Role of Inflammatory Cytokines in Obese and Nonobese Diabetic Children

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Abstract

BACKGROUND: Obesity is an expanded health problem worldwide and it is blamed for a startling rise in type 1 diabetes (T1DM), the interaction between obesity, autoimmune processes, and glucose homeostasis is a growing field of study.

AIM: This study was undertaken to predict the role of the inflammatory cytokines (interleukin [IL]-17 and IL-10) as biomarkers in early screening for obesity and T1DM and to determine the relation of inflammatory cytokines with diabetic complications especially nephropathy.

SUBJECTS AND METHODS: The target group consisted of 92 children with type 1 diabetes children who were diagnosed according to the criteria provided by American Diabetes Association Diabetic; cases were divided into two groups, Group 1 (overweight and obese diabetics) and Group 2 (normal weight diabetic children). The levels of serum IL-17 and IL-10 were assayed in these children by an enzyme-linked immunosorbent assay. Serum triglycerides (TG) and cholesterol levels were measured as well as urinary microalbumin level was estimated for detection of nephropathy.

RESULTS: Diabetic overweight and obese children exhibited significantly 3.8 folds more at risk to be bad glycemic control than diabetic children with normal body mass index (BMI). Furthermore, overweight and obese diabetic children displayed significantly 15 times more at risk of having nephropathy than diabetic children with normal BMI. Low serum level of IL 10 and high level of IL 17 showed a significant association with high BMI in diabetic children. High HBA1c, low IL 10, and long disease duration were significantly considered as predominant risk factors for diabetic nephropathy in diabetic children.

CONCLUSION: The obtained data from these investigations proved that overweight and obese children have a low serum level of IL-10 and high serum IL-17 levels. The relationship between IL-10/IL-17 can be applied as a good marker for the inflammatory state and these inflammatory interleukins can be employed as biomarkers in early screening for obesity and T1DM. Furthermore, these interleukins can be utilized as a predictor for early diabetic complications, particularly nephropathy.

Introduction

Overweight and obesity in children are growing global health issues. Obesity is defined as an excessive accumulation of fat that occurred due to entertaining a lot of calories than the body can consume. They have emerged as one of the major global health problems. In fact, previous studies have estimated that more than 2 billion adults worldwide are overweight (body mass index [BMI] ≥25 kg/m^2), and 671 million of them are clinically obese (BMI ≥30 kg/m²) [1]. Accordingly, it was suggested that more than 51% of the population all over the world will be obese by 2030 [2].

Excessive weight gain leads to severe complications such as hypertension, diabetes, atherosclerosis, and hyperlipidemia, which have been defined as "metabolic syndrome." However, only half of the obese patients with BMI from 30 to 50 kg/m^2 had metabolic disorders [3].

Type 1 diabetes mellitus (T1DM) is an autoimmune disease characterized as multifactorial disorders attributable to T cell-mediated destruction of the pancreatic β cells caused by the interaction between inherited and ecological factors [4]. It accounts for 80–90% in diabetic children and adolescents [5] and its incidence was 387 million in 2014, and a raise of approximately 205 million new cases are expected to occur by 2035 [6]. Some of the diabetic patients are asymptomatic, particularly in children with absolute insulin insufficiency who may undergo polyphagia, polydipsia, polyuria, blurred vision, and weight loss. Uncontrolled diabetic individuals may cause stupor, coma, and ketoacidosis or nonketotic hyperosmolar

syndrome that may lead to death [7], DM1 is strongly related to chronic low-grade inflammation, which is largely presented in obese individuals, it is related to the fact that, in obese individuals, visceral white adipose tissue (AT) is characterized by hyperplasic and hypertrophic adipocytes, with infiltration of inflammatory macrophages, endothelial cells activation, and fibrosis. Another important factor is the phenomena called inflammaging, which consists of the positive regulation of the chronic low-grade inflammatory. Thus, high levels of pro-inflammatory cytokines like IL-17 combined with the reduction of anti-inflammatory cytokines, like IL-10, lead to an imbalance in the inflammatory composition of the innate and acquired immune system and have been related to the development and maintenance of several chronic diseases like T1DM [8].

