol/l), while in 40.4% of the cases, the increase was twice or more. Serum growth hormone levels rose more than three times the usual level (0.4-14 ng/ml) in half of cases. The prevalence of macroadenoma was 78.8%, the waist circumference was abnormally raised in 94.2% of cases, and a normal BMI value was reported in 5.8% of the cases, while 28.8% of patients were overweight and the others were obese (class 1 obesity, 48.1%, class 2 obesity, 7.7%, and class 3 obesity, 9.6%).

Table 1: distribution of studied cases according to studied variables

Parameter		*n*(%)
Gender	Male	35(67.3)
	Female	17(32.7)
Age (Year)	< 40	24(46.2)
	≥ 40	28(53.8)
Serum IGF1	<2 x normal	31(59.6)
	≥2 x normal	21(40.4)
Serum Growth hormone	<3 x normal	26(50.0)
	≥ 3 x normal	26(50.0)
Size of adenoma	Macroadenoma	41(78.8)
	Microadenoma	11(21.2)
Waist circumference	Normal	3(5.8)
	Abnormal	49(94.2)
Body Weight	Normal	3(5.8)
	Overweight	15(28.8)
	Obese G1	25(48.1)
	Obese G2	4(7.7)
	Obese G3	5(9.6)
Blood Pressure	Normotensive	26(50.0)
	Hypertensive	26(50.0)
Family history of DM	Negative	23(44.2)
	Positive	29(55.8)

Patients with hypertension (50%) and a family history of diabetes (55.8%) comprised the majority of participants in this study. In Figure 1, 81% of acromegaly patients had triglyceride levels (TG) of less than150 mg/dL, and 38% had HDL values that were within the normal ranges. In addition, 65% of the acromegaly patients had serum LDL cholesterol levels below 100 mg/dL, and 75% had non-HDL cholesterol levels below 130 mg/dL.

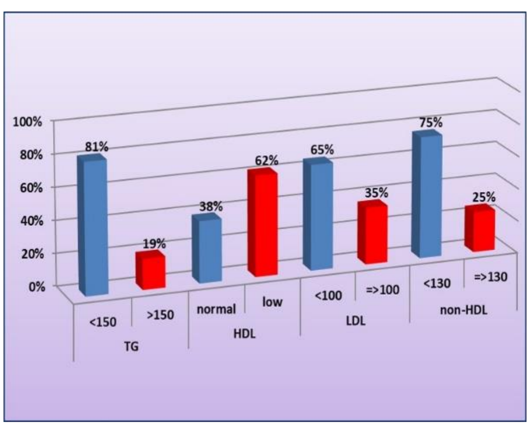

Figure 1: Distribution of the acromegaly patients according to their lipid profile.

Table 2 shows the association between lipid profile variables and the glycemic status of the acromegaly patients. There was no significant association (P>0.05) between each of the lipid profile components (triglycerides, HDL cholesterol, LDL cholesterol, and non-HDL) with the different glycemic status subgroups (normal, diabetic, and pre-diabetic).

Table 2: Association between lipid profile variables and glycemic status according to Fisher Exact test.

Variables		Total	Normal *n*(%)	Pre DM *n*(%)	DM *n*(%)	*P*-value
TG	<150	42	9(81.8)	18(85.7)	15(75.0)	0.454
	≥150	10	2(18.2)	3(14.3)	5(25.0)	
P-value			Reference	1	1	
HDL	Normal	20	3(27.3)	8(38.1)	9(45.0)	0.756
	Low	32	8(72.7)	13(61.9)	11(55.0)	
P-value			Reference	0.703	0.452	
LDL	<100	34	7(63.6)	15(71.4)	12(60.0)	0.520
	≥100	18	4(36.4)	6(28.6)	8(40.0)	
P-value			Reference	0.703	1	
non-HDL	<130	39	9(81.8)	15(71.4)	15(75.0)	1
	≥130	13	2(18.2)	6(28.6)	5(25.0)	
P-value			Reference	0.681	1	

