Evaluation of Meteorin-like (Metrnl), Profile Hormones and Other Biochemical Variables in Iraqi Hypothyroidism children

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ABSTRACT

Adipose tissue browning and energy expenditure are regulated by thyroid hormone and Meteorin-like (Metrnl). Given their many comparable modes of action, it would seem necessary to investigate how these chemicals might affect the body in tandem.This research aims to assess Metrnl serum, Profile hormones, and other Biochemical Variables in prepubertal patients with hypothyroidism and pubertal patients with hypothyroidism. Ninety participated in this study. Sixty children with Hypothyroidism were divided into two groups: thirty(G1) pre-pubertal with hypothyroidism, thirty(G2) pubertal with hypothyroidism, and thirty(G3) healthy controls. A highly significant different decrease at (P <0.001) was noted between the study groups for (D3, TT4 and FT4). A highly significant increased (P < 0.001) was noted between G1 and G3, and between G2 and G3, for TSH. Increased significant difference (P < 0.05) was observed for every one of BMI, FBS, TC, TG, non-HDL-C, and LDL-C among the study groups. A significant increase was recorded between study groups for cortisol (P < 0.05), and a highly significant increase was observed for IGF-1 and PTH (P < 0.01). There was a significant difference (P < 0.05) in Meteorin-like (Metrnl) levels among the study groups. Conclusion: It can be concluded that decreased levels of meteorin-like (Metrnl) in pre-pubertal and pubertal hypothyroid patients may have a future impact on the early-onset diseases like diabetes and heart diseases in children and adolescents, because Metrnl has an influential role in enhancing energy expenditure in metabolic diseases. Also profile hormonal imbalance in children with hypothyroidism is a factor affecting metabolism, leading to disease.

Keyword: Hypothyroidism, hormone profile, lipid profile, meteorin-like (Metrnl), pre-pubertal and pubertal.

INTRODUCTION

Hypothyroidism is an endocrine disorder that arises when the thyroid gland produces insufficient amounts of thyroid hormone. Constipation, growth, weight gain, and exhaustion are all possible symptoms of an underactive thyroid in children[1]. Children may have congenital thyroid problems. Timely identification and treatment of thyroid disease is crucial, particularly during the first three years of life, because thyroid hormone plays a significant role in early brain development, growth retardation, and childhood development; hypothyroidism may result in permanent intellectual and motor disabilities[2,3]. The prevalence increases with age, but even the incidence of children is increasing[4].

The frequency of hypothyroidism in children and adolescents can range from 1.7 to 9.5% when subclinical hypothyroidism is taken into account[5]. Meteorin-like protein (METRNL), also referred to as subfatin, interleukin-41, and Meteorin-β, is a recently discovered hormone that regulates metabolism and is considered a potential biomarker of metabolic syndrome[6]. Upon thermogenic activation, METRNL is substantially stated in brown adipose tissue (BAT), and following exercise, it is also highly expressed in skeletal muscle[7]. By inducing alternatively stimulated macrophages in adipose depots. It has been demonstrated that METRNL increases adipose tissue browning, which raises glucose tolerance and energy expenditure[8]. via the peroxisome proliferator-activated receptor (PPAR) and AMP-activated protein kinase (AMPK) pathways. Additionally, METRNL lowers skeletal muscle inflammation and insulin resistance[9].

METRNL and thyroid hormones both contribute to controlling energy expenditure and adipose tissue browning. It becomes necessary to look at how these compounds might affect the body in a reciprocal manner because of their similar mechanisms of action[10]. The levels of specific cytokines that circulate throughout the body, such as neuregulin 4 (Nrg4), irisin, fibroblast growth factor 21 (FGF21), and Metrnl, may be impacted by thyroid issues[11]. The quantities of these cytokines may be influenced by thyroid function, which can have implications of the body's metabolism and overall health[12]. This leads one to assume that TH influences the body's overall metabolism via interacting with cytokines produced by the liver, skeletal muscle, or adipose tissue[13].

