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Evaluation of Laboratory Investigations for Neuropathy in Children and Adolescent with Type I Diabetes Mellitus (TIDM)

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Objectives: The study aimed to evaluate different laboratory parameters in children and adolescent with type 1 diabetes mellitus (T1DM) with and without diabetic neuropathy.
Methods: 60 children and adolescents with T1DM was enrolled in this study, they were classified into: 30 cases with T1DM from 2 to 5 years, 30 cases with T1DM for more than 5 years and 30 healthy children matched for age and sex as a control group. Blood samples were obtained from all cases to assess different laboratory investigation including hemoglobin (Hb) level, liver function test (ALT and AST), renal function test (urea and serum creatinine), fasting blood sugar (FBS), 2 h post

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prandial glucose (2hPP), lipid profile (serum cholesterol and triglycerides) and thyroid function tests.
Results: There was significant value in serum creatinine, serum cholesterol, FBS and 2hPP glucose level between the studied groups.
Conclusion: Patients with DM duration more than five years are associated with impaired renal function, hypercholesteremia and less glycemic control.

Keywords: Type 1 diabetes mellitus; laboratory investigation; hypercholesterinemia.

1. INTRODUCTION

Diabetes Mellitus (DM) can be categorized into many types: type 1 diabetes mellitus (T1DM) that is due to the autoimmune destruction of β cells resulting in absolute insulin deficiency. Whereas in type 2 diabetes Mellites (T2DM), there is a progressive loss of β-cell that produce insulin and increased insulin resistance. There are other types of diabetes as monogenic diabetes and drug induced diabetes [1].

In T1DM, there is destruction of beta cells, resulting in hyperglycemia which leads to a lifelong insulin-dependent state. T1DM has a complex pathogenesis and exact mechanism is not clearly understood but it is multifactorial disease. These factors include family history and genetic predisposition (HLA and non-HLA genes) besides environmental and metabolic factors [2].

The finding of insulin in 1922 transformed T1DM from a fatal condition to a treatable one. Despite advancements in management, DM is linked with significant medical, psychological, and financial stress. A life-threatening complication as hypoglycemia and ketoacidosis can occur [3].

Microvascular consequences of DM include retinopathy, neuropathy, and nephropathy, but they may also impact cognitive significance, the heart, and other organs. Hyperglycemia is the key risk factor for microvascular illness, and decreasing HbA1c by comprehensive DM care, especially in the early stages of the disease, is linked with large reductions (about 70%) in prevalence and slower development of microvascular disease. Variations in HbA1c do not, however, completely account for complications and disease severity. Variations in glucose levels (daily and long-term) and glycosylation rates may potentially play a role in individual variances [4].

Heart, peripheral artery, and brain atherosclerosis and thrombosis are macrovascular consequences of T1DM. In contrast to microvascular issues, stringent glycemic management does not seem to minimize the risk of cardiovascular events. An elevated risk to develop macrovascular complications is associated with diabetic nephropathy which can be presented with as microalbuminuria, macroalbuminuria, or decreased glomerular filtration rate [5].

The study aimed to evaluate different laboratory parameters in children and adolescent with T1DM.

2. METHODOLOGY

60 children and adolescents with T1DM were enrolled in this study who were diagnosed and followed up at pediatric endocrinology and diabetes unit and Endocrinology and diabetes clinic of Pediatric Department, Tanta university hospital.

2.1 They were Classified Into

1. 30 children and adolescents with duration of diabetes two to five years.
2. 30 children and adolescents with duration of diabetes more than five years [6].
3. 30 healthy children matched for age and sex as a control group.

2.1.1 Inclusion criteria

- Children and adolescents aged 5-18 years old.
- Children and adolescents with T1DM criteria:

FBG more than 126 mg/dl (7mmol/L) and 2hPP more than 200 mg/dl (11.1 mmol/L), or RBS more than 200mg/dl (11.1 mmol/L), HbA1c more than 6.5 % with signs of DM (polyuria, polydipsia, polyphagia, weight loss, tiredness and lethargy)

2.1.2 Exclusion criteria

connective tissue diseases, e.g., SLE., acute or chronic illness, neurodegenerative diseases, malignancy &renal diseases.

The adequate provision to maintain privacy of the participants and confidentiality of the data were as follows:

- We put code number to every patient symbol to the name and
- address that was kept in a special file.
- We hid the patient's name when we used the research.
- We used the results of the research only in scientific aim and not used it in any other aim.

