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Assessment of Melanocortin-4 Receptor Levels in Obese Individuals

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Abstract

Obesity is a multifactorial metabolic disorder influenced by genetic and environmental factors and represents a major global health problem. The *melanocortin-4 receptor* (*MC4R*) gene is important for regulating appetite and energy balance. This study aimed to evaluate serum MC4R levels in an Iraqi population. A case–control study was conducted including 45 obese individuals (BMI = 38.44 ± 5.42 kg/m²) and 35 healthy controls (BMI = 22.3 ± 1.8 kg/m²), aged 18–69 years. Serum MC4R levels were significantly elevated in obese individuals (1170.36 ± 108.22 ng/mL) compared with controls (759.35 ± 41.92 ng/mL) (P = 0.002). No significant gender differences were observed within controls (P = 0.089) or obese subjects (P = 0.609), although obese females showed slightly higher levels than males. Group comparison confirmed significantly higher *MC4R* levels in both obese males (P = 0.011) and females (P = 0.042) compared to controls. In conclusion, Obesity is associated with high serum levels of MC4R suggesting the potential role of MC4R in obesity pathophysiology and this association appears to be independent of gender.

Keywords: Obesity, MC4R, Serum levels.

تقييم مستويات مستقبلات الميلانوكورتين-4 لدى الأفراد المصابين بالسمنة

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الخلاصة

تُعدّ السمنة اضطرابًا أيضيًا متعدد العوامل يتأثر بالعوامل الوراثية والبيئية، وتمثل إحدى المشكلات الصحية العالمية الرئيسة. ويؤدي جين مستقبل الميلانوكورتين-4 (MC4R)دورًا مهمًا في تنظيم الشهية وتوازن الطاقة. هدفت هذه الدراسة إلى تقييم مستويات MC4Rالمصلية لدى عينة من السكان العراقيين . أُجريت دراسة من نوع الحالات والشواهد شملت 45 فردًا مصابًا بالسمنة، إذ بلغ متوسط مؤشر كتلة الجسم لديهم (38.44 ± 5.42 كغم/م²)، إضافةً إلى 35 شخصًا سليمًا بوصفهم مجموعة ضابطة، بمتوسط مؤشر كتلة جسم بلغ (22.3 ± 1.8 كغم/م²)، وتراوحت أعمار المشاركين بين 18 و69 عامًا .أظهرت النتائج ارتفاعًا معنويًا في مستويات MC4Rالمصلية لدى الأفراد المصابين بالسمنة، إذ بلغت (1170.36 ± 108.22 نانوغرام/مل) مقارنةً بالمجموعة الضابطة التي بلغت مستوياتها (759.35 ± 41.92 نانوغرام/مل)، مع وجود فرق ذي دلالة إحصائية (P = 0.002). كما لم تُسجَّل فروق معنوية مرتبطة بالجنس داخل مجموعة الضبط (P = 0.089)أو داخل مجموعة المصابين بالسمنة (P = 0.609)، على الرغم من أن الإناث المصابات بالسمنة أظهرن مستويات أعلى قليلًا من الذكور. وأكدت المقارنة بين المجموعات وجود ارتفاع معنوي في مستويات MC4Rلدى الذكور المصابين بالسمنة (P = 0.011) وكذلك لدى الإناث المصابات بالسمنة (P = 0.042)مقارنةً بالأصحاء .وفي الختام، ترتبط السمنة بارتفاع مستويات MC4Rالمصلية، مما يشير إلى الدور المحتمل لهذا المستقبل في الفيزيولوجيا المرضية للسمنة، ويبدو أن هذا الارتباط مستقل عن عامل الجنس .

1. Introduction

Obesity is a multifactorial and complex disease that results in excess body fat and impacts health adversely, including the development of metabolic syndrome, type 2 diabetes, and cardiovascular disease [1]. Its development results from the interaction between environmental factors and genetic susceptibility, with genetic influences accounting for a considerable proportion of individual variability in body weight [2]. While there is a lack of national data in Iraq, some studies reported high prevalence rates of overweight and obesity among Iraqi adults and adolescents [3] [4] [5].

The melanocortin 4 receptor (MC4R) gene is a key regulator of appetite and energy homeostasis through its action in the hypothalamus [6]. Genetic variations in this gene have been widely associated with obesity, particularly the rs17782313 T<C polymorphism, which has been linked to increased body mass index and higher obesity risk in different populations [7] [8]. Activation of MC4R results in decreased appetite and increased energy expenditure, whereas inactivating mutations may lead to hyperphagia and early-onset obesity [9] [10].

