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Article

Estimation of Serum Levels of Interleukin-6, Malondialdehyde and Glutathione in Pediatric Type 1 Diabetes Mellitus: A Case-Control Study

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Abstract: Type 1 Diabetes Mellitus (T1DM) is a disease of metabolic and immunological dysregulations in paediatric population. The aim of this study was to measure the serum levels of Interleukin-6 (IL-6), Malondialdehyde (MDA), and Glutathione (GSH) in T1DM children and their effects on systemic inflammatory, oxidative stress and antioxidant status in Tikrit City. One hundred and twenty children aged 1-12 years were included, and were split into 2 groups: 60 T1DM and 60 age matched healthy controls. The concentration of IL-6 (ELISA), MDA and GSH were measured and statistically analyzed in serum by SPSS. The serum levels of pro-inflammatory cytokine (IL-6) and lipid peroxidation marker (MDA) were significantly increased in T1DM group compared to healthy controls ($p \leq 0.05$). On the other hand diabetic children showed significant reduction in the level of serum GSH compared to the control group ($p \leq 0.05$). Pediatric T1DM is associated with increased systemic inflammation and lipid peroxidation and decreased antioxidant defenses. These are markers of the biochemical interactions between diabetic glycemic control and cell damage.

Keywords: Interleukin-6 (IL-6), Malondialdehyde (MDA) and Glutathione (GSH), Diabetes Mellitus 1, Tikrit

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1. Introduction

Type 1 diabetes mellitus (T1DM) is a serious autoimmune condition influenced by multiple factors, marked by the destruction of pancreatic β cells due to T-cell activity accompanied by an infiltration of leukocytes [1], consequently, there is a marked impairment in both the synthesis and secretion of insulin. Beyond inherent genetic predisposition, several environmental factors may precipitate islet autoimmunity, including infectious agents, early nutritional patterns, serum vitamin D concentrations, the composition of the gut microbiota, vaccination protocols, and exposure to various pollutants and toxins [2].

IL-6 is a glycopeptide cytokine characterised by four helices, contributing to the maturation and activation of both innate and adaptive immune responses, having a molecular weight of 26 kD [3]. IL-6 is a major pro-inflammatory cytokine, in situations of inflammation, infection and autoimmunity, it is important for the initiation of a number of inflammatory responses in tissues, through its ability to facilitate the infiltration and activation of mononuclear white blood cells, whilst preventing infiltration of neutrophils; IL-6 signalling has also been associated with the upregulation of anti-apoptotic factors that increase the longevity of T cells [4]. IL-6 additionally governs the synthesis of immunoglobulin and facilitates the maturation of T follicular helper cells, which

subsequently aids in the differentiation of activated B cells into plasma cells [5]. The activation of the IL-6 pathway may be shared by both T1DM and autoimmunity as the STAT3 and STAT1 response to IL-6 are strongly up-regulated in both CD4 and CD8 T cells of T1DM [6]. T1DM can be an onset of primary disease and many mechanisms involving altered T cell trafficking via an IL-6 signal pathway can be involved.

Free radicals induce lipid oxidation, which produces MDA, the primary metabolite of arachidonic acid, and is highly toxic when combined with proteins and phospholipids. [8,9]. In T1DM, the increase in oxidative stress causes lipid peroxidation, resulting in an increase of malondialdehyde in the serum of T1DM patients, which is an indicator of lipid peroxidation and helps in measuring the total oxidative stress in T1DM [10].

Glycine, cysteine, and glutamic acid make up GSH, which is an efficient antioxidant that shields cells from oxidative stress. It is also a cofactor for Glutathione peroxidase (GPx), another antioxidant that guards against peroxides and stops the build-up of reactive oxygen species (ROS), preventing cellular damage [11]. The present study intended to evaluate and estimate the serum level of IL-6, MDA and GSH in diabetic children who suffered from T1DM in comparison with healthy children in Tikrit City to evaluate the level of response of inflammatory markers, lipid peroxidation markers and antioxidant defense markers in children with T1DM.

2. Materials and Methods

2.1. Patients and Blood Collection

The present study has been carried out on "120 numbers of blood samples from 1st January 2026 to August 2026 with the age group ranging from 1-12 years. Blood samples from the offspring of T1DM patients were obtained and separated into two groups; the first group (60 samples) included T1DM patients, whilst the second group (60 samples) comprised healthy normal children as a control. Disposable syringes and clean, dry, plain tubes devoid of anticoagulants were used to extract venous blood samples, which were then allowed to coagulate for five milliliters at room temperature. After that, the serum was centrifuged for ten minutes at 4000 rpm to remove any" hemolysis.

