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A COMPARATIVE STUDY OF CHANGES IN IMMUNOGLOBULINS LEVELS IN PATIENTS WTH IDDM 1 AND NIDDM 2 TYPES OF DIABETES

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Abstract

Diabetes mellitus (DM) is defined as a disease that results from an increase in the level of glucose in the blood (Hyperglycemia) over the normal level as a result of lack or reduction of insulin hormone secretion (from the beta cells of islets of Langerhans located within the pancreas) of most vertebrates. Also, it occurs if there is a weakness in the insulin mechanism of action, or both together. In addition, the defect in the Insulin receptors as a result of epidemiological genetic disorders. Diabetes mellitus is caused as a result of the deficiency of β cells in the pancreas, so the production of insulin by these cells is either little or no, and this is known as Type 1 diabetes mellitus insulin-dependent diabetes mellitus (IDDM 1). The body's use of insulin correctly (insulin resistance) is known as type 2 diabetes mellitus noninsulin-dependent diabetes mellitus (NIDDM 2). The work aims to Evaluate some immunological indicators and knowledge of the immunological effects of type 1 diabetics and knowledge of the relationship of age, sex, and duration of disease for patients.

Key Words: Diabetes Mellitus, Immunology, type 2 Diabetes and Immunoglobins

INTRODUCTION:

Diabetes mellitus (