In addition to genetic variation, circulating MC4R levels may provide further insight into obesity-related mechanisms [11]. The aim of the current study is to evaluate MC4R serum levels in an obese individuals from Wasit Province-Iraq.

2. Material and Methods

This study is a case-control study, which carried out from 1 July 2025 to 15January 2026. The research performed at the Department of Biology, College of Education for Pure Sciences, University of Wasit.A total of 45 obese participants were enrolled in this study. All individuals were classified as obese according to body mass index (BMI ≥30 kg/m²).The participants' ages ranged from 18 to 69 years, with a mean age ± SD of **31.98** ± 10.94 years (Median: 28 years). Body weight ranged from 72 to 150 kg, while height ranged from 1.52 to 1.88 meters.The BMI values ranged from 30.4 to 47.8 kg/m², with a mean BMI ± SD of 38.44 ± 5.42 kg/m² (Median: 36.4 kg/m²), indicating that the majority of participants were classified within Class II and Class III obesity categories.

All participants were residents of Wasit Province, Iraq, and were recruited according to the study inclusion criteria.

A volume of 5 mL blood samples was drawn from each individual by aseptically venipuncture technique. Sera were used to measure quantitative levels of serum MC4R using the enzyme-linked immunosorbent assay (ELISA) method using Human Melanocortin 4 Receptor (MC4R) ELISA Kit, BT LAB Bioassay Technology Laboratory,China

Data were analyzed using SPSS software version 21.0 (SPSS Inc., Chicago, IL, USA). Serum MCR4 levels were presented as mean ± standard error (SE) and compared between groups using Student's t-test.

3. Results

Determination of serum MC4R levels in obese individuals and healthy controls was performed using the Enzyme-Linked Immunosorbent Assay (ELISA). The results are presented in Table (1). The findings revealed highly significant differences, where serum MC4R levels in obese patients were higher than those in the control group (1170.36 ± 108.22 ng/mL vs. 759.35 ± 41.92 ng/mL, P = 0.002).

Table 1- The mean value of serum MC4R levels in obese subjects compared with control

Group/Parameter	ng/ml Mean ±SE
Control	759.350±41.918
Obese	1170.360±108.221
P-value	0.002
Significant level	Sig. **

ng/mL = nanogram per milliliter; SE = standard error; P = P-value; **Sig. P < 0.01 = highly significant

3.1 Gender differences in serum MC4R levels

Serum MC4R levels were evaluated according to gender in both obese individuals and healthy controls (Table 2). In the control group, males had a mean ± SE serum MC4R level of 835.04 ± 64.68 ng/mL, whereas females had 690.41 ± 48.50 ng/mL, with no statistically significant difference between genders (P = 0.089). Among obese subjects, males showed a mean ± SE of 1119.38 ± 81.48 ng/mL compared with 1234.31 ± 216.33 ng/mL in females, and this difference was also not statistically significant (P = 0.609). Comparison between groups revealed that serum MC4R levels were significantly higher in obese individuals than in controls for both males (P = 0.011) and females (P = 0.042), indicating that obesity is associated with elevated MC4R levels, while gender does not have a significant effect within each group.

Table 2- The mean value of serum MC4R levels by gender in obese subjects and healthy controls

Group/Parameter	**ng/ml Mean ±S E**			
	Male	**Female**	**P-value**	**Significant level**
Control	835.044±64.678	690.405±48.496	0.089	NS.
Obese	1119.377±81.479	1234.310±216.329	0.609	NS.
P-value	0.011	0.042		
Significance level	Sig. **	Sig.*		

ng/mL = nanogram per milliliter; SE = standard error; P = P-value; ** = P < 0.01 (highly significant), * = P < 0.05 (significant), NS = not significant

4. Discussion

The elevated serum levels of MC4R in obese individuals in the present study may reflect a compensatory response or dysregulation of the MC4R pathway in obesity. These findings are consistent with previous studies reporting that the C allele of MC4R rs17782313 is associated with increased BMI, adiposity, and obesity risk [12] [7] [13].

Furthermore, studies investigating the interaction between MC4R and biomarkers of appetite and metabolism support the functional role of MC4R in obesity. Hammad et al. reported that carriers of the rs17782313 C allele exhibited elevated levels of ghrelin, visfatin, and other metabolic regulators, suggesting a mechanistic association between MC4R variation and altered energy homeostasis [14]. Gene–environment interactions affecting obesity risk have also been documented, particularly regarding dietary and metabolic influences on MC4R activity [15].