2.2. Determination of Parameters

The levels of the cytokines were measured by an ELISA kit provided by My BioSource (USA) for IL-6. The level of malondialdehyde in the serum was determined by a modified method of "Guidet and Shah (1989) [12]. GSH was quantified by a modified procedure of Tietz (1986)" [13].

2.3. Statistical Analysis

The "IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA) software was used for data analysis. Values of continuous variables were presented as mean ± SD. Independent sample t-test was used to compare the differences between the two study groups (T1DM patients and healthy controls). All analyses were given a p-value of ≤0.05".

3. Results

The fasting blood glucose concentration (FBG) in the T1DM group was significantly higher ($p \leq 0.05$) during the experimentation period (169.00 ± 15.28 mg/dl) than in the control group (86.00 ± 8.21 mg/dl), as Figure (1) illustrates.

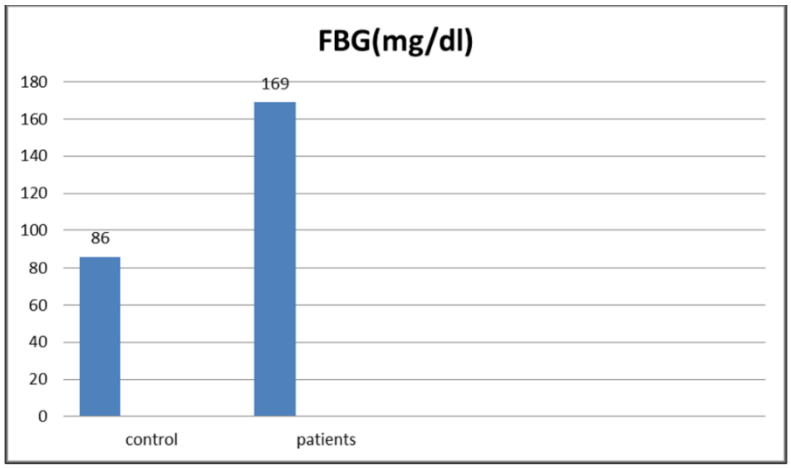


Figure 1. Concentrations of Fasting Blood Glucose (mg/dl) in the study groups.

The findings are in line with the hyperglycaemia seen in type 1diabetes, as a consequence of insulin deficiency [14]. This increase in fasting blood glucose is caused mostly by the absolute deficiency of insulin resulting from destruction of the insulin-producing pancreatic beta cells, which is caused by the absence of insulin's effects on peripheral glucose uptake and results in accelerated glycogenolysis and gluconeogenesis in the liver to produce an accelerated increase in hepatic glucose production [15]. The T1DM group's "blood serum pro-inflammatory cytokine IL-6 concentrations were significantly higher ($p \leq 0.05$) during the trial period (Figure 2) (31.22± 4.23 pg/ml) than the control group's" (7.97± 2.03 pg/ml).

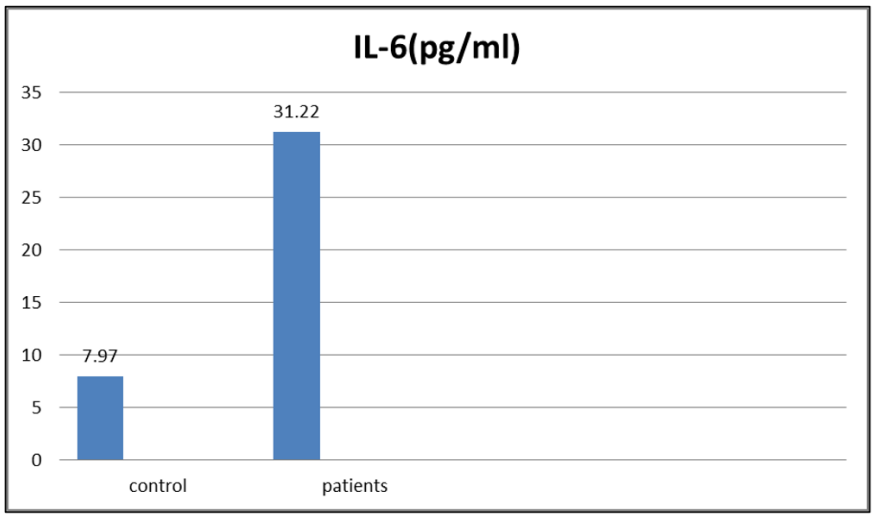


Figure 2. Shows the study groups' blood serum IL-6 concentrations (pg/ml).