This research aims to assess Metrnl serum, Profile hormones, and other Biochemical Variables in prepubertal patients with hypothyroidism and pubertal patients with hypothyroidism.

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MATERIAL AND METHODS

Ninety participated in this study. Sixty children with Hypothyroidism were divided into two groups: thirty (G1) pre-pubertal with hypothyroidism, thirty (G2) pubertal with hypothyroidism, aged between 4 and 17 years, and thirty (G3) healthy controls, aged between 4 and 17 years, from December 2024 to the end of April 2025. Each participant's age, weight, and height were recorded, and their BMI was calculated. MiniVidas measured serum levels of D3, TT3, TT4, FT4, and TSH using Biomerix Kits. Assays conducted on blood samples for the laboratory study included fasting serum glucose (FSG), lipid profiles (Total Cholesterol (TC) triglycerides (TG) high-density lipoprotein (HDL-C); and low-density lipoprotein (LDL-C)), non-HDL- C was calculation by (TC-HDL-C).

Hormone profiles (serum cortisol, Adrenocorticotropic Hormone (ACTH), insulin-like growth factor-1 (IGF-1), and parathyroid hormone (PTH)) were measured using the cobas e411. An ELISA kit was used to calculate the amount of Meteorin-like protein (METRNL) catalog (EL013718HU).

Excel was used to do the statistical analysis. The means and standard deviation (SD) of the data are expressed. 'A P-value was considered significant if it was less than 0.05, and highly significant if it was less than 0.01[14,15].

RESULTS

The clinical features and biochemical parameters of children are given in Table 1. demonstrating significant variations among the pre-pubertal G1, pubertal G2, and healthy G3 groups. A highly substantial distinct decreased at (P <0.001) was noted between (G_1 vs $G_{3)}$ and (G_2 vs G_3) for (D3, TT4 and FT4), and a highly significant different increased at (P <0.001) was observed between (G_1 vs G_3)and (G_2 vs G_3) for TSH, while a different in significant increase (P <0.05) for each of BMI, FBS, TC, TG, non-HDL-C, and LDL-C among study groups. Additionally, statistical values had been suggested; There are no appreciable differences between the groups for either TT3 or HDL-C.

In Table 2, a significant increase was shown between G1 vs G2, G1 vs G3, and G2 vs G3 for cortisol at (P <0.05), and a highly significant difference at (P <0.01) for IGF-1 and PTH. At the same time, For ACTH, there were no discernible differences between the research groups.

The values of Meteorin-like (Metrnl) levels were expressed in Table 3, where it was noted that a significant difference at (P< 0.05) among the groups G_1, G_2, and G_3.

The optimum cut-off value for Meteorin-like (Metrnl) is determined to be Prepubertal and Pubertal with a sensitivity of 100.0% and

Table 1. Clinical Parameters of study groups (prepubertal with Hypothyroidism patients, pubertal with Hypothyroidism patients, and Control).

Parameter	G1 Mean ± SD N (30)	G2 Mean ± SD N (30)	G3 Mean ± SD N (30)	P-Value (G1 vs G2)	P-Value (G1vs G3)	P-Value (G2vs G3)
Sex (Male/Female)	(14/16)	(17/13)	(15/15)	/	/	/
BMI (kg/m2)	21.77 ±2.71	27.77±2.58	24.77±2.35	0.05	0.05	0.05
FBS (mg/dl)	86.27±4.94	96.87±8.58	72.87±4.25	0.05	0.05	0.05
TC(mg/dl)	154.77±37.07	183.57±13.11	126.2±13.28	0.05	0.05	0.05
TG (mg/dl)	98.93±7.70	112.33±9.44	70.87±12.50	0.05	0.05	0.05
HDL-C (mg/dl)	42.77 ±8.76	41.3±3.03	53±5.66	NS	NS	NS
non- HDL-C (mg/dl)	73.22 ±14.51	95.52 ±18.23	62.26 ±13.2	0.05	0.05	0.05
LDL-C (mg/dl)	55.62 ±14.67	77.31 ±24.31	66.8 ±13.7	0.05	0.05	0.05
D3 (ng/ml)	8.79 ±3.36	10.23 ±2.45	22.77 ±1.66	0.01	0.001	0.001
TT3 (nMole\L)	1.16±0.39	1.04±0.31	2.02±0.29	NS	NS	NS
TT4 (nMole\L)	68.3±13.05	65.57±8.64	92.17±17.04	NS	0.01	0.01
FT4 (nMole\L)	6.25±1.31	6.75±2.74	12.51±2.58	NS	0.01	0.01
TSH (uU/L)	12.47±5.31	13.95±6.90	2.56±2.31	NS	0.01	0.01