2.2 All Participants Underwent

2.2.1 Complete history taking

- Age and sex of participants, onset and duration of DM, symptoms of neuropathy as numbness, tingling of hands & feet, pain, burning sensation, paresthesia, foot ulcers, gloves & socks sensation etc.
- Insulin regimen and total daily dose.
- History suggestive of chronic diabetic complication as retinopathy with persistent blurring of vision.
- Family history: detailed history about similar condition in the family

2.2.2 Through clinical examination

Including weight, height, BMI, vital signs, signs of diabetic neuropathy including pin prick test, monofilament test, vibration test and thermal discrimination and motor examination [6].

2.2.3 Laboratory investigations

Laboratory investigation were done in clinical pathology department at Tanta university hospital.

2.2.4 Laboratory investigation including

Hemoglobin (Hb) level, liver function test (ALT and AST), renal function test (urea and serum creatinine), fasting blood sugar (FBS), 2 h Post prandial glucose (2hPP), lipid profile (serum cholesterol and triglycerides) and thyroid function tests.

The duration of the research was about 12 months.

2.3 Statistical Analysis

Data were entered into the computer and analysed using version 20.0 of the IBM SPSS software suite. (Armonk, New York: IBM Corporation) Quantitative and percentage descriptions were provided for qualitative data. The Shapiro-Wilk test was employed to evaluate the distribution's normality. The range (minimum and maximum), mean, standard deviation, median, and interquartile range were used to characterise quantitative data (IQR). The acquired findings were deemed significant at the 5 percent level.

3. RESULTS

The age of subjects was between 5.0 – 17.0 years with median (IQR)= 11.60 (6.50 – 14.60) in group 1 and between 7.0 – 17.0 years with median (IQR) = 10.25(9.0 – 15.90) in group 2 and between 5.0 – 16.0 years with median (IQR) = 9.25 (6.5 - 13) in control group. There was no significant difference among studied groups (P = 0.956).

As regard gender: In group 1, sixteen male patients (53.3 %) and fourteen female patients (46.7%) were involved; in group 2, fifteen male patients (50%) and fifteen female patients (50%) were involved; while in control group sixteen male patients (53.3 %) and fourteen female patients (46.7%) were involved with no significant difference in the studied groups (P = 0.104).

Comparison between studied groups in height and weight, according to height: Group I showed patients heights between 95.0 – 167.0 cm with median (IQR) = 143.50, group II showed heights between 124.0 – 169.0 cm with median (IQR) = 154.75 and control group showed heights between 108.0 – 161.0 cm with median (IQR) = 135.50. Height in group 1 was significantly reduced than in group 2, group 2 was significantly elevated than control group while there was no significance difference among group 1 and control group (P < 0.001).

During evaluation of the patients' weights group 1 showed mean = 40.28 ± 18.10, group 2 showed mean = 49.32 ± 14.59 and control group showed mean = 37.43 ± 13.74. Weight in group 1 and 2 showed no statistically significance difference, also group 1 and control group also showed no statistically significant difference while weight in group 2 was significantly elevated than control group (P = 0.011).

Laboratory investigations for diabetic individuals included in the studied groups:

The mean Hb level in group 1 was 12.23 ± 1.23 g/dl (range 10.20 – 14.70 g/dl) and in group 2 the mean Hb level was 12.42 ± 1.12 g/dl (range 9.60 – 14.70 g/dl). There was no statistically significant difference between studied groups (P = 0.521).

Serum creatinine level was ranged between 0.45 – 0.80 mg/dl with mean = 0.65 ± 0.10 mg/dl in group 1 while the level was ranged between 0.38 – 1.20 mg/dl with mean = 0.75 ± 0.16 mg/dl in group 2. Serum creatinine level in group 1 was significantly lower than group 2 (P = 0.01).

Urinary albumin level was ranged between 2.0 – 629.0 mg/dl with mean = 30.89 ± 113.14 mg/dl while in group 2 urinary albumin ranged between 1.70 – 528.0 mg/dl with mean = 58.75 ± 109.08. There was no significant variance among studied groups (P = 0.706).

Serum triglycerides level mean in group 1 was 84.93 ± 25.75 mg/dl and in group 2 was 103.33 ± 50.45 mg/dl. There was no statistically significant difference between both studied groups (P= 0.133).