The findings are consistent with a study performed by Hameed et al., 2012 [16] which found that the IL-6 levels in the blood serum of T1DM patients was significantly higher than in the control group. IL-6 is an indicator of an inflammatory process because it raises the activity of nuclear factor (NF-κB), mitogen-activated protein kinase, and protein kinase C. This enhances the transcription and release of higher IL-6 by the monocytes in hyperglycemia during T1DM [19,20]. Moreover IL-6 production is increased by the up regulation of these two activities during hyperglycemia [19,20]. The blood serum concentration of MDA was significantly ($p \leq 0.05$) higher in T1DM group (3.98±0.94 μmol/L) than in the control group (1.48±0.13 μmol/L) (Figure 3)

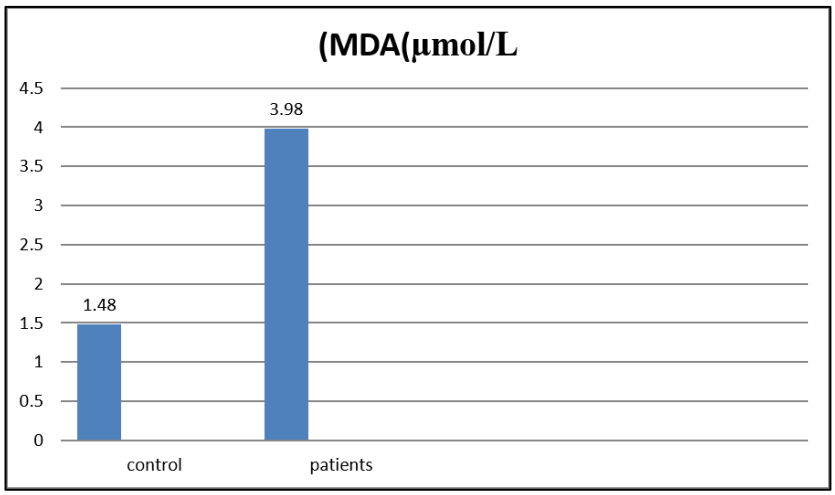


Figure 3. Shows the study groups' blood serum MDA concentrations (µmol/L).

The findings agreed with Abdel-Moneim et al. (2020) [20] and Stambouli-Guerriche et al. (2015) [21], who informed that the blood serum MDA level in patients was significantly higher than the control group. Type1 diabetes is associated with hyperglycaemia which leads to increased levels of MDA as a result of chemical modifications of proteins, lipids and DNA [23] and a raised production of ROS, leading to increased lipid peroxidation and decreased antioxidant defenses [24]. The level of GSH was significantly reduced in the T1DM group (1.67 ±0.12µmol/L) during the trial period when compared to the control group (4.86 ±0.44µmol/L) ($p \leq 0.05$) (Figure 4).

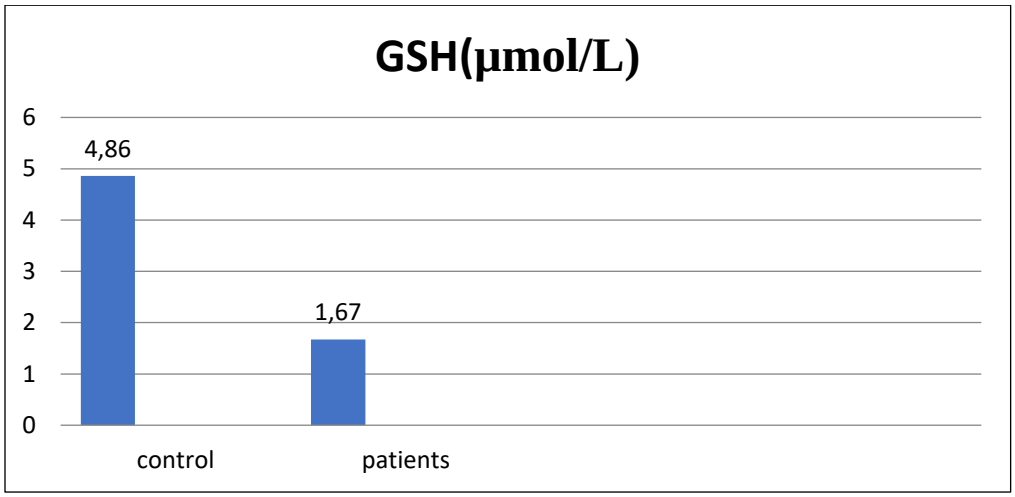


Figure 4. Shows the study groups' blood serum GSH concentrations (µmol/L).