Diabetic nephropathy occurs in 30% of people with T1DM, mostly in post adolescents. Albumin excretion rate increases until frank albuminuria occur which may result in renal failure [9].

Cytokines are extracellular proteins of low molecular weight that acts as immune response mediators. They perform in highly complex pathways that regulate the inflammatory process, and they are essential to conduct response to the lesion site. Obesity is associated with low-grade chronic inflammation. Indeed, AT in obese individuals are the former site of progressive infiltration by pro-inflammatory immune cells, which, together with increased inflammatory adipokine secretion, induce adipocyte insulin resistance. IL-17 and IL10 cells are part of obese AT infiltrating cells and are likely to be promoted by adipose [3].

Low-grade chronic inflammation and stimulation of the innate immune system are identified to be strongly linked to the pathogenesis of DM [10]. Pro- and anti-inflammatory cytokines have been suggested to be implicated in the events of diabetes [11]. Previous reports revealed that definite pro- and/or anti-inflammatory cytokines are able to interfere with insulin-responsive glucose uptake and stimulate insulin resistance [12]. IL-10 and IL-17 have been found to be connected with the pathophysiology of DM1; however, their interplay in the modulation of diabetogenic T-cells remains unknown.

IL-10 plays a central role in regulating immune response and limiting inflammation. IL-10 suppresses inflammation through various mechanisms, including inhibition of the synthesis of pro-inflammatory cytokines such as IL12 and TNFα through suppression of p65 NF-kB and c-Rel activity in macrophages [13]. IL-10 is also important in the downregulation of the release of reactive oxygen species and nitrogen intermediates, regulation of antigen presentation capacity and immune tolerance [14], and suppression of proliferative and cytotoxic T cell responses [15].

IL-17 was discovered as cytotoxic T-lymphocyte associated antigen 8 in 1993 [16].

After 10 years, it was identified that the cellular source of this cytokine is Th17 cells [17].

Th17 cells are likely to play a major role in the propagation of inflammation and in the immunometabolism, which can be easily modified with a hypercaloric diet as it was mentioned before that the hypercaloric diet induces enrichment of pathogenic Th17 cells, in several metabolic organs [18]. However, data obtained from human T1DM studies and mouse models suggest the involvement of Th17 in the pathogenesis of this disease [19].

This study was intended to explore the mechanism behind the role of IL-10 and IL-17 in inflammation associated with obesity in diabetic children. Furthermore, the study was extended to find out the possibility of utilizing these cytokines as early predictors for T1DM complications, particularly nephropathy.

Subjects and Methods

Between October 2019 and March 2020, 92 diabetic children (T1DM) attending the Unit for Pediatric Diabetes and Endocrinology, Children Hospital, Ain Shams University, were selected for this study. The study group of T1DM children was diagnosed according to the criteria provided by the American Diabetes Association. The parents gave informed consent and children of 10 years of age or older signed their informed consent by themselves after full explanation of the aim of the work, plan of action and blood as well as urine sampling, the protocol of the study was approved by the Ethics Committees for Medical Research of the National Research Centre, Egypt. The diabetic children age ranged between 5 and 15 years were divided into two groups: 34 overweight and obese diabetics (Group 1) and nonobese diabetics (Group 2). All anthropometric parameters have been obtained using standardized equipment and following the recommendations of the International Biological Program [20]. Obesity was considered when BMI exceeded 95th percentile while overweight was considered when BMI was from 85th to 95th percentile and other normal weight diabetic children [21]. Assessment of BMI was done using categories reported by the World Health Organization (WHO) Child Growth Charts Standards for age and sex [22].

Participants were excluded for any of the following reasons: The presence of other chronic or inflammatory disease, drugs or medications (other than insulin), presence of known renal disease or systemic disease, or acute infection at the time of testing.