Serum cholesterol level mean in group 1 was 133.67 ± 31.74 mg/dl and in group 2 was 166.87 ± 39.03 mg/dl. Serum cholesterol in group 1 was significantly reduced than group 2 (P = 0.001).

During evaluation of liver function for the studied groups: Group 1 showed ALT mean value = 18.47 ± 9.39 while group 2 showed ALT mean = 25.97 ± 52.79. There was no significant difference among both studied groups (P = 0.853).
Group 1 showed AST mean value = 25.57 ± 25.43 while group 2 showed AST mean value = 32.43 ± 76.20. There was no significant difference among both studied groups. (P = 0.459).

FBS in group 1 was ranged between 90.0 – 292.0 mg/dl with mean = 172.90 ± 57.19 mg/dl and in group 2 was ranged between 105.0 – 520.0 mg/dl with mean = 216.63 ± 81.43 mg/dl, group 2 showed significantly higher FBS than group1. (P= 0.019).

2hPP glucose level in group 1 was ranged between 129.0 – 412.0 mg/dl with mean = 224.93 ± 75.26 mg/dl while group 2 was ranged between 120.0 – 640.0 mg/dl with mean = 279.07 ± 104.49 mg/dl. Group 2 showed significantly higher 2hPP than group 1 (P = 0.032*).

Thyroid function evaluation in the studied groups, TSH in group 1 showed mean value **=** 1.91 ± 1.01, Free T4 mean value = 1.46 ± 0.93 and Free T3 mean value = 2.14 ± 1.37 while in group 2 TSH mean value = 1.89 ± 0.95, Free T4 mean value = 2.06 ± 1.63 and Free T3 mean value =2.01 ± 1.25. There was no significant difference among both groups in thyroid function.

Table 1. Demographic data of studied groups

		Group I (n = 30)	Group II (n = 30)	Group III (n = 30)	P value
Sex	**Male**	16 (53.3%)	15 (50.0%)	16 (53.3%)	0.956
	Female	14 (46.7%)	15 (50.0%)	14 (46.7%)	
Age (years)		10.87 ± 4.37	12.14 ± 3.72	9.96 ± 3.65	0.104
Height (cm)		137.38 ± 22.56	152.67 ±10.93	135.53 ± 16.45	<0.001*
Weight (kg)		40.28 ± 18.10	49.32 ± 14.59	37.43 ± 13.74	0.011*

*Data expressed as mean ± SD or frequency (%), *: significant as P value ≤ 0.05*

Table 2. Comparison between the two studied groups according to different laboratory parameters

	Group I (n = 30)	Group II (n = 30)	P value
Hemoglobin	12.23 ± 1.23	12.42 ± 1.12	0.521
Serum creatinine	0.65 ± 0.10	0.75 ± 0.16	0.010*
Microalbuminuria	9.50 (5 - 14)	7.05 (4.90 - 65)	0.706
Triglycerides	84.93 ± 25.75	103.33 ± 50.45	0.133
Cholesterol	133.67 ± 31.74	166.87 ± 39.03	0.001*
ALT	16.0 (13 - 21)	16.0 (12 - 23)	0.853
AST	21.0 (16 - 25)	18.0 (14 - 25)	0.459
FBS	172.90 ± 57.19	216.63 ± 81.43	0.019*
2h PP	224.93 ± 75.26	279.07 ± 104.49	0.032*

