EVALUATION OF MANNOSE BINDING LECTIN LEVEL AND THYROID FUNCTIONS IN PATIENTS WITH HYPERTHYROIDISM DISEASE

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ABSTRACT

Objective: The study aimed to evaluate thyroid function and mannose binding lectin level in Sudanese patients with hyperthyroidisms disease in comparison with apparently healthy controls.

Methods: This is an analytical, hospital based- case control study conducted on 50 Sudanese patients with hyperthyroidism and 100 apparently healthy control groups between the periods from January 2016 to December 2016.

Results: The study showed a highly significant difference (P=0.009) between the means and SD of serum levels of MBL (ng/ml) of the test hyperthyroidism group and the control group (1119.4±137.9 ng/ml) versus (1046.6±133.2 ng/ml), respectively.

Conclusion: There was increased level of serum mannose binding lectin in Hyperthyroidism patients. There was a significant negative correlation between the serum levels of TSH and the serum MBL level in hyperthyroidism patients.. Readability of copy is of paramount importance.

Keywords:
Hyperthyroidism disease
Mannose Binding Lectin (MBL)
Thyroid Stimulating Hormone (TSH)

I. INTRODUCTION

Hyperthyroidism and hypothyroidism are common conditions that have lifelong effects on health [1]. Complications as consequences of thyroidism include cardiovascular disorders such as atrial fibrillation, Coronary heart disease, congestive heart failure, osteoporosis, neuropsychiatric disorders [2, 3] and immunological disorders [4].

Recent studies have indicated the existence of causal links between both the endocrine system and the Immune system with cardiovascular diseases [5-7]. Mannose-binding lectin (MBL) may constitute the connection between these fields.

MBL is a member of the collectin family of proteins found in serum [8, 9]. Human MBL is derived from a single gene on chromosome 10 [10, 11]. Mannose-binding lectin (MBL), also called mannose binding protein (MBP), is a calcium-dependent serum protein that plays a role in the innate immune response by binding to carbohydrates on the surface of a wide range of pathogens (viruses, bacteria, fungi, protozoa) where it can activate the complement system or act directly as an opsonin [11]. Mannose-binding lectin is a member of the collectin family of proteins, which are made in the liver and can opsonize bacteria by tagging the surface of a pathogen to facilitate recognition and ingestion by phagocytes. Collecting's get their name because they have a collagen-like region and a lectin region. Lectins are proteins that bind sugar molecules, usually on the surface of bacteria. The collagen domain interacts with the effector parts of the innate immune system. The MBL2 gene on human chromosome 10 produces MBL, an oligomer of 248-amino acid protein subunits composed of three identical polypeptide chains comprising a cysteine rich region, a collagen-like region, a neck, and a carbohydrate recognition domain. Three MBL polypeptide chains assemble into a biologically active trimmer found in vivo [12].

The normal structural MBL allele is named A, while the common designation for the 3 variant structural alleles B (mutation in codon 54, Gly to ASP), C (mutation in codon 57, Gly to Glu), and D (mutation in codon 52, Arg to Cys) [9,11]. Complement mannan-binding lectin (MBL) deficiency is associated with increased susceptibility to infections and autoimmune diseases. Previous studies suggested that the production of MBL is stimulated by thyroid hormones [13,14]. The levels of these hormones are regulated by the secretion of thyroid stimulating hormone (TSH) from the pituitary gland and TSH secretion is regulated by thyrotropin-releasing hormone (TRH). If the levels of T4 are within the normal ranges, the person is said to be euthyroid. However, if a person has elevated or suppressed TSH levels with normal T4 levels, they may be described as having a subclinical thyroid disorder. Increased or decreased production of thyroid hormones has important consequences on all cells of the body, including the brain and as a result can affect mental health [15].

Concentration of TSH increases with age, requiring age-corrected tests [16]. Hyperthyroidism is the result of excess synthesis and release of thyroid hormones. Thyrotoxicosis is the hyper metabolic state associated with elevated levels of free thyroxine (fT4), free triodothyronine (fT3), or both [17].

Nonspecificchanges due to excessive thyroid hormone include weight loss,nervousness, fatigue, heat intolerance, and rapid heartbeat orpalpitations sometimes associated with atrial fibrillation and high outputcongestive heart failure (CHF) [18]. Thyroid hormones excess cause leftventricular thickening, which is associated with an increased riskof CHF. Thyrotoxicosis has been associated with dilatedcardiomyopathy, right heart failure with pulmonary hypertension, and diastolic dysfunction [19].

