# Angiopoietin-like protein 5: a potential culprit of cardio-metabolic risk in Egyptian obese children

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**Background**
Obesity has recently been identified as a risk factor for coronavirus disease-19. There is a significant correlation between obesity rates with metabolic syndrome and coronavirus disease-19 in children worldwide. Owing to the high expression in adipose tissue, angiopoietin-like protein 5 (ANGPTL5) might be assumed to have a broad range of physiological processes in lipid, glucose homeostasis, and inflammatory responses.
**Objective**
To examine the association between childhood obesity and plasma ANGPTL5 levels in an attempt to demonstrate the probable relationships of plasma levels of ANGPTL5 with unacylated ghrelin and obestatin and its relevance to metabolic parameters in obese versus normal-weight children and adolescents.
**Patients and methods**
A total of 90 children between 5 and 15 years of age were randomly enrolled in this cross-sectional case–control study. They were classified into obese patients ($n$=45) and nonobese controls ($n$=45). BMI for age was calculated following WHO guidelines. Serum levels of ANGPTL5, obestatin, and unacylated ghrelin were measured and correlated with the anthropometric measurements and biochemical markers of metabolic syndrome.
**Results**
A highly significant positive correlation was observed between the serum level of ANGPTL5 and the weight $z$ score. Moreover, a significant positive correlation between ANGPTL5 and the investigated diabetic parameters (glucose, insulin, and homeostasis model assessment for insulin resistance) and high sensitivity C-reactive protein was detected. The increased weight in children was associated with a higher level of ANGPTL5 in parallel with the observed elevated insulin resistance.
**Conclusion**
ANGPTL5 might be considered a promising sensitive assessment biomarker to be applied for early diagnosis and prognosis of obese children with a high risk of cardio-metabolic diseases.

**Keywords:**
angiopoietin-like protein 5, cardio-metabolic diseases, metabolic parameters, obesity

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## Introduction

One-third of the world's population has obesity. According to an analysis of relevant data from the WHO, in 2016, more than 1.9 billion people and 400 million children and adolescents were overweight or obese [1]. The well-known consequences of obesity are noncommunicable diseases like cardiovascular disease and type 2 diabetes. Furthermore, it is responsible for more than 40 million deaths annually worldwide [2]. Obesity has recently been identified as a risk factor for coronavirus disease-19. The Centers for Disease Control and Prevention in the United States found that four out of five hospitalized patients with coronavirus disease-19 in the United States were either overweight or obese [3].

High-income countries remained at the epidemic's center, while similar patterns emerged in many low-income and middle-income countries [4]. Millions of individuals will risk major health problems if early intervention and fast action are not implemented. Obesity is a complicated disorder affecting people of all ages and socioeconomic backgrounds, with major social and psychological implications that threat to overrun developing and developed nations. Furthermore, the prevalence of metabolic syndrome has become one of the most rising general health crises

worldwide. It is manifested clinically by an increase in weight and laboratory by dyslipidemia, hyperglycemia, and hypertension [5]. Dyslipidemia is the most important factor in several health problems, such as obesity, diabetes mellitus, and cardio-metabolic syndrome. Numerous biomarkers have been frequently applied in clinical diagnosis, evaluation, and prognosis. Therefore, the researchers must apply sensitive and specific biomarkers to promote primary and secondary intervention strategies for metabolic syndrome [6]. Newly found is a family of secreted glycoproteins called angiopoietin-like proteins (ANGPTLs), with the designations ANGPTL1 through ANGPTL8 [7]. ANGPTL1 through ANGPTL7 have comparable biological structures and opposing actions [8]. ANGPTL5 has been the target of numerous investigations, and it has been found to have a variety of physiological roles in the metabolism of lipids and glucose, in addition to the inflammatory process as being expressed in adipose tissue [9]. In contrast to other ANGPTL proteins, the effect of ANGPTL5 on the occurrence of metabolic diseases and obesity is still unknown.