P-value is significant at P<0.05, and high significant at P<0.01 and at p<0.001. prepubertal with Hypothyroidism patients (G_1) vs pubertal with Hypothyroidism patients (G_2), prepubertal with Hypothyroidism patients (G_1) vs Control (G_3 pubertal with Hypothyroidism patients (G_2) vs Control (G_3).

Table 2. Profile hormones among study group (prepubertal with Hypothyroidism patients, pubertal with Hypothyroidism patients, and Control).

	Prepubertal patients with hypothyroidism (G1) Mean ± SD N (30)	Pubertal patients with Hypothyroidism (G2) Mean ± SD N (30)	Control (G3) Mean ± SD N (30)	p-value (G1 vs G2)	p-value (G1 vs G3)	p-value (G2 vs G3)
ACTH (Pmol/L)	7.45± 3.94	7.28±3.61	5.67±1.68	NS	NS	NS
Cortisol (ug/dl)	12.47±5.31	14.10±2.29	9.17±2.09	0.05	0.05	0.05
IGF-1 (ng/ml)	85.26±20.51	111.06±36.52	135.23±2.31	0.01	0.01	0.01
PTH (ng/ml)	63.03 ±13.0	68.56±8.63	46.26±3.40	0.05	0.01	0.01

P-value is significant at P<0.05, and high significant at P<0.01 and at p<0.001. prepubertal with Hypothyroidism patients (G_1) vs pubertal with Hypothyroidism patients (G_2), prepubertal with Hypothyroidism patients (G_1) vs Control (G_3 pubertal with Hypothyroidism patients (G_2) vs Control (G_3).

Table 3. Meteorin-like (Metrnl) levels among the study groups (prepubertal with Hypothyroidism patients, pubertal with Hypothyroidism patients, and Control).

Parameter	G1 Mean± SD N (30)	G2 Mean± SD N (30)	G3 Mean± SD N (30)	p-value (G1 vs G2)	p-value (G1 vs G3)	p-value (G2 vs G3)
Meteorin-like (Metrnl) levels (ng/ml)	2.35±1.11	0.79±1.08	4.12±1.24	0.05	0.05	0.05

P-value is significant at P<0.05, and high significant at P<0.01 and at p<0.001. prepubertal with Hypothyroidism patients (G_1) vs pubertal with Hypothyroidism patients (G_2), prepubertal with Hypothyroidism patients (G_1) vs Control (G_3 pubertal with Hypothyroidism patients (G_2) vs Control (G_3).