The most reliable screening measure of thyroid function is a TSH level. TSH levels usually are suppressed to immeasurable levels (<0.05 mU/L) in thyrotoxicosis. To estimate the degree of thyrotoxicosis, TSH measurement should be combined with serum levels of free T4 (and T3 if T4 levels are normal). Of patients with thyrotoxicosis, 5% have only elevated T3 levels. The most specific autoantibody estimation for autoimmune thyroiditis is an enzyme-linked immune sorbent assay (ELISA) for anti-TPO antibody (thyroperoxidase). The titers usually are significantly elevated in the most common type of hyperthyroidism, Graves' thyrotoxicosis; toxic multi-nodular goiter and toxic adenoma are also associated with elevated thyroid hormones. A significant number of healthy people without active thyroid disease have mildly positive TPO antibodies, thus the test should not be performed for screening purposes. TSI, if elevated, helps establish the diagnosis of Graves' disease. A positive anti thyroglobulin antibody test does not predict the development of thyroid dysfunction and should not be measured [20].

This study aimed to compare the mean level of mannose binding lectin between Sudanese patients with hyperthyroidisms disease and apparently healthy controls.

II. MATERIALS AND METHODS

2.1. Subjects

The study was conducted from January 2016 to December 2016 at Fedail Hospital. A total number of one hundred and fifty subjects were enrolled in this study. 50 Sudanese patients with hyperthyroidism and 100 apparently healthy control groups with adjusted mean age to the patients were enrolled in the study. All participants have No other diseases or infections that may interfere with the levels of MBL. The local ethics committee approved the study. Before participation, volunteers were fully informed of the nature and purpose of the study and written consent was obtained from each.

2.2. Samples

In a sterile condition by using a local antiseptic for skin, 5 ml of venous blood was collected in serum separating gel tubes from patients and controls. The blood samples were separated after complete clotting by centrifugation at 4000 rpm for 5 minutes and serum was collected and stored in tubes at -20°C for measurement of MBL and thyroid hormones.

2.3. Measurement of TSH, FT4 and FT3:

Serum for TSH, FT4 and FT3 was measured by Electro chemiluminesent (ECL) immunoassay on Roche analyzer COBAS e411.

2.4. Measurement of MBL:

Serum for MBL level was measured by ELISA methods using Human MBL kit Hycult Biotech. Test procedure as instructed by the manufacturer was followed. In brief the plate was inactivated using inactivation buffer, duplicate patients samples, calibrator and standard were added into each wells and incubated. The plate was washed and diluted tracer was added and incubated. The plate was washed again and antibody conjugate with streptavidin peroxidase was added to each wells and incubated. Tetramethylbenzidin (TMB) substrate was added and the plate was incubated in the dark. Stop solution was then added and the optical density (OD) was measured using ELISA reader.

III. STATISTICAL ANALYSIS

All statistical analyses were conducted using SPSS version 17.0 for Windows (SPSS, Inc., Chicago, IL), and significant correlation was detected when the P value ≤ to 0.05. Measurement data were expressed as mean ± standard deviation.

IV. RESULTS

The study conducted in Khartoum state during the period from 1st of January 2016 until 30th December 2016 (12 months). This study showed a highly significant difference (P=0.009) between the means ± SD of serum levels of MBL (ng/ml) of the test hyperthyroidism group and the control group (1119.4±137.9 ng/ml) versus (1046.6±133.2 ng/ml), respectively (Table 1). The result revealed a highly significant strong negative correlation between the serum levels of TSH (µIU/ml), and the level of MBL (ng/ml) in the hyperthyroidism group (r = - 0.638, P = 0.000) was seen (figure 1), and revealed a significant positive correlation between the serum levels of FT4 and FT3 (pmol/l), and the level of MBL (ng/ml) in the hyperthyroidism group (r = + 0.66, P = 0.0000) (figure 2, 3) respectively.

Table 1
Comparison of the means of serum levels MBL of the hyperthyroidism group and the control group.

Hyperthyroidisms		Mean ±SD	P Value
MBL [ng/ml]	Case No.= 50	1119.4 ± 137.9	0.009
	Control No.= 100	1046.6± 133.2	

. The table shows the mean ± SD and probability (P) range between brackets.
. t-test or mann-whitney test were used for comparison.
. P value ≤ 0.05 is considered significant.

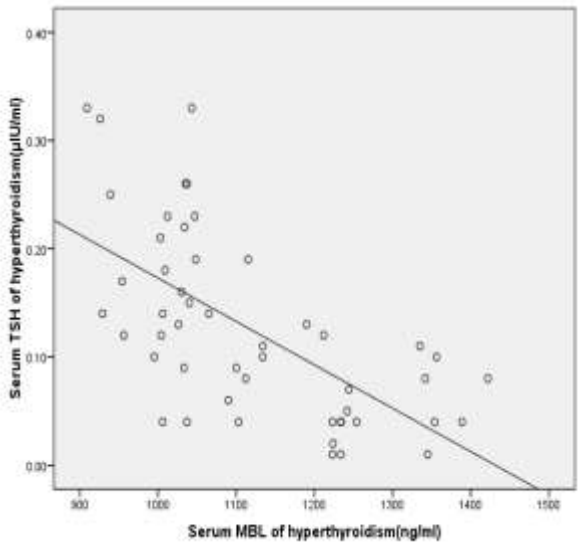

Figure 1 : The relationship between the serum level of MBL (in ng/ml) and the serum levels of TSH in hyperthyroidism group (r=-0.638, P=0.00).

