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Short Report

Elevated Plasma Leptin Levels in Autistic Children of Sultanate of Oman

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ABSTRACT

Autistic spectrum disorders (ASD) are mysterious, complex, childhood pervasive developmental disorders characterized by impairments in social interaction, deficits in verbal and non-verbal communication, and restricted repetitive and stereotyped patterns of behavior and interests. The etiology of this disorder is poorly understood and no biomarkers have yet been identified as characteristic of ASD. Leptin, a peptide hormone mainly secreted by adipose tissue, is involved in the regulation of body weight and energy expenditure. Leptin also play a role in regulation of neuroendocrine functions, immune system and inflammatory response and development. Recent evidences suggest that leptin might be implicated in the pathophysiology of autism. Availability of biochemical data related with leptin for Omani autistic children is scarce. So, the current study was aimed to compare the levels of leptin in the plasma of ASD children in Sultanate of Oman. Significant higher levels of leptin were found in Omani autistic children as compared with controls. Our results corroborate with the previous findings and also suggest that there might be some relationship between leptin and the pathophysiology of autism. The exact mechanism is still unknown and further extensive research needed.

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1. Introduction

Autistic spectrum disorders (ASD) are mysterious, complex, childhood pervasive developmental disorders characterized by impairments in social interaction, deficits in verbal and non-verbal communication, and restricted repetitive and stereotyped patterns of behavior and interests [1]. Studies suggest that there might be involvement of genetic factors [2] and the etiology of this disorder is poorly understood and no biomarkers have yet been identified as characteristic of ASD. Although the precise mechanism underlying the pathophysiology of autism remains to be determined, accumulating evidence suggests that a combination of environmental or perhaps in utero risk factors, autoimmune risk factors and abnormality of inflammatory events along with localized inflammation of the central nervous system

may contribute to the pathogenesis of ASD [3-13]. Despite numerous reports suggesting a high rate of inheritance, no specific single genes have been identified that are more than risk factors [14-15]. The identification of specific biochemical correlates of autism might increase the reliability of the behavioral diagnosis of this disorder.

Sultanate of Oman is a developing Arab country located in the South Eastern of the Arabian Peninsula and the total population is approximately 3.5 million, about half of which is below the age of 15 years [16]. 113 diagnosed cases of ASD were reported nationwide and the prevalence of ASD in Oman was reported low (1.4 cases per 10,000 children aged 0-14 years) compared to western countries, which is attributed to under-diagnosis and under-reporting. More prevalent cases were among boys (75%) and among low-income families in Oman also reported [17].

Leptin, a peptide hormone mainly secreted by adipose tissue, is involved in the regulation of body weight and energy expenditure at the hypothalamic level [13]. Serum leptin concentrations are related to fat tissue and body mass index (BMI) in children and adults [18-20]. It has become increasingly evident that leptin may

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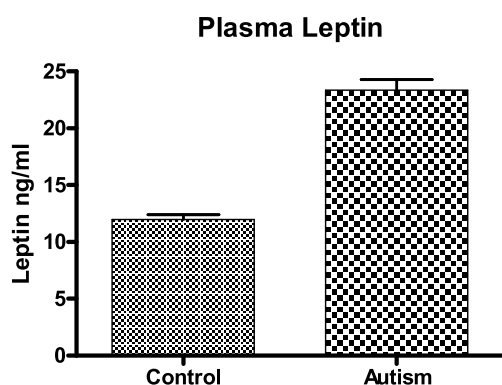
be considered a cytokine-like hormone with pleiotropic actions since it may be involved in the regulation of neuroendocrine functions, immune system, inflammatory response, in addition to playing a role in development [21-23]. Involvement of some of cytokine like hormones and pro-inflammatory adipokines are implicated in the pathophysiology of autism [6, 13, 24] reported. According to literature survey, there is no scientific data available related with leptin in the autistic children of Sultanate of Oman. So, there is a need for scientific and biochemical studies which can explore the cause of autism and helps for early detection of autism in Oman and worldwide. Therefore, the current study was conducted to analyze the levels of plasma leptin in Omani autistic children and find out the link between ASD and leptin.