*Data expressed as mean ± SD or median (IQR), *: significant as P value ≤ 0.05*

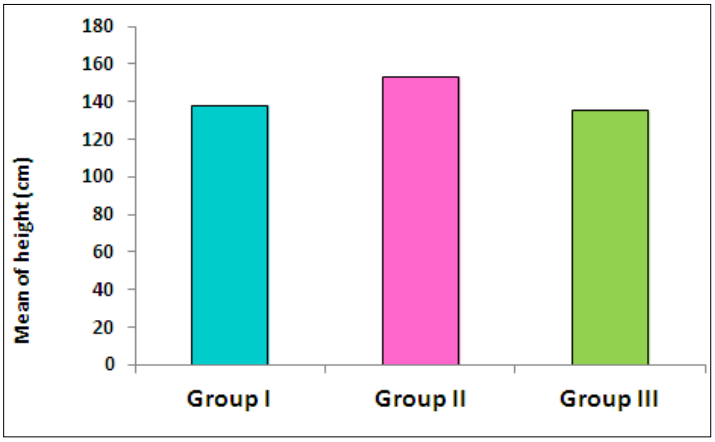

Fig. 1. Comparison between studied groups according to height

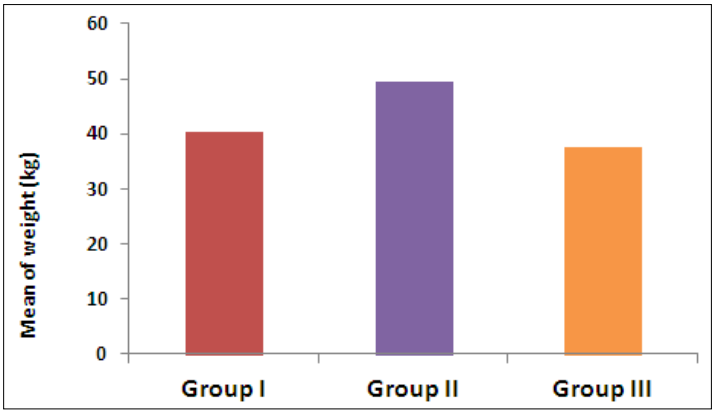

Fig. 2. Comparison between studied groups according to weight

Table 3. Comparison between the two studied groups according to thyroid function profile

	Group I (n = 30)	Group II (n = 30)	P value
TSH	1.67 (1.09 – 2.65)	1.69 (1.3 – 2.25)	0.871
Free T4	1.20 (1.02 – 1.64)	1.62 (1.18 – 1.96)	0.051
Free T3	1.80(1.36 – 2.16)	1.65(1.30 – 2.16)	0.478

Data expressed as median (IQR)

4. DISCUSSION AND CONCLUSION

In this study, the age of subjects was between 5.0 – 17.0 years with median (IQR)= 11.60 (6.50 – 14.60) in group 1 and between 7.0 – 17.0 years with median (IQR) = 10.25(9.0 – 15.90) in group 2 and between 5.0 – 16.0 years with median (IQR) = 9.25 (6.5 - 13) in control group. In group 1, sixteen male patients (53.3 %) and fourteen female patients (46.7%) were involved; in group 2, fifteen male patients (50%) and fifteen female patients (50%) were involved; while in control group sixteen male patients (53.3 %) and fourteen female patients (46.7%) were involved, both age and sex did not show any significant difference in this study.

Li et al. conducted on 568 Type 1 or 2 diabetic and healthy control subjects, group 1 included 218 diabetic patients without neuropathy with age between 43.3–60.6 years with median (IQR) = 51.4 while group 2 included 214 patients with neuropathy with age between 40.0–64.8 years with median (IQR) = 52.3 and control group included 136 subjects with age between 38.6–61.9 years with median (IQR) = 52.5 [7].

While Sandhu et al., conducted on 72 T1DM or T2DM and healthy control subjects, group 1 included 22 diabetic patients without neuropathy with age between 42.8-67.6 years with median (IQR) = 55.2 with male to female ratio 2.25: 1 while group 2 included 24 patients with

neuropathy with age between 47.3-71.9 years with median (IQR) = 59.6 with male to female ratio 3.4: 1 and control group included 26 subjects with age between 26.8-61.6 years with median (IQR) = 44.2. with male to female ratio 3: 1 [8].

In the current study, height and weight for included patients were measured. Group I showed patients heights between 95.0 – 167.0 cm with median (IQR) = 143.50, group II showed heights between 124.0 – 169.0 cm with median (IQR) = 154.75 and control group showed heights between 108.0 – 161.0 cm with median (IQR) = 135.50. Height in group 1 was significantly reduced than in group 2, group 2 was significantly elevated than control group while there was no significance difference among group 1 and control group.

During evaluation of the patients' weights group 1 showed mean = 40.28 ± 18.10, group 2 showed mean = 49.32 ± 14.59 and control group showed mean = 37.43 ± 13.74. Weight in group 1 and 2 showed no statistically significance difference, also group 1 and control group also showed no statistically significant difference while weight in group 2 was significantly elevated than control group.