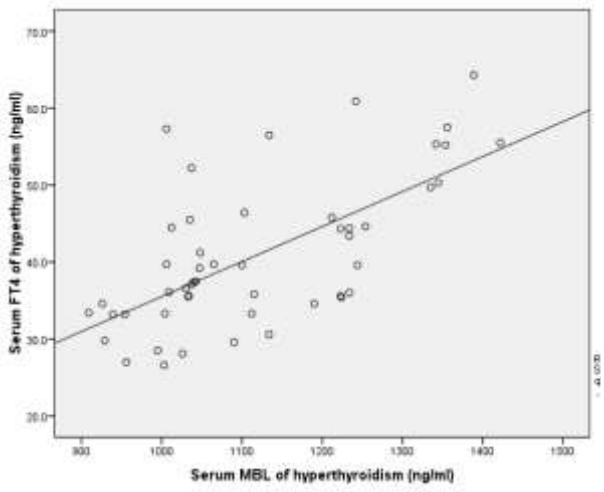

Figure 2 : The relationship between the serum level of MBL (in ng/ml) and the serum levels of T4 in hyperthyroidism group (r=+0.66, P=0.00).

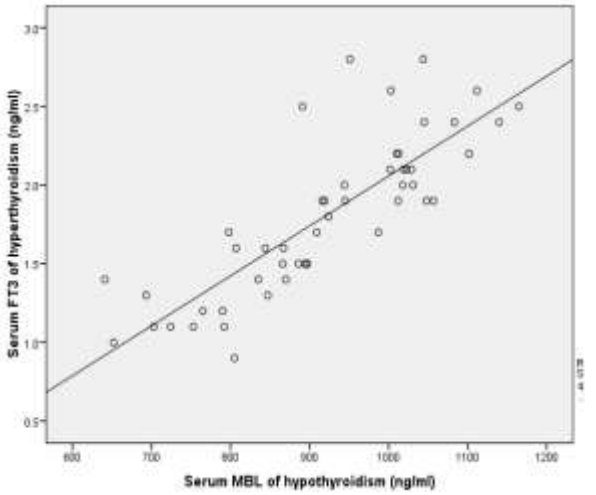

Figure 3 : The relationship between the serum level of MBL (in ng/ml) and the serum levels of T3 in hypothyroidism group (r=+0.84, P=0.00).

V. DISCUSSION

Thyroid disease is recognized as one of the leading causes of morbidity and mortality in the world. A hypothyroid and hyperthyroid disease usually develops in childhood and adolescence. The disease complicated with cardiovascular disease which increases the prognosis of the disease. The facts that thyroid homones may control our body immune response allow us to think about the effects of thyroid hormones on MBL serum levels which by facts affect the complement lectin pathway, in addition to opsonisation – phagocytic activity of the body and finally affecting the natural immune response.

The results of this study showed a significant difference between the means of serum levels of MBL (ng/ml) in the hyperthyroidism test group when compared with the control healthy group (P = 0.009). This result agrees with the result of Riis et al (6) who reported that, thyroid hormone increases mannan-binding lectin levels. While it is agrees with the result of Potlukova et al. [14] who reported that serum levels of MBL tightly correlated with thyroid hormones, leading to strongly increased MBL levels in hyperthyroidism and decreased levels in hypothyroidism respectively.

The results of the current study showed significant, negative correlation between the serum levels of TSH in µIU/ml and the levels of MBL ng/ml in hyperthyroidism groups (r =-0.638, P=0.00). This result in consistent with the result of Riis et al [6] and Potlukova et al [14], who reported that serum levels of MBL tightly correlated with thyroid hormones, leading to strongly increased MBL levels in hyperthyroidism and decreased levels in hypothyroidism. With normalization of the thyroid function during follow-up, MBL levels decreased or increased respectively (r = - 0.34, P = 0.0001)

Our results revealed a significant positive correlation between the serum levels of FT4 and FT3 in pmol/l and the levels of MBL in hyperthyroidism groups (r=+0.66, P=0.00), (r=+0.84, P=0.00) respectively. This result was in consistent with the result of Riis, et al [6] who reported that the thyroid hormone regulates MBL levels and there was a significant correlation between the serum levels of FT3 in pmol/l and the levels of MBL in hypothyroidism and hyperthyroidism (P 0.01). And also in consistent with the result of Potlukova, et al. (14) who reported that serum levels of MBL tightly correlated with thyroid hormones, leading to strongly increased MBL levels in hyperthyroidism and decreased levels in hypothyroidism. With normalization of the thyroid function during follow-up, MBL levels decreased or increased respectively (r = +0.22, P = 0.0123).

VI. CONCLUSION

This study concluded that there patients with hyperthyroidism had increased the levels of MBL compared to healthy group, positive correlation was noted between the levels of T3 and T4 with MBL and negative correlation was noted between the level of TSH and MBL.

Evaluation of mannose binding lectin level and Thyroid functions in patients with hyperthyroidism disease

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