Laboratory and clinical data

The background information of subjects such as age, gender, weight, height, daily dose of insulin injection, disease duration, and family history of diabetes was recorded. Furthermore, detailed medical history and physical examination were carried out. Disease

duration was defined in this study as the day of the initial diagnosis of diabetes to the day of blood collection.

Samples collection for biochemical analysis

From each child, 5 ml of fasting blood samples were withdrawn; 4 ml were collected in a vacuum tube free from EDTA for separation of serum, and 1 ml was put in another tube with anticoagulant for determination of glycated hemoglobin. Serum samples were separated using a cooling centrifuge (4°C) at 1800× g for 10 min and stored at −20°C until analysis. Triglycerides and cholesterol were quantified using colorimetric techniques on Synchron Cx7 (Beckman Instruments Inc., Brea, California, USA) [23]. Glycated hemoglobin was measured in whole blood colorimetrically using a kit obtained from Biosystems (Spain) according to the method of Roberts *et al.* [24].

According to the manufacturer's protocol, IL-10 and IL-17 were assayed by employing the Human cytokine ELISA set. IL-10 ELISA kit was purchased from SinoGeneClon Biotech Co., Ltd., China, for the quantitative determination of Human IL-10 concentrations, Catalog No: SG-10271. IL-17 ELISA kit was purchased from SinoGeneClon Biotech Co., Ltd., China, for the quantitative determination of Human IL-17 concentrations, Catalog No: SG-10278. For random urinary microalbumin measurement, an early morning midstream urine specimens were used. The cloudy samples were centrifuged before use and the clear supernatants were stored at −20°C until analysis. Microalbumin concentrations were estimated in urine using a Minineph Microalbumin kit based on the nephelometry method on a Minineph nephelometer (AD200) (Birmingham, UK). The diagnosis of nephropathy was established when microalbumin in the urine was more than 30 μgldl [25].

Statistical analysis

Data entry was carried on Excel sheet and statistical analysis was done using the SPSS software program, version 18.0 (SPSS Inc., PASW Statistics for Windows, Version 18.0. Chicago, USA). Chi-square was done for qualitative data that were presented by numbers and percentages. t-test was done for comparison between two means. A simple linear correlation (Pearson's correlation) for quantitative data was also done. P value was considered statistically significant when p < 0.05 and considered statistically highly significant when its value was <0.01.

Results

A total number of 92 Egyptian diabetic children were included in this study. The study group was divided into two groups: Group 1 (38 overweight and obese diabetic) and Group 2 (52 normal weight diabetic cases). Diabetic cases were further classified according to their glycated hemoglobin (HbA1c) level into Group A (67 controlled HbA1c <8%) and Group B (25 uncontrolled HbA1c >8%) diabetic groups. All children were age- and sex-matched.

The mean age was 9.58 ± 2.585 years old in overweight and obese diabetes versus 9.56 ± 2.377 years old in normal-weight diabetes with no significant difference between them (p > 0.05), as shown in Table 1. The data presented in Table 1 also shows a statistically significant difference between obese and normal-weight diabetic children regarding cholesterol, IL10, IL17, HBA1c, and insulin dose. Meanwhile, there is no significant difference between both groups regarding age, disease duration, or triglyceride level (p > 0.05).

Table 1: Comparison between both diabetic groups regarding some clinical and biochemical findings according to BMI

Items	Group 1 Mean ± SD	Group 2	t-test	p
Age (years)	9.58 ± 2.585	9.56 ± 2.377	0.045	0.964
Disease duration (years)	6.50 ± 1.484	6.37 ± 1.218	0.459	0.647
Cholesterol (mg/dL)	181.63 ± 22.114	152.57 ± 15.162	7.482	0.000*
Triglycerides (mg/dL)	76.63 ± 11.034	72.67 ± 11.384	1.666	0.099
IL10 (pg/ml)	3.608 ± 0.9763	7.959 ± 0.9591	−21.269	0.000*
IL17 (pg/ml)	196.947 ± 21.5825	141.930 ± 13.8687	14.884	0.000*
HBA1c (g%)	10.182 ± 2.1145	8.156 ± 1.5811	5.259	0.000*
Insulin dose (unit/kg/day)	1.382 ± 0.3083	1.104 ± 0.1843	5.400	0.000*

Group 1 (Overweight and obese) *p<0.05 is significant, Group 2 (Normal BMI). BMI: Body mass index, HBA1c: Glycated hemoglobin, IL: Interleukin.