The findings supported research by Benson et al. (2023) [25] and Pastore et al. (2012) [26] that showed individuals with T1DM had considerably lower GSH levels than the control group. Increased blood glucose levels in diabetes mellitus cause oxidative stress and weaken antioxidant defences; a persistent loop of "metabolic stress, tissue damage, and cell death may exacerbate oxidative stress" [27]. It causes reduced levels of GSH as it leads to more free radicals production and impaired the free radical scavenger system as a result of increased GSH utilization to combat free radicals to prevent oxidative damage in Type 1 diabetic patients [28].

4. Discussion

In this study, the difference among markers of inflammatory and oxidant stress of the children with T1DM and healthy children was found to be significant. "There was significant increase in the levels of IL-6 and MDA, and significant decrease in the level of

GSH in diabetic children serum compared to the control group". The serum IL-6 and MDA levels were significantly high while the level of GSH was significantly low in the diabetic children compared to control group.

The hyperglycemia seen in diabetic children is the hallmark of the classic diabetic pathogenesis of T1DM due to the immune destruction of pancreatic β-cells [14, 15]. Chronic hyperglycemia leads to increased production of the ROS and activates the intracellular pro-inflammatory signaling pathways such as PKC, MAPK, and NF- κB, which subsequently increase the production of IL-6 [16–19].

The marked elevation in serum IL-6 further indicates the systemic inflammatory state in pediatric T1DM which is in line with Hameed et al. [16]. At the same time, increased MDA levels are related to increased lipid peroxidation and cell membrane damage as reported earlier [20, 21, 23]. Endogenous antioxidants are constantly used up to combat overproduction of ROS. The marked reduction in serum GSH indicates that diabetic children have a defective antioxidant defense system which supports the results of Benson et al. [25] and Pastore et al. [26].

Together, the combination of increased levels of IL-6 and MDA with a decreased GSH indicates a definite relationship among chronic hyperglycemia, systemic inflammation, and oxidative damage. Some constraints need to be recognized, however [30]. There are two main limitations with the cross-sectional design: firstly, generalizability is restricted due to the limited geographical scope, and secondly, causal inferences cannot be drawn. Second, important clinical parameters (e.g., diabetes duration, insulin regimens, HbA1c levels, and direct correlation analyses between Biomarkers) were not studied. More longitudinal studies with greater numbers of subjects and exhaustive metabolic phenotyping are needed to validate the clinical relevance of these biomarkers in the surveillance of pediatric T1DM.

5. Conclusion

The current study showed that the serum levels of IL-6 and MDA were significantly elevated while the "GSH was significantly decreased in children with T1DM compared to healthy children in Tikrit city ($p \leq 0.05$)". Among the 120 children aged 1–12 years, the diabetic group (n = 60) had higher fasting blood glucose (169.00 ± 15.28 versus 86.00 ± 8.21 mg/dL), IL-6 (31.22 ± 4.23 versus 7.97 ± 2.03 pg/mL), and MDA (3.98 ± 0.94 versus 1.48 ± 0.13 μmol/L), whereas GSH was lower (1.67 ± 0.12 versus 4.86 ± 0.44 μmol/L) than in the control group (n = 60). This result shows a relationship between T1DM in children and a higher systemic inflammatory state and lipid peroxidation, and lower antioxidant defense. The results could be relevant to a deeper understanding of inflammatory and oxidative stress profiles in children with the disease, but are not necessarily causal or clinically diagnostic in themselves. Further studies with larger numbers of patients, over longer periods and measurement of glycemic control and disease duration could confirm the clinical significance of these biomarkers.

Ethics Approval

"This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Institutional Review Board (IRB) at the University of Tikrit (Approval No. USS-IRB-2025/041). Prior to enrollment, written informed consent was obtained from the parents or legal guardians of all participating children".

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