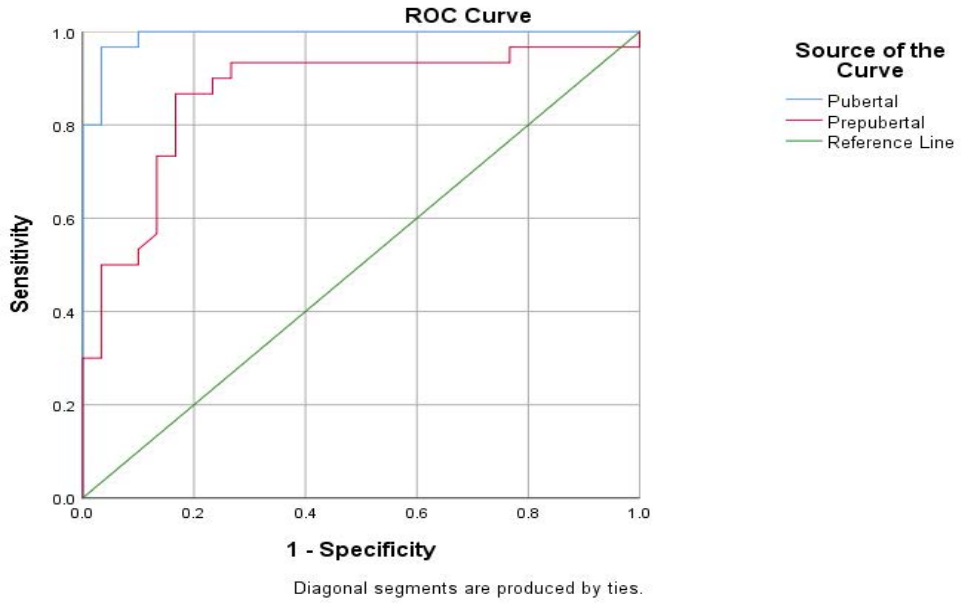

Figure 1. The accuracy of the diagnosis using the Receiver Operating Characteristic (ROC) curve of serum Meteorin-like (Metrnl) levels in hypothyroidism disease between prepubertal and pubertal.

a specificity of 100.0%. This suggests a high level of accuracy in uniqueness between the sets. These findings are graphically represented in Table 4 and Figure 1, which visually illustrate the robustness and efficacy of the Meteorin-like (Metrnl) test across the groups.

Table 4. The Meteorin-like (Metrnl) levels' performance criterion and area under the ROC curve for discrimination between the pubertal, prepubertal, and control groups.

	Pubertal	Prepubertal
AUC	0.992	0.876
Cut off	1299	1024
Sensitivity (%)	100	78
Specificity (%)	100	68
PPV (%)	100	85.8
NPV (%)	98	75
Accuracy (%)	96	95

DISCUSSION

Adipokines are a category of bioactive peptides and proteins that are expressed and released by adipose tissue, making it a highly active endocrine organ. Critical physiological processes, including insulin sensitivity, cardiovascular health, immunological response, inflammation, and glucose and lipid metabolism, are regulated by these adipokines[16]. The body's largest endocrine organ is adipose tissue, adipokines releases that are involved in several signaling pathways and regulate homeostasis. The interaction between adipose tissue and systemic lipid and glucose metabolism is believed to be explained by adipokines[17]. Meteorin-like (Metrnl) is an adipokine that was recently found. By promoting the insulin-induced phosphorylation of AKT, Metrnl can improve the action of insulin in adipose tissue[18,19]. Energy metabolism is another area in which thyroid hormones have a significant impact[20].

Overweight and obesity in children are essential promoters of chronic and lipid buildup and lo grade inflammatory conditions in children with hypothyroidism[19]. According to Löffler et al.[22], children who are obese have higher levels of Metrnl in their adipocytes than children who are not obese. In addition to promoting adipocyte development by upregulating PPARγ and increasing adipocyte lipid accumulation, these interactions with adipose tissue dynamics point to a possible link between Metrnl and obesity[23].

In this study, Metrnl was shown a significant lower in children (prepubertal) and adolescents (pubertal) when compared with control groups. These findings concur with those reported by Moradi et al[24]. Patients with hypothyroidism had significantly lower levels of circulating Metrnl. Moreover, hypothyroidism was independently linked to lower serum Metrnl levels. These results are in agreement with[25,26] and shed light on the therapeutic implications of Metrnl in individuals with hypothyroidism. The β-oxidation of fatty acids, lipolysis, and cholesterol synthesis are all regulated by thyroid hormone (TH). Additionally, by promoting the transcription of the LDL receptor gene, TH promotes the transporting cholesterol in reverse to the liver for elimination.