The imbalance between oxidants and antioxidants in either obesity or overweight had resulted in the noticed oxidative stress [10]. Ghrelin and obestatin are hormones with an orexigenic property and are mainly secreted in the stomach. It has been demonstrated that they improve the antioxidant defense. Both ghrelin and obestatin have been linked to obesity-related insulin resistance in metabolic syndrome [7]. Ghrelin is a 28-amino acid hormone mainly produced by the stomach and pancreas. It increases appetite and, through the action of its receptor, is a powerful growth hormone stimulator [11]. Furthermore, there are two types of ghrelin: acylated and desacyl ghrelin. They gradually rise in the plasma. Even though some of its effects are debatable and its receptor is unidentified, biological activities of desacyl ghrelin have been documented, including gastric motility [12], adiposity, and glucose metabolism [13]. Obestatin is chemically composed of a 23-amino acid peptide produced via the posttranslational modification of the protein precursor that generates ghrelin. According to scientific-based evidence, the effect of obestatin on food consumption is controversial to ghrelin [14]. Ghrelin might have a crucial role in adipogenesis and energy storage in adipose tissue [15], suggesting the role of ghrelin as an 'energy saving or storage' effect on adipose tissue and suppressing adipogenesis by stimulating cell proliferation in the adipocyte cell [16]. Ghrelin also inhibits the expression of adiponectin.

As lipid peroxidation might be a sensitive indicator of any suspected oxidative stress in clinical disorders [17], the relationship between ghrelin, obestatin, and lipid peroxide was also evaluated. To our knowledge, there are limited research papers concerning laboratory monitoring of ANGPTL5 in obese children. With this, we aimed to evaluate the association between childhood obesity and serum level of ANGPTL5 by examining the probable relationships of plasma level of ANGPTL5 with unacylated ghrelin and obestatin and its relevance to metabolic parameters in obese versus normal-weight children and adolescents.

## Patients and methods

### Study populations

A total of 90 children between 5 and 15 years of age were chosen randomly in this cross-sectional case–control study from the follow-up clinics of Child Health and Complementary Medicine, Medical & Scientific Centre of Excellence, National Research Center. They were classified into obese patients ($n$=45) and nonobese patients (control) ($n$=45). A full history, anthropometric measurements, and clinical examination were carried out for all participants. The participants did not change their normal eating habits or underwent any nutritional intervention and followed their routine lifestyle. Children with genetic or endocrine obesity, those with prolonged debilitating conditions, or those who were prescribed medications influencing a person's blood pressure, lipids, or blood glucose were excluded.

The BMI percentiles were performed according to the guidelines of the National Center of Health and Statistics; the remarked percentiles on growth charts above 95th were considered obese children. On the contrary, participants with BMI in the 5th to 85th percentiles served as controls. A seca scale (Seca, Hamburg, Germany) was used when measuring weight, whereas on measuring height, a Seca 225 stadiometer was used. They were calibrated to within 0.1 kg and 0.1 cm, respectively, and used considering recommended instructions [18]. Following the International Biological Program's recommendations, the mean of three consecutive readings was used for each measurement [19]. BMI for age was calculated using the AnthroPlus software for personal computers following WHO guidelines [20]. All BMI $z$ score calculations, height-for-age ratio, and weight-for-age ratio followed the most recent WHO guidelines [21]. Waist and hip circumference, waist/hip ratio, and blood pressure had been also determined.

### Biochemical measurements

Following an overnight fast of 8–12 h, a 3-ml venous blood sample was taken in the morning and allowed to clot in a plain tube. After centrifuging for 10 min at 5000 rpm, the serum was separated; it was kept at −20°C until the assays could be performed. Serum ANGPTL5 level was measured by using a commercial enzyme-linked immunosorbent assay (ELISA) kit produced by AFG Bioscience Company, 1818 Skokie Boulevard Northbrook, IL 60062 USA, Catalog number: EK700028, with optimal dilution 1 : 25. Commercial ELISA kits manufactured by Glory Science Co. Ltd (Del Rio, Texas, USA), was used to determine the serum's obestatin and unacylated ghrelin concentrations. Obestatin and Ghrelin kit catalog numbers were 17526 and 95622. Quantitative analysis of serum insulin concentration was performed using a commercially available ELISA kit (Chemux Bioscience Inc., USA). The assay's detection limit was found to be 2.0 IU/ml. A bio-diagnostic kit was used to enzymatically colormetrically quantify fasting serum glucose, total cholesterol, and triglycerides (TG) using a Biosystems BTS-302 photometer (Egypt) [22]. To assess high-density lipoprotein-cholesterol, we used the precipitation end point method; we collected the supernatant and then followed the same procedure as we did for total cholesterol. The Friedewald method was used to determine low-density lipoprotein-cholesterol levels in the serum [low-density lipoprotein-cholesterol=total cholesterol–high-density lipoprotein-cholesterol–(TG/5)] [23]. With the use of the homeostasis model assessment for insulin resistance (HOMA-IR), insulin resistance was determined by the following formula: [fasting insulin (mIU/ml) fasting glucose (mg/dl)/405]. If HOMA-IR was more than 3.16, it was considered insulin resistance [24].