The data depicted in Table 2 shows a statistically significant difference between diabetic children with good and bad glycemic control regarding BMI percentile, cholesterol, IL10, and insulin dose (p < 0.05) but there is no significant difference between both groups regarding age, disease duration, TG, or IL17 (p > 0.05).

Table 2: Comparison between the diabetic groups regarding some clinical and biochemical findings according to the glycemic control

Items	Group 1 Mean ± SD	Group 2	t-test	p
Age (years)	9.20 ± 1.756	9.70 ± 2.663	−0.872	0.386
Disease duration (years)	6.20 ± 1.323	6.51 ± 1.330	−0.988	0.326
BMI centile	56.72 ± 19.974	74.10 ± 22.329	−3.414	0.001*
Cholesterol (mg/dL)	155.80 ± 18.690	167.85 ± 24.021	−2.263	0.026*
Triglycerides (mg/dL)	75.84 ± 13.576	73.73 ± 10.459	0.791	0.431
IL10 (pg/ml)	7.256 ± 1.8301	5.754 ± 2.4148	2.819	0.006*
IL17 (pg/ml)	155.504 ± 27.9879	168.069 ± 33.3187	−1.676	0.097
Insulin dose (unit/kg/day)	1.048 ± 0.1323	1.282 ± 0.2923	−3.855	0.000*

Group A (controlled HbA1c <8%), Group B (uncontrolled HbA1c >8%), *p<0.05 is significant. BMI: Body mass index, HBA1c: Glycated hemoglobin, IL: Interleukin.

Table 3 shows that diabetic overweight and obese children displayed significantly 3.8 folds more at risk to be bad glycemic control than diabetic children with normal BMI (Table 3).

Table 3: Association between glycemic control and obesity

Items	Glycemic control Group A (controlled HbA1c <8%)	Group B (uncontrolled HbA1c >8%)	Total
Obesity			
Overweight and obese			
Count	33	5	38
% within obesity	86.8	13.2	100.0
Normal BMI			
Count	34	20	54
% within obesity	63.0	37.0	100.0

Odds ratio=3.882, 95% CI 1.304–11.556, p=0.015*, *p<0.05 is significant. BMI: Body mass index, HBA1c: Glycated hemoglobin, CI: Confidence interval.

The data in Table 4 show that overweight and obese diabetic children displayed significantly 15 times more at risk of having nephropathy than diabetic children with normal BMI (Table 4).

Table 4: Association between obesity and diabetic nephropathy

Items	Nephropathy		Total
	Yes	No	
BMI			
Overweight and obese			
Count	14	24	38
% within obesity	36.8	63.2	100.0
Normal BMI			
Count	2	52	54
% within obesity	3.7	96.3	100.0

Odds ratio=15.167, 95%, CI 3.192–72.070, p=0.001*, *p<0.05 is significant. BMI: Body mass index, HBA1c: Glycated hemoglobin, CI: Confidence interval.

The data presented in Table 5 showed a statistically significant negative correlation between IL10 and IL17, BMI, cholesterol, HBA1c, and insulin dose, while there is a significant positive correlation between IL17 and BMI, cholesterol, and HBA1c.