Additionally, patients with thyroid disorders showed enhanced lipid oxidation and skeletal muscle metabolism[27]. We found in this study that there were substantial differences in TC, LDL-C, and TG among the study groups, and that a correlation existed between TC, TG, and LDL-C and MERTRNL. According to earlier research, a lack of adipose tissue MTRNL worsened hypertriglyceridemia[28,29]. It also caused an increase in TG production, which reduced TG buildup in hepatocytes. Furthermore, we found that Metrnl uses an AMPK-dependent mechanism to positively regulate fatty acid oxidation (FAO) in the liver and skeletal muscle.

These findings have significant ramifications for the systemic control levels of TG and demonstrate the surprising function of Metrnl in maintaining hepatic lipid[30]. In skeletal muscle, Metrnl therapy decreased fatty acid oxidation and inflammation brought on by AMPK or PPAR signaling[28]. Thus, the effects of TH on lipid metabolism, thermogenesis, and energy homeostasis may be partially mediated by increased circulating Metrnl levels in patients with thyroid disorders[26]. Although they are distinct disorders, hypothyroidism and adrenal insufficiency may have a shared origin. Adrenal insufficiency and autoimmune thyroid illness are two conditions that can result from autoimmune disease, which frequently affects many organs. There was no discernible group difference in ACTH among the study group prepubertal with hypothyroidism patients, pubertal with hypothyroidism patients, and controls. This is in agreement with other studies[31,32]. Cortisol levels were significantly increased in pubertal and prepubertal children with hypothyroidism when compared with control groups, which is consistent with the findings of a previous similar study[31,34]. Normal thyroid epithelial cell function depends on several factors. These include TSH and IGF-I, both of which are essential for the synthesis of thyroid hormones. Tyrosine kinase receptors are crucial in the interaction between TSH and IFG-1. Additionally, IGF-I continuously improved TSH effects in thyroid epithelial cells and demonstrated cooperation in terms of tyrosine kinase activation and cell proliferation[35].

Elevated parathyroid hormone (PTH) levels in children with hypothyroidism may be due to several interrelated causes related to the body's functions and compensation in the case of a thyroid disorder. When children and adolescents suffer from hypothyroidism at the same time as low levels of vitamin D3 and a parathyroid hormone (PTH) disorder, this constitutes a complex condition that may lead to disturbances in mineral and bone balance, and requires careful follow-up and treatment[36], also thyroid hormones are deficient, the body reacts in various ways to compensate. This can lead to disturbances in calcium and phosphate levels, which can stimulate the parathyroid glands to produce more parathyroid hormone [37].

Finally, Metrnl was regarded as an adipokine and attracted considerable interest from scientists because of its essential roles in preserving the balance of glucose metabolism, enhancing insulin sensitivity, encouraging the browning of adipose tissue, and raising energy expenditure in metabolic disorders[37]. Adipose tissue is one of TH's primary targets. By upregulating the expression of UCP-1 and PGC, thyroid hormone stimulates adaptive thermogenesis in brown adipocytes. TH also encourages the browning/beiging of WAT by elevating mitochondrial biogenesis and UCP-1 expression[37].

CONCLUSION

It can be concluded that decreased levels of meteorin-like (Metrnl) in pre-pubertal and pubertal hypothyroid patients may have a future impact on the onset of early-onset diseases like diabetes and heart diseases in children and adolescents, because Metrnl has an influential role in enhancing energy expenditure in metabolic diseases. Also, the profile of hormonal imbalance in children with hypothyroidism is a factor affecting metabolism, leading to the disease.

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Potential Conflicts of Interest: None

Competing Interest: None

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