2. Materials & Methods

Subjects: A total of thirty eight Omani Children, between the age of 3 to 10 years (19 autistic, 15 males and 4 females and their age matched normal children (19, 10 males and 9 females) from 19 different families were recruited for this study. The autistic children were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) (25) American Psychiatric Association, 2000). Ascertainment of ASD diagnosis was further supplemented by completing a standardized and validated Arabic version of the Childhood Autism Rating Scale (CARS) questionnaire. A written consent was obtained from the parents in each individual case, according to the guidelines of the Ethical Committee of Sultan Qaboos University, Oman.

3. Results

The plasma levels of leptin were significantly higher in autistic children as compared to their age matched controls (n=19). All values are mean \pm SD, compared by using unpaired student's t test, $p \leq 0.05$ was considered as significant.



Control	Autism	P value
11.96 \pm 0.45 (N=19)	23.34 \pm 0.94 (N=19)	0.0001 (***)

4. Discussion

Leptin, a peptide hormone mainly secreted by adipose tissue, is involved in the regulation of body weight and energy expenditure at the hypothalamic level [13] and serum leptin is a marker related to fat tissue and body mass index (BMI) in children and adults [18-20]. It may be considered a cytokine-like hormone with pleiotropic actions since it may be involved in the regulation of

neuroendocrine functions, immune system, inflammatory response, in addition to playing a role in development [21-23]. Recent evidences suggest that some of pro-inflammatory cytokines like hormones are implicated in the pathophysiology of autism, which may be due to the abnormal inflammation in autism [6-13, 24].

It was recently hypothesized that the leptin might involve in the clinical manifestations other than development and regulation of body weight and energy expenditure in ASD and other psychiatric disorders such as Rett syndrome [7, 16, 20]. ASD children are predisposed to malnutrition was reported and recent study from our group found that ASD children of Oman at preschool age level showed a general tendency towards malnutrition (19). Recent studies from Japan and Italy suggest that there is a link between the elevated leptin levels might be implicated in the pathophysiology of autism [7, 16] and Rett syndrome [20].

5. Conclusion

Our results suggest that Omani autistic children have significantly elevated levels of leptin when compared with control subjects, which was supported by the previous studies from other countries. And also confirms the hypothesis of elevated levels of leptin might be implicated in pathophysiology of autism and could also be involved in the clinical manifestation of autism. This is the first study related with leptin in autism in Oman and furthermore, this study has the limitation in the sample size (n=19). Identification of biochemical markers related to autism will be advantageous for an early clinical diagnosis and intervention. The exact mechanism is still unclear and further extensive research needed to be done in larger samples with broader age spectrum to find the link between autism and leptin.

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Conflict of Interest- None

6. References

- [1] American Psychiatric Association . Diagnostic and statistical manual of mental disorders, fourth ed., Text Revision (DSM-IV-TR). Washington, DC.2002; p. 70.
- [2] Folstein SE, Rosen-Sheidley B. Genetics of autism: complex aetiology for a heterogeneous disorder. *Nat Rev Genet* 2001;2:943-955.
- [3] Nelson KB, Grether JK, Croen LA. Neuropeptides and neurotrophins in neonatal blood of children with autism or mental retardation. *Ann Neurol*. 2001;49:597-606.
- [4] Vargas DL, Nascimbene C, Krishnan C, Zimmerman AW, Pardo CA. Neuroglial activation and neuroinflammation in the brain of patients with autism. *Ann Neurol*. 2005;57:67-81.
- [5] Zimmerman A, Jyonouchi H, Comi A, Connors S, Milstien S, Varsou A, Heyes M. Cerebrospinal fluid and serum markers of inflammation in autism. *Pediatr Neurol*. 2005;35:195-201.
- [6] Ashwood P, Wakefield AJ. Immune activation of peripheral blood and mucosal CD3+ lymphocyte cytokine profiles in children with autism and gastrointestinal symptoms. *J Neuroimmunol*. 2006;173:126-34
- [7] Licinio J, Alvarado I, Wong ML. Autoimmunity in autism. *Mol Psychiatry*. 2002;7:329.