### Ethical considerations

Written illustrative consent form was signed by all parents/caregivers of the participating children. This study was performed according to the ethical rules for medical research involving human participants of the Declaration of Helsinki (1964). The study received approval from the Ethics Committee, National Research Center. An ethical approval number was obtained.

### Statistical analysis

Data were gathered, authenticated, encoded, and analyzed using the Statistical Package for the Social Sciences (SPSS), version 22. (SSPS Inc., Philadelphia, Pennsylvania, USA). Descriptive statistics were used to assess the baseline characteristics of the research population. The mean and SD were presented for continuous variables. The independent *t* test was used to compare quantitative data between the two groups. Pearson's correlation analysis was used when looking at the relation between two quantitative variables within the same group. The variables that had the greatest effect on inflammatory mediators between cases were identified using multiple linear regressions. Two-tailed *P* values were used for this study.

## Results

Anthropometric and blood pressure values are outlined in Table 1. Obese children were shown to have a significantly higher serum level of ANGPTL5 and unacylated ghrelin compared with the control group ($P<0.001$) (Fig. 1).

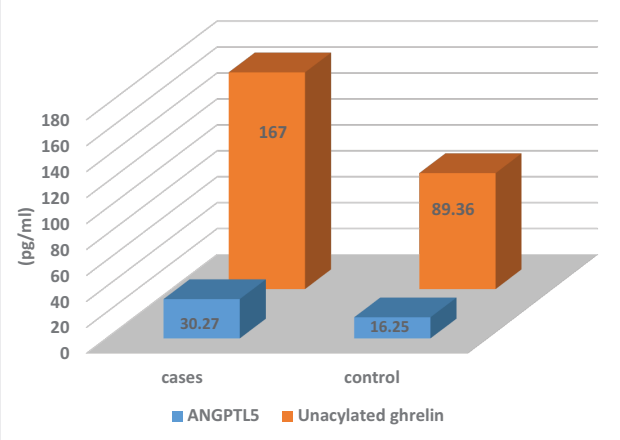
On the contrary, the serum concentration of obestatin was markedly diminished in obese versus the controls, as shown in Table 2. A highly significant positive relationship was observed between ANGPTL5 serum levels, weight *z* score, and diastolic blood pressure. ($r=0.434$, $P=0.017$, and $r=0.401$, $P=0.028$, respectively). The hormonal biomarkers in obese patients, such as unacylated ghrelin, showed a significant positive relationship with both skin-fold

**Table 1 Anthropometric and blood pressure values in obese children and controls**

| Variables | Obese children (*N*=45) (mean±SD) | Control group (*N*=45) (mean±SD) | *P* value |
|---|---|---|---|
| Age (years) | 15.56±1.94 | 14.92±2.72 | 0.135 |
| Wt (*z* score) | 2.39±1.02 | 0.87±0.57 | <0.001** |
| Ht (*z* score) | −0.98±1.02 | −0.91±1.34 | 0.816 |
| BMI | 35.52±8.69 | 25.56±1.86 | <0.001** |
| BMI (*z* score) | 2.78±0.81 | 1.49±0.4 | <0.001** |
| Waist circumference | 99.37±17.45 | 64.7±10.9 | <0.001** |
| Hip circumference | 113.74±18.91 | 82.5±14.4 | <0.001** |
| Waist/hip ratio | 0.89±0.08 | 0.74±0.2 | 0.04* |
| Skin-fold thickness(mm) | 20.6±4.78 | 10.10±2.58 | <0.001** |
| Mid-arm circumference | 34.09±8.4 | 19.6±4.7 | <0.001** |
| Systolic blood pressure | 0.4234±1.07529 | 0.1258 ±0.87520 | 0.178 |
| Diastolic blood pressure | 0.7140±0.81049 | 0.3348±0.3348 | 0.013 |

Ht *z* score, height to age according to the *z* score; Wt *z* score, weight to age according to *z* score. **P* value less than or equal to 0.05=significantly different. ***P* value less than 0.01=highly significant different.