Table 5: Correlation between different variables in diabetic children

Items	IL10 (pg/ml)	IL17 (pg/ml)
Age (years)		
r	−0.036	−0.060
p	0.736	0.567
Disease duration (years)		
r	−0.085	−0.073
p	0.421	0.491
BMI centile		
r	−0.837**	0.742**
p	0.000	0.000
Cholesterol (mg/dL)		
r	−0.667**	0.493**
p	0.000	0.000
Triglycerides (mg/dL)		
r	−0.188	0.033
p	0.072	0.755
IL10 (pg/ml)		
r	1	−0.732**
p		0.000
IL17 (pg/ml)		
r	−0.732**	1
p	0.000	
HBA1c (g%)		
r	−0.500**	0.400**
p	0.000	0.000
Insulin dose (unit/kg/day)		
r	−0.527**	0.393**
p	0.000	0.000

**Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed). BMI: Body mass index, HBA1c: Glycated hemoglobin, IL: Interleukin.

Table 6 and Figures 1 and 2 showed that low level of IL 10 and high level of IL 17 were significantly associated with high BMI in diabetic children.

Table 6: Multiple linear regression analysis of factors affecting BMI in diabetic children

Items	Unstandardized coefficients		Standardized coefficients	t	Sig.
	B	SE	Beta		
(Constant)	20.213	24.367		0.830	0.409
HBA1c (g%)	1.382	0.761	0.125	1.816	0.073
IL10 (pg/ml)	−4.655	0.971	−0.478	−4.795	0.000*
IL17 (pg/ml)	0.206	0.056	0.289	3.666	0.000*
Cholesterol (mg/dL)	0.113	0.071	0.115	1.598	0.114
Triglycerides (mg/dL)	0.198	0.111	0.098	1.779	0.079
Insulin dose (unit/kg/day)	−1.488	5.770	−0.018	−0.258	0.797

*p<0.05 is significant. HBA1c: Glycated hemoglobin, IL: Interleukin.

Table 7 showed that high HBA1c, low IL 10, and long disease duration are all considered as risk factors of diabetic nephropathy in diabetic children.
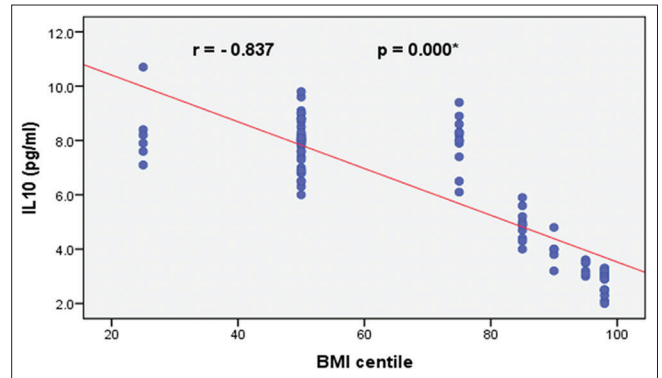

Figure 1: Correlation between body mass index and interleukin-10

Discussion

Long-term complications of DM1 are secondary to the damaging impacts of the metabolic consequences of insulin deficiency on tissues of different body organs. Maintaining good control of diabetes by preventing prolonged hyperglycemia is essential to avoid developing complications it in later life [9].
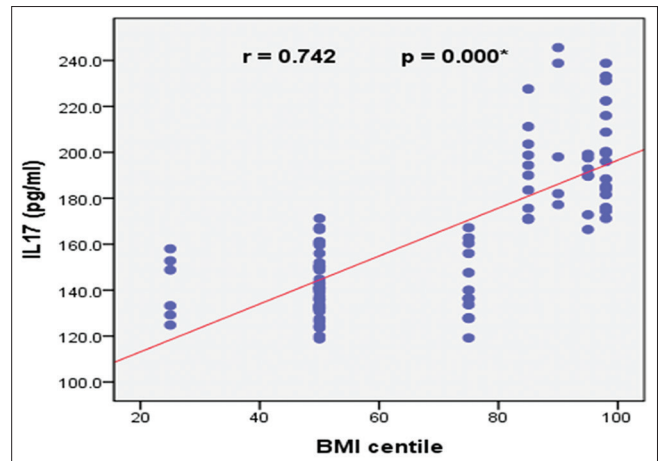

Figure 2: Correlation between body mass index and interleukin-17

Obesity is well known to predispose individuals to metabolic syndrome (MetS). The mechanisms involved in obesity-related pathological processes involve various immune cells, which release IL10 and IL17 [18].