DISCUSSION

It has been widely accepted that active acromegaly is associated with a condition of lipotoxicity and visceral adiposity dysfunction, and insulin resistance is one of the key metabolic changes that characterize it [11-13]. The present study showed that the vast majority of the participants who are treated with octreotide LAR had low levels of TG, LDL cholesterol, and non-HDL cholesterol; however, the HDL cholesterol value was found to be low in 62% of them. Octreotide LAR is successful in decreasing GH in acromegaly patients, and it is linked to improvements in plasma lipids and lipoproteins [14,15]. Similar to these findings, Tan *et al*. have observed a reduction in plasma triglyceride and LDL cholesterol after octreotide LAR treatment [16]. Except for the reported fall in blood HDL cholesterol levels, this finding was determined to be compatible with the findings of the current investigation. This could be attributed to the initial rapid drop in GH after starting octreotide LAR medication, which results in a 10-fold fall in GH by week 8 and then levels off. However, given the study's small sample size, the likelihood that some of these alterations were temporary could not be ruled out. Moreover, the changes in plasma lipids and lipoproteins after lowering GH in patients with acromegaly may be partly secondary to the effects of improving insulin resistance and glycemic control [17,18]. The presented results showed that the lipid profile was comparable across all glycemic status subgroups, with no significant association between any of the lipid profile variables and glycemic status, and that most patients with diabetes and prediabetes were within the target for LDL cholesterol, non-HDL cholesterol, and triglyceride. In this study, 60% of the acromegaly patients had diabetes, and 71.4 percent of those categorized as prediabetics had LDL cholesterol levels of less than 100 mg/dl and non-HDL cholesterol levels of less than 130 mg/dl. Non-HDL levels of less than 130 mg/dl were seen in 75% of diabetics. Furthermore, 75% of diabetics and 85.7% of participants with pre-diabetes had TG levels below 150 mg/dl. These findings were in line with those of Tan *et al*. and Colao *et al*., who discovered that octreotide LAR is linked to improved plasma lipid profiles and a decrease in small dense LDL [16,19].

Conclusion

Lipid profile parameters were not associated with the different glycemic control status of acromegaly patients treated with octreotide LAR and not maintained on statins.

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Conflicting interests

Nothing declared.

Data sharing statement

Supplementary data will be provided by the corresponding author based on reasonable request.

REFERENCES

1. Colao A, Ferone D, Marzullo P, Lombardi G. Systemic complications of acromegaly, epidemiology, pathogenesis, and management. *Endocr Rev*. 2004;25:102-152. doi: 10.1210/er.2002-0022.

2. Berg C, Petersenn S, Lahner H, Herrmann BL, Buchfelder M, Droste M, et al. Investigators, Cardiovascular risk factors in patients with uncontrolled and long-term acromegaly, comparison with matched data from the general population and the effect of disease control. *J Clin Endocrinol Metab*. 2010;95:3648-3656. doi: 10.1210/jc.2009-2570.

3. Pivonello R, Auriemma RS, Grasso LF, Pivonello C, Simeoli C, Patalano R, et al. Complications of acromegaly, cardiovascular, respiratory and metabolic comorbidities. *Pituitary*. 2017;20:46-62. doi: 10.1007/s11102-017-0797-7.

4. Biagetti B, Herance JR, Ferrer R, Aulinas A, Palomino-Schätzlein M, et al. Metabolic fingerprint of acromegaly and its potential usefulness in clinical practice. *J Clin Med*. 2019;8(10):1549. doi: 10.3390/jcm8101549.

5. Briet C, Ilie MD, Kuhn E, Maione L, Brailly-Tabard S, et al. Changes in metabolic parameters and cardiovascular risk factors after therapeutic control of acromegaly vary with the treatment modality. Data from the Bicêtre cohort, and review of the literature. *Endocrine*. 2019;63(2):348-360. doi: 10.1007/s12020-018-1797-8.

6. Giordano C, Ciresi A, Amato MC, Pivonello R, Auriemma RS, Grasso LF, et al. Clinical and metabolic effects of first-line treatment with somatostatin analogues or surgery in acromegaly, a retrospective and comparative study. *Pituitary*. 2012;15:539-551. doi: 10.1007/s11102-011-0365-5.