- [8] Cohly HH, Panja A. Immunological findings in autism. *Int RevNeurobiol.* 2005;71:317-41.
- [9] Pardo CA, Vargas DL, Zimmerman AW. Immunity, neuroglia and neuroinflammation in autism. *Int Rev Psychiatry* 2005;17:485-495.
- [10] Okada K, Hashimoto K, Iwata Y, Nakamura K, Tsujii M, Tsuchiya JK, et al. Decreased serum levels of transforming growth factor-beta1 in patients with autism. *Prog Neuropsychopharmacol Biol Psychiatry.* 2007;31:187-190.
- [11] Tsuchiya JK, Hashimoto K, Iwata Y, TsujiiM, Sekine Y, Sugihara G, et al. Decreased serum levels of platelet-endothelial adhesion molecule (PECAM-1) in subjects with highfunctioning autism: a negative correlation with head circumference at birth. *Biol Psychiatry.* 2007;62:1056-1058.
- [12] Li X, Chauhan A, Sheikh AM, Patil S, Chauhan V, Li XM, et al. Elevated immune response in the brain of autistic patients. *J Neuroimmunol.* 2009;207:111-116.
- [13] Fujita-Shimizu A, Suzuki K, Nakamura K, Miyachi T, Matsuzaki H, Kajizuka M, Shinmura C, Iwata Y, Suda S, Tsuchiya KJ, Matsumoto K, Sugihara G, Iwata K, Yamamoto S, Tsujii M, Sugiyama T, Takei N, Mori N. Decreased serum levels of adiponectin in subjects with autism. *Progress in Neuro-Psychopharm and Biological Psychiatry.* 34: 455-458.
- [14] Bernalova LN, Buxbaum JD. Disease susceptibility gene for autism. *Ann Med* 2003; 3:274-281.
- [15] Santangelo SL, Tsatsanis K. What is known about autism: genes, brain, and behavior. *Am J Pharmacogenomics* 2005; 5:71-92.
- [16] Annual Health Report. Ministry of Health, Sultanate of Oman, 2008.
- [17] Yahya M. Al-Farsi, Marwan M. Al-Sharbaty, Omar A. Al-Farsi, Mohammed S. Al-Shafae, Daniel R. Brooks and Mostafa I. Waly. Prevalence of Autistic Spectrum Disorders in the Sultanate of Oman. *Journal of Autism and Developmental Disorders.* 2011; 41(6) 821-825.
- [18] R. Pilcova, J. Sulcova, M. Hill, P. Bláha, L. Lisá, Leptin levels in obese children: effects of gender, weight reduction and androgens, *Physiol. Res.* 2003; 52: 53-60.
- [19] W.F. Blum, P. Englaro, S. Hanitsch, A. Juul, N.T. Hertel, J. Muller, N.E. Skakkebaek, M.L. Heiman, M. Birkett, A.M. Attanasio, W. Kiess, W. Rascher, Plasma leptin levels in healthy children and adolescents: dependence on body mass index, body fat mass, gender, pubertal stage, and testosterone. *J Clin Endocrinol Metab.* 1997;82: 2904-2910.
- [20] R.V. Considine, J.F. Caro, Leptin and the regulation of body weight. *Int J Biochem Cell Biol.* 1997; 29: 1255-1272.
- [21] S.R. Bornstein, J. Licinio, R. Tauchnitz, L. Engelmann, A.B. Negrão, P. Gold, G.P. Chrousos, Plasma leptin levels are increased in survivors of acute sepsis: associated loss of diurnal rhythm, in cortisol and leptin secretion. *J Clin Endocrinol. Metab.* 1998; 83 : 280-283.
- [22] G. Fantuzzi, R. Faggioni, Leptin in the regulation of immunity, inflammation, and hematopoiesis. *J Leukoc Biol.* 2000; 68: 437-446.
- [23] R.S. Ahima, C.B. Saper, J.S. Flier, J.K. Elmquist, Leptin regulation of neuroendocrine systems, *Front. Neuroendocrinol.* 2000; 21: 263-307.
- [24] Bardi P, de Lalla, A, Ceccatella L, Vanessa, G, Auteri, A, and Hayek, J. Variations of plasma leptin and adiponectin levels in autistic patients. *Neuroscience Letters.* 2010; 479: 54-57.
- [25] American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fourth ed., Text Revision (DSM-IV-TR). Washington. 2000; DC.p.70.