**Figure 1**




Comparison between case and control regarding serum levels of ANGPTL5 and unacylated ghrelin.

**Table 2 Laboratory investigations for obese children and controls**

| Variables | Obese children (*N*=45) (mean±SD) | Control group (*N*=45) (mean±SD) | *P* value |
|---|---|---|---|
| ANGPTL5 (pg/ml) | 30.27±6.56 | 16.25±2.95 | <0.001** |
| Unacylated ghrelin (pg/ml) | 167.23±24.47 | 89.36±31.11 | <0.001** |
| Obestatin (ng/l) | 137.47±18.63 | 222.75±78.0 | <0.001** |
| Insulin (μIU/ml) | 15.58±10.56 | 37.57±7.8 | <0.001** |
| Glucose (mg/dl) | 99.93±17.48 | 55.18±6.59 | <0.001** |
| HOMA-IR | 4.33±3.25 | 1.82±2.46 | 0.002** |
| Total cholesterol (mg/dl) | 196.9±44.07 | 109.92±12.86 | <0.001** |
| Triglycerides (mg/dl) | 114.49±42.01 | 69.86±12.2 | <0.001** |
| HDL-cholesterol (mg/dl) | 43.53±9.16 | 93.93±11.25 | <0.001** |
| LDL-cholesterol (mg/dl) | 120.33±29.33 | 87.11±22.54 | <0.001** |
| Hs-CRP | 4.97±2.34 | 2.79±1.23 | <0.001** |
| Lipid peroxide | 32.87±16.11 | 22.88±11.65 | 0.009 |

ANGPTL5, angiopoietin-like protein 5; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment for insulin resistance; Hs-CRP, high sensitivity C-reactive protein. ***P* value less than 0.01=highly significant difference.

thickness and MAC, but the serum level of obestatin showed a significant negative correlation with the weight *z* score (Table 3). The correlation between the measured biochemical parameter is outlined in Table 4. The correlation analysis revealed a positive relationship between serum level of ANGPTL5 and unacylated ghrelin and a significant negative relationship with obestatin ($r$=0.572, $P$=0.001, and $r$=−0.620, $P$=0.000, respectively) (Table 4). Moreover, the blood concentration of ANGPTL5 was found to be significantly positively linked with the serum concentration of glucose, insulin, HOMA-IR (Fig. 2), and high sensitivity C-reactive protein (Hs-CRP). HOMA-IR showed a significant positive correlation with unacylated ghrelin and a negative correlation with obestatin. Moreover, glucose was significantly positively correlated only with ANGPTL5 ($r$=0.401, $P$=0.028).

## Discussion

Childhood obesity is a global pandemic. It is considered a major public health challenge regarding detection, prevention, and treatment that might reduce the future risk of metabolic disorders [2]. A family of eight proteins called ANGPTL is thought to play a special and significant function in several metabolic illnesses. One of these, ANGPTL5, is thought to control how TGs are metabolized and is elevated in those with diabetes and obesity. Although ANGPTL5 was mostly detected in adipose tissue, it was also found in some organs, including the skin, ovaries, testis, and heart, but at lesser levels [13].

The best that we can state is that the current study demonstrated for the first time the correlation between circulating plasma levels of ANGPTL5 and unacylated ghrelin and obestatin in diagnosed obese children. We also evaluated the long-term alterations in the plasma lipid panel in obese children. The primary outcome was a striking rise in the levels of circulating plasma ANGPTL5 in obese children versus nonobese ones, associated with a positive correlation with weight *z* score and diastolic blood pressure as well as Hs-CRP. In contrast to the lipid profile, fasting plasma glucose, fasting insulin, and HOMA of insulin resistance were all significantly positively linked with serum ANGPTL5 in the obese group. Thus, ANGPTL5 has been shown to affect the metabolic pathway of glucose metabolism.