7. Colao A, Grasso LFS, Giustina A, Melmed S, Chanson P, Pereira AM, et al. Acromegaly. *Nat Rev Dis Primers*. 2019;5:20. doi: 10.1038/s41572-019-0071-6.

8. Caron PJ, Petersenn S, Houchard A, Sert C, Bevan JS, Group PS. Glucose and lipid levels with lanreotide autogel 120 mg in treatment-naïve patients with acromegaly, data from the PRIMARYS study. *Clin Endocrinol*. 2017;86:541-551. doi: 10.1111/cen.13285.

9. Chen X, Shen G, Jiang J, Liu H, Hu K, Darstein C, et al. Pharmacokinetics and safety of subcutaneous pasireotide and intramuscular pasireotide long-acting release in Chinese male healthy volunteers, a phase I, single-center, open-label, randomized study. *Clin Ther*. 2014;36:1196-1210. doi: 10.1016/j.clinthera.2014.06.006.

10. Ciresi A, Amato MC, Pivonello R, Nazzari E, Grasso LF, Minuto F, et al. The metabolic profile in active acromegaly is gender-specific. *J Clin Endocrinol Metab*. (2013) 98:E51-59. doi: 10.1210/jc.2012-2896.

11. Freda PU, Shen W, Heymsfield SB, Reyes-Vidal CM, Geer EB, Bruce JN, et al. Lower visceral and subcutaneous but higher intermuscular adipose tissue depots in patients with growth hormone and insulin-like growth factor I excess due to acromegaly. *J Clin Endocrinol Metab*. 2008;93(6):2334-2343. doi: 10.1210/jc.2007-2780.

12. Ciresi A, Amato MC, Pizzolanti G, Giordano Galluzzo C. Visceral adiposity index is associated with insulin sensitivity and adipocytokine levels in newly diagnosed acromegalic patients. *J Clin Endocrinol Metab*. 2012;97(8):2907-2915. doi: 10.1210/jc.2012-1518.

13. Ciresi A, Amato MC, Pizzolanti G, Giordano C. Serum visfatin levels in acromegaly: Correlation with disease activity and metabolic alterations. *Growth Horm IGF Res*. 2015;25(5):240-246. doi: 10.1016/j.ghir.2015.07.002.

14. James RA, Møller N, Chatterjee S, White M, Kendall-Taylor P. Carbohydrate tolerance and serum lipids in acromegaly before and during treatment with high dose octreotide. *Diabet Med*. 1991;8(6):517-523. doi: 10.1111/j.1464-5491.1991.tb01644.x.

15. Cohen R, Chanson P, Bruckert E, Timsit J, Legrand A, Harris AG, et al. Effects of octreotide on lipid

metabolism in acromegaly. *Horm Metab Res*. 1992;24(8):397-400. doi: 10.1055/s-2007-1003343.

16. Tan KC, Pang RW, Tiu SC, Lam KS. Effects of treatment with Sandostatin LAR on small dense LDL and remnant-like lipoproteins in patients with acromegaly. *Clin Endocrinol (Oxf)*. 2003;59(5):558-564. doi: 10.1046/j.1365-2265.2003.01849.x.

17. Ben-Shlomo A, Melmed S. Somatostatin agonists for treatment of acromegaly. *Mol Cell Endocrinol*. 2008;286(1-2):192-198. doi: 10.1016/j.mce.2007.11.024.

18. Öberg K, Lamberts SW. Somatostatin analogues in acromegaly and gastroenteropancreatic neuroendocrine tumors: past, present and future. *Endocr Relat Cancer*. 2016;23(12):R551-R566. doi: 10.1530/ERC-16-0151.

19. Colao A, Marzullo P, Ferone D, Spinelli L, Cuocolo A, Bonaduce D, et al. Cardiovascular effects of depot long-acting somatostatin analog Sandostatin LAR in acromegaly. *J Clin Endocrinol Metab*. 2000;85(9):3132-3140. doi: 10.1210/jcem.85.9.6782.