Table 7: Multiple logistic regression analysis of risk factors of diabetic nephropathy

Items	B	Adjusted OR	95% CI for OR		Sig.
			Lower	Upper	
HBA1c	1.161	3.192	1.193	8.543	0.021*
BMI centile	−0.084	0.919	0.813	1.039	0.177
IL10	−1.710	0.181	0.034	0.955	0.044*
IL17	0.020	1.020	0.960	1.084	0.521
Cholesterol	−0.030	0.971	0.906	1.039	0.393
Disduration	1.377	3.963	1.089	14.418	0.037*
Age	0.427	1.533	0.900	2.612	0.116
Insulin dose	−1.188	0.305	0.004	25.414	0.599
Triglycerides	0.042	1.043	0.943	1.154	0.409
Constant	−12.218	0.000			0.344

*p < 0.05 is significant. BMI: Body mass index, HBA1c: Glycated hemoglobin, IL: Interleukin, OR: Odds ratio, CI: Confidence interval.

There is growing evidence linking IL10 and IL17 to obesity [26]. metabolic syndrome (MetS) and cardiovascular disease are also linked to IL10 and IL17 [27].

This research provides relevant information on the influence of body composition on inflammatory and biochemical markers in overweight and obese diabetic and normal weight diabetic children. We demonstrate how body composition interferes with the balance of cytokines, especially IL-10 and IL-17, and how it may exert an effect on the biochemical parameters and risk factors associated with T1DM.

The purpose of this study was to predict if the inflammatory cytokines (IL-17 and IL-10) were beneficial as biomarkers in early screening for obesity and T1DM and to determine the relation of inflammatory cytokines with diabetic complications, especially nephropathy.

Comparison of different variables in both obese and normal-weight groups according to BMI group revealed that serum cholesterol, IL-10, IL-17, HBA1c levels, and insulin dose are the factors showing a significant difference between both groups. And to some extent, the findings of previous researches came in accordance with our conclusion as the study done by Israel et al. [8]. We next performed multiple linear regression analysis to predict variants that are independently associated with BMI and we found that IL-10 and IL-17 concentration are strongly associated with BMI. This study showed that IL-10 concentration is negatively correlated with blood cholesterol but not triglycerides. Moreover, this comes in agreement with a study done by Jung and Choi, who stated that IL-10 exerts essential control over the biochemical parameters such as LDL, VLDL, HDL, triglycerides, and glucose [28]. While on the contrast of our findings Jung and Choi reported that such a correlation pattern is not detected in overweight women, in whom IL-10 showed a negative correlation only with total cholesterol and LDL.

In the current study, the overweight and obese diabetic children had a low level of IL-10 and this agrees with a study done by Jung et al. [29], in which when compared overweight and obese with their normal-weight counterparts, overweight and obese children had lower serum IL-10. In contrast, a study done by Pereira et al. revealed that obese women have higher serum concentrations of IL-10 as feedback generated from the elevated expression of pro-inflammatory cytokines as a result of obesity [30]. However, that increase is not sufficient to govern the development of the pro-inflammatory profile [31].

Many other studies investigating IL10 in children and young adolescents with obesity have yielded conflicting results [32], [33], [34], [35]. Another study, included 80 obese and 80 nonobese Egyptian children, agreed with our results as these authors stated that serum levels of IL-10 are significantly lower in the former group [32]. This could be explained by a study done by Lauridsen et al., gave accentual evidence concerning this as they demonstrated that in the prefrontal cortex of neurologically and psychiatrically healthy humans, a gradual increase in BMI is associated with discrete signs of altered gene expression, that leads to downregulation of mRNA expression of the anti-inflammatory cytokine IL-10 [33].

However, this comes in conflict with Calcaterra et al. in a study, including 70 severely obese and 30 normal-weight children aged 11.46±3.42 years old, Calcaterra et al. stated that serum IL-10 concentrations are higher in severely obese children compared to normal weight [34]. Tam et al. recorded no differences in IL-10 concentration between normal and overweight children at 8 years old; however, at 15 years old, serum IL-10 is elevated in overweight and obese girls when compared to normal weight girls of the same age [35].