This was in line with Liu *et al.* [25], who noticed that in patients with metabolic syndrome, plasma ANGPTL5 was more closely associated with abnormalities in glucose and insulin metabolism than lipid metabolism. As a result, this suggests that it is possible to monitor the involvement of ANGPTL5 and the effect on insulin resistance and sensitivity, which will provide thorough information on glucose metabolism throughout the development of metabolic syndrome.

However, current findings found a relationship between impaired glucose tolerance and elevated

**Table 3 Correlations between studied hormonal biomarkers and anthropometric measures in cases**

| Parameters | Unacylated ghrelin (pg/ml) | | Obestatin (ng/l) | | ANGPTL5 (pg/ml) | |
|---|---|---|---|---|---|---|
| | *r* | *P* | *r* | *P* | *r* | *P* |
| Wt (*z* score) | 0.235 | 0.211 | –0.462* | 0.010* | 0.434* | 0.017* |
| Ht (*z* score) | 0.045 | 0.814 | –0.081 | 0.670 | 0.067 | 0.726 |
| BMI (*z* score) | –0.007 | 0.970 | –0.119 | 0.532 | 0.071 | 0.711 |
| Waist circumference | 0.252 | 0.179 | 0.044 | 0.816 | 0.187 | 0.322 |
| Hip circumference | 0.314 | 0.092 | –0.113 | 0.552 | 0.181 | 0.34 |
| Waist-hip ratio | –0.107 | 0.575 | 0.107 | 0.574 | –0.046 | 0.809 |
| Skin-fold thickness | 0.515** | 0.004** | –0.276 | 0.140 | 0.261 | 0.164 |
| Mid-arm circumference | 0.367* | 0.046* | –0.334 | 0.071 | 0.404* | 0.027 |
| Systolic blood pressure | 0.079 | 0.677 | –0.006 | 0.976 | 0.183 | 0.333 |
| Diastolic blood pressure | 0.206 | 0.276 | –0.089 | 0.639 | 0.401* | 0.028* |

ANGPTL5, angiopoietin-like protein 5; Ht *z* score, height to age according to the *z* score; Wt *z* score, weight to age according to *z* score. **At 0.01 level (2-tailed)=correlation is significant. *At 0.05 level (2-tailed)=correlation is significant.

**Table 4 The comparative correlations among the studied hormonal biomarkers with the resulted other biochemical measures in cases**

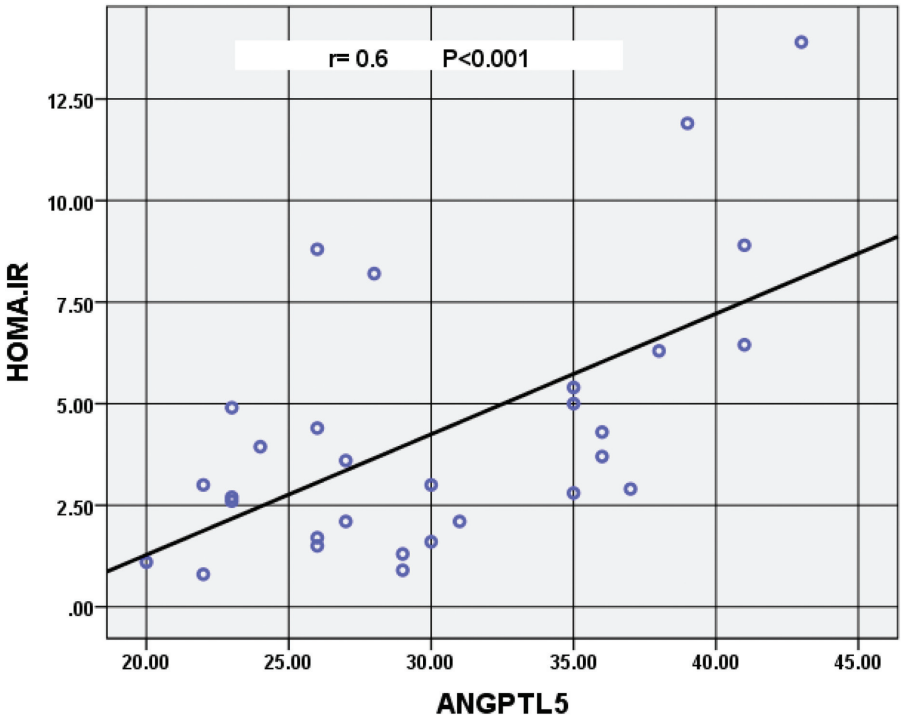
| Laboratory investigated | Unacylated ghrelin (pg/ml) | | Obestatin (ng/l) | | ANGPTL5 (pg/ml) | |
|---|---|---|---|---|---|---|
| Unacylated ghrelin (pg/ml) | | | –0.538** | 0.002** | 0.572** | 0.001** |
| Obestatin (ng/l) | –0.538** | 0.002** | | | –0.620 | 0.000** |
| ANGPTL5 | 0.572** | 0.001** | –0.620** | 0.000** | | |
| Glucose | 0.260 | 0.166 | –0.278 | 0.136 | 0.401* | 0.028* |
| Insulin | 0.480** | 0.007** | –0.355 | 0.054 | 0.473** | 0.008** |
| HOMA-IR | 0.395* | 0.031* | –0.444* | 0.014* | 0.600** | 0.000** |
| Total cholesterol (mg/dl) | –0.114 | 0.549 | –0.145 | 0.446 | –0.077 | 0.684 |
| Triglycerides (mg/dl) | 0.102 | 0.591 | –0.098 | 0.605 | –0.046 | 0.809 |
| HDL-cholesterol (mg/dl) | 0.221 | 0.240 | –0.341 | 0.065 | 0.293 | 0.116 |
| LDL-cholesterol (mg/dl) | 0.196 | 0.300 | –0.243 | 0.196 | 0.211 | 0.264 |
| Hs-CRP | 0.243 | 0.195 | –0.303 | 0.103 | 0.522** | 0.003** |
| Lipid peroxide | 0.597** | 0.001** | –0.408* | 0.025* | 0.597** | 0.001 |

ANGPTL5, angiopoietin-like protein 5; HDL, high-density lipoprotein; HOMA-IR, homeostasis model assessment for insulin resistance; Hs-CRP, high sensitivity C-reactive protein. **Significant correlation at the level of 0.01 (2-tailed). *Significant correlation at the 0.05 level (2-tailed).

ANGPTL4 levels [26]. It has been demonstrated that ANGPTL4 enhances lipolysis [27]. A research paper reported that the elevated level of ANGPTL4 highly influences the hydrolysis of triacylglycerols, resulting in the release of FFA into the bloodstream [28]; this might indicate that the relationship between ANGPTL4 and FFA levels is stronger than the relationship with ANGPTL5 plasma levels.

In support of our result, Hammad *et al.* [29] reported a significant increase in plasma levels of ANGPTL5 and Hs-CRP in obese patients versus normal-weight and overweight ones. Obesity was considered a minimal stage of inflammatory disorder in which various oxidative stress biomarkers were thought to rise [30]. Hs-CRP is a potent marker for mild inflammatory activities and is implicated in a variety of disorders. It is also frequently used to diagnose and predict systemic inflammation [31]. In response to inflammatory signals and cytokines, the liver produces Hs-CRP. Elevated CRP levels have been associated with a higher risk of heart disease in adults [32], as well as insulin resistance and diabetes in adults, children, and adolescents [33]. This showed that ANGPTL5 and Hs-CRP are both implicated in the progression of obesity via a similar pathway. The increased circulating plasma level of Hs-CRP is assumed to be due to macrophage infiltration of enlarged adipose tissue, which is essential for synthesizing pro-inflammatory signals and producing cytokines like IL-6. The induced release of inflammatory cytokine production can stimulate hepatocytes to produce Hs-CRP [34]. As dyslipidemia and its associated cardio-metabolic disorders are strongly linked to multiple inflammatory responses, recent attention has shifted to composing and implementing the relationship between ANGPTL5 and inflammatory biomarkers such as Hs-CRP [35]. Even though Hs-CRP is an important pro-inflammatory biomarker, limited studies have assessed the potential relationship

**Figure 2**




ANGPTL5 serum level showed a significant positive correlation with HOMA-IR. HOMA-IR, homeostasis model assessment for insulin resistance.

between ANGPTL5 and the Hs-CRP. Our results reveal a strong positive association between ANGPTL5 plasma levels and Hs-CRP [36]. The remarkable positive link between plasma level ANGPTL5 and unacylated ghrelin in obese children might be explained by the ANGPTL proteins being one of the key pathways that are dysregulated in metabolic syndrome. They have been proven to affect metabolic pathways like lipid and glucose metabolism, in addition to inflammation. The first four members of the ANGPTL family (ANGPTL1–4) and ANGPTL6/angiopoietin-related growth factor has been found to influence angiogenesis. ANGPTLs 3, 4, 5, and 8, as well as ANGPTL6/angiopoietin-related growth factor, appear to be participating in other processes such as lipid metabolism and glucose and energy homeostasis. As a result, higher ANGPTL protein levels have been associated with diabetes and metabolic syndrome [37].