The association analysis between the rs17782313 polymorphism of the MC4R gene and obesity risk is consistent with several previous reports identifying the C allele as a significant obesity risk factor linked to increased body mass index and altered energy homeostasis [7] [13].

5. Conclusion

Obesity is associated with high serum levels of MC4R suggesting the potential role of MC4R in obesity pathophysiology and this association appears to be independent of gender.

References

[1] W. H. Organization, "Obesity and overweight," World Health Organization, Geneva, 2023.

[2] J. F. Loos and G. S. H. Yeo, "The genetics of obesity: From discovery to biology," *Nature Reviews Genetics,* vol. 23, no. 2, pp.120-133, 2022. https://doi.org/10.1038/s41576-021-00414-z

[3] "W. Al-Kubaisy, H. Alwan, and A. Al-Mossawi, “Prevalence of overweight and obesity among Iraqi adults and associated factors from a national survey," *BMC Public Health,* vol. 21, no. 1, pp. 1–9, 2021.

[4] W. Al-Kubaisy, R. K. Mohammed and S. H. Al-Jubour, "Overweight and obesity among adolescents in Babylon Province, Iraq," *Journal of Public Health Research,* vol. 11, no. 3, pp. 1–7, 2022.

[5] H. Ahmed, S. M. Hussein and N. A. Kareem, "Prevalence of overweight and obesity in Erbil city among adults," *Zanco Journal of Medical Sciences,* vol. 21, no. 2, pp. 1800–1808, 2017.

[6] R. D. Cone, "The central melanocortin system and energy homeostasis," *Trends in Endocrinology & Metabolism,* vol. 27, no. 7, pp. 521–530, 2016.

[7] R. F. Loos, C. M. Lindgren, S. Li, E. Wheeler, J. H. Zhao, I. Barroso and et al., "Common variants near MC4R are associated with fat mass, weight and risk of obesity," *Nature Genetics,* vol. 40, no. 6, pp. 768–775, 2008. doi: 10.1038/ng.140

[8] B. Xi, Y. Takeuchi, S. Chandak and T. Kato, "MC4R polymorphisms and obesity risk: A meta-analysis,” Obesity Reviews," vol. 13, no. 7, pp. 659–667, 2012.

[9] D. Huszar, C. A. Lynch, V. Fairchild-Huntress , J. H. Dunmore, Q. Fang, L. R. Berkemeier, W. Gu, R. A. Kesterson, B. A. Boston, R. D. Cone, F. J. Smith, L. A. Campfield, P. Burn and F. Lee, "Targeted disruption of the melanocortin-4 receptor results in obesity in mice," *Cell,* vol. 88, no. 1, pp. 131–141, 1997. https://doi.org/10.1016/S0092-8674(00)81865-6

[10] I. S. Farooqi, J. M. Keogh, G. S. Yeo, E. Lank, T. Cheetham and S. O. Rahilly, "Clinical spectrum of obesity and mutations in the melanocortin 4 receptor gene," *New England Journal of Medicine,* vol. 348, no. 12, pp. 1085–1095, 2003. DOI: 10.1056/NEJMoa022050

[11] J. R. Speakman, "Obesity: genetics and physiology," *Physiological Reviews,* vol. 101, no. 4, pp. 1607–1662, 2021.

[12] Z. Cheraghi, M. R. Rahimi and F. Hosseini, "Association of MC4R polymorphism with obesity susceptibility in different populations," *Gene Reports,* vol. 38, pp. 101–109, 2025.

[13] L. Qi, K. Kraft, D. J. Hunter and F. B. Hu, "The common obesity variant near MC4R gene is associated with higher intakes of total energy and dietary fat, weight change and diabetes risk in women," *Human Molecular Genetics,* vol. 17, no. 22, pp. 3502–3508, 2008. doi: 10.1093/hmg/ddn242

[14] A. Hammad, N. Al-Husseini and R. Al-Domi, "Association of MC4R rs17782313 polymorphism with ghrelin, visfatin, and metabolic biomarkers in obesity," *Diabetes & Metabolic Syndrome: Clinical Research & Reviews,* vol. 14, no. 5, pp. 1449–1455, 2020.

[15] A. Adamska-Patruño, M. Ostrowska and A. Goscik, "Gene–diet interactions of MC4R variants in obesity and metabolic traits," *Nutrients,* vol. 13, no. 4, pp. 1–14, 2021.