The study done by Chang et al. suggested that the effect of obesity on IL-10 serum concentration varies with age, but in this current study, we did not find a correlation between IL-10 and IL-17 and age neither in the obese group nor in the normal-weight group [29].

In the present study, IL17 is significantly increased in overweight and obese diabetic compared to normal weight diabetic and this agrees with a study of Sumarac-Dumanovic who observed significant enhancement in circulating IL-17 and IL-23 cytokines in obese as compared with lean individuals [36]. The relationship between obesity and serum level of IL-17 has been further demonstrated in a sheep model, where maternal obesity provoked an inflammatory state in the fetal intestine, with increased levels of inflammatory cytokines, particularly IL-17 [37]. Infiltrating IL-17+-secreting cells have also been noticed more abundant, in obese versus lean AT, and in visceral versus subcutaneous AT [38]. Dalmas et al. have shown that single populations of IL-17+ IL-22− and IL-17−IL-22+ and double populations of IL-17+ IL-22+ CD4+ T cells are highly induced in the mucosal tissues of obese subjects, as compared with non-obese [39]. Supporting the implication of IL-17 in the MetS, the levels of IL-17 expression in liver or muscle were shown to correlate with insulin resistance [38], and the blockade of IL-17 resulted in the decrease of hepatic inflammation in the non-alcoholic steatohepatitis syndrome (NASH) [40].

This current study also demonstrated that pro-inflammatory cytokine IL-17 and the anti-inflammatory IL-10 are significantly negatively correlated and this matches the findings of Winer et al. which showed that in obese rats the increase of IL-6 due to obesity causes maturation of Th17 and secretion of IL-17which inhibits IL-10 secretion and Treg development and this, in turn, intensified inflammation in the body [41].

Comparing the two groups of diabetics according to their glycemic control level using HbA1c 8% as a cutoff (controlled [<8%] and uncontrolled [>8%]

diabetic group), a significant difference between good and bad glycemic control has been found regarding BMI, IL10, cholesterol and insulin dose. Diabetic overweight and obese children were significantly 3.8 folds more at risk to be bad glycemic control than diabetic children with normal BMI. This result comes in line with that of El-Wakeel _et al._'s study [42]; this strong association was confirmed by many other studies [8], [18].

The current study showed that overweight and obese diabetic children are significantly at higher risk of having nephropathy than diabetic children with normal BMI. This coincides with the study done by Zu _et al._ which explained this as obesity is associated with hyperleptinemia, which contributes to a decline in eGFR and pathological processes [43]. Changwei _et al._ did not agree with this result in their study, where 481 patients with nephropathy were finally enrolled in the study. There was no significant difference in clinical and pathological characteristics among the four-group patients categorized by BMI. After matching with propensity scores, no significant correlation between BMI and renal outcomes was seen [44]. These findings spotlight the effect of impaired control of hyperglycemia and BMI on the risk of premature development of complications in the pediatric diabetic population. There are several limitations in our study; the cross-sectional nature of the current study and the relative small sample size are the common limitations of the study. However, in the light of data documented by the results of the present study, we put forward the evidence that high serum IL17 and lower IL10 levels in type 1 diabetic children together with obesity might be collateral to deterioration in diabetic cases and more emerging of diabetic complications as nephropathy.

Conclusion

This study proved that overweight and obesity in children T1DM are associated with low serum IL-10 concentration and high serum IL-17. The changes in these interleukins in overweight and obese diabetic children may further implicate to the inflammatory environment associated with obesity. The relationship between IL-10/IL-17 can be applied as a good marker for the inflammatory state, and we encourage further studies with a large sample size to confirm this hypothesis. This study is considered as innovative and relevant research in children population showing that serum IL-10 and IL-17 levels can be served as predictors of obesity and diabetes-associated complications.

Acknowledgment

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