Current knowledge of circulating ghrelin levels in healthy humans reveals that circulating ghrelin levels rise during fasting and fall after meal consumption. This is consistent with its unique mechanism of action on orexigenic hormone evolution for energy storage and seeking [38]. As a result, ghrelin is thought to raise the likelihood of obesity.

Serum obestatin, on the contrary, possesses a significant negative relationship with ANGPTL5 and unacylated ghrelin. It is possible that obestatin may regulate appetite and body weight by counteracting the effects of ghrelin. Although the roles of leptin and ghrelin in obesity have been the patient of numerous studies in both children and adults, very little is known about the physiological role of obestatin in humans, especially children [39].

Converse to our result, Balagopal *et al.* [40] had reported that the levels of obestatin and ghrelin were lower in lean controls but not in obese cases ($P$=0.003 for obestatin and $P$<0.001 for ghrelin). Similarly, obese people had lower obestatin levels than lean people. As a result, a negative relationship between obestatin and obesity-related indices such as BMI was established. In contrast, an insignificant relationship between inflammatory factors and obestatin was detected.

Unacylated ghrelin had a significant positive association with other variable parameters such as skin-fold thickness, mid-arm circumference, insulin, and HOMA-IR. These findings were partially consistent with the published data by Fittipaldi *et al.* [41], who found a positive correlation between unacylated ghrelin with insulin and HOMA-IR,

especially in children who are obese or overweight. Ghrelin, an octanoylated peptide hormone, regulates appetite and glycemic control. Desacyl ghrelin abolishes some of the effects of ghrelin but does not bind to the ghrelin receptor. In contrast, several studies have found that ghrelin levels in adults and children are negatively associated with circulating insulin and insulin resistance [42]. Furthermore, the regulation of ghrelin and obestatin concentrations appears to be intimately linked to glucose and insulin metabolism.

For both children and adults, there is an inverse relationship between these satiety hormones and insulin resistance indices [43]. Ultimately, circulating serum obestatin concentrations range around 5 and 10% of ghrelin-equivalent serum levels [7]. As a result, obestatin is more localized than ghrelin. The aforementioned findings, as well as the distinct roles of ghrelin and obestatin in appetite and obesity in pediatrics, require further investigation in carefully designed research, necessitating additional analyses that thoroughly examine alteration in energy balance and satiety hormone levels in future research. Consequently, adiposity is believed to be the main generator of reactive oxygen species, and fat storage is associated with increased oxidative stress. Mitochondrial dysfunction is implicated in the production of insulin resistance and is a primary investigator of the adiposity progression of cardiovascular risk and diabetes [44].ANGPTLs have been shown in studies to regulate angiogenesis potently [45]. Still, some also have pleiotropic functions such as suppression of lipoprotein lipase and endothelial lipase, increased energy expenditure, and stimulation of inflammatory processes [46]. The higher level of ANGPTL proteins regulates important metabolic processes such as the TG metabolism. So the elevated ANGPTL5 might influence TG metabolism. ANGPTL5 has formerly been found to reduce TG lipolysis in collaboration with ANGPTL3, 4, and 8 by suppressing lipoprotein lipase activity [47].

Furthermore, few studies have found no variations in ANGPTL3 and ANGPTL8 levels among standard and overweight children [48]. Thus, our supportive results might encourage the researchers to consider ANGPTL5 as a useful clinical marker for predicting and monitoring children at high risk of cardio-metabolic diseases.

## Conclusion

The blood levels of ANGPTL5 are much higher in patients with obesity and insulin resistance. As a result, ANGPTL5 may be considered a unique and promising biomarker for the early diagnosis of cardio-metabolic disorders in children.

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**Conflicts of interest**

There are no conflicts of interest.

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