In present study, cross-sectional study for laboratory investigations for diabetic individuals in group 1 were shown that the mean Hb level was 12.23 ± 1.23 g/dl (range 10.20 – 14.70 g/dl) and in group 2 the mean Hb level was 12.42 ± 1.12 g/dl (range 9.60 – 14.70 g/dl) which showed no statistically significant difference.

While serum creatinine level was ranged between 0.45 – 0.80 mg/dl with mean = 0.65 ± 0.10 mg/dl in group 1 while the level was ranged between 0.38 – 1.20 mg/dl with mean = 0.75 ± 0.16 mg/dl in group 2 which showed that group 1 was significantly lower than group 2.

However, In Li et al creatinine clearance was done, showing mean creatinine clearance in group 1 was 81.9 ± 7.3 while in group 2 was 82.5 ±18.4 which denoted no statistically significant value. Furthermore, in the current study group 1, urinary albumin level was ranged between 2.0 – 629.0 mg/dl with mean = 30.89 ± 113.14 mg/dl while in group 2 urinary albumin ranged between 1.70 – 528.0 mg/dl with mean = 58.75 ± 109.08 which showed no statistically significant value. In Li et al., group I showed albumin/creatinine ratio (ACR) = 24 ± 6.2 mg/g while in group 2 ACR was 25 ± 7.2 mg/g that showed no statistically significant value [7]. However, In Sandhu et al., group 1 ACR was 6.6 ± 0.87 mg/mmol while in group 2 ACR was 8.2 ± 2.0 mg/mmol which donated a statistically significant value between group 1 and group 2 [8].

There is evidence that albuminuria is a substantial risk factor for the advancement of diabetic kidney disease, hence it is recommended that frequent albumin/creatinine ratio (ACR) testing be performed (DKD). In addition, serum urea and creatinine are commonly used parameters to indicate renal dysfunction. A comparison of kidney parameters i.e., urea and creatinine across different stages of DPN patients and controls showed a significant increase in urea across stages reaching maximum in stage 3, indicative of increasing renal abnormality across stages. A previous study also concluded that diabetic nephropathy was found to be related with proliferative diabetic retinopathy, neuropathy and cardiovascular disease by univariate analysis [9].

In the current study, serum cholesterol level mean in group 1 was 133.67 ± 31.74 mg/dl and in group 2 was 166.87 ± 39.03 mg/dl that showed serum cholesterol in group 1 was significantly reduced than group 2, while in contrast serum triglycerides level mean in group 1 was 84.93 ± 25.75 mg/dl and in group 2 was 103.33 ± 50.45 mg/dl that demonstrated no significant difference among both groups.

In Li et al., both serum cholesterol and triglycerides levels didn't show any significance for both groups [7].

A higher incidence of dyslipidemia was found in both T1DM and T2DM with close relation to diabetic neuropathy. Certain variables may be implicated in the processes through which plasma lipids affect DN, albeit they have not been completely explained. First, dyslipidemia patients are characterised by insulin resistance and chronic inflammation, both of which may lead to insulin resistance. Moreover, there is a correlation between insulin resistance and peripheral neuropathy. Secondly, oxidative stress is a significant DN risk factor. In addition, LDL contributes to neuronal damage, which increases superoxide generation. Demyelination caused by lipid profile disturbances is a third possible route for lipid-induced nerve damage. Important hallmark of DN cases is segmental demyelination, and myelin breakdown with focal

demyelination has been seen in high-fat fed mice [10].

Concerning glycemic control of diabetic individuals in this research, the mean of FBS in group 1 was 172.90 ± 57.19 mg/dl and in group 2 was 216.63 ± 81.43 mg/dl which showed that group 2 was significantly higher FBS than group1.

While in Li et al., the mean of FBS in group 1 was 133 ± 41 mg/dl and in group 2 was 142 ± 46 mg/dl which showed P value = 0.03 [8].

From previous studies, Hyperglycemia leads to a diversion of surplus glucose via an active polyol pathway that impairs brain Na+/K+-ATPase, producing intra-axonal Na+ buildup, which in turn leads to failure of the energy-dependent axonal Na+/K+ pump. HbA1c indicates glycemia over a period of two to three months. Elevated HbA1c readings are often linked with greater diabetes complications, such as neuropathy [11].

5. LIMITATION OF STUDY

The small size of studied group and short duration of follow up.

CONSENT

As per international standard or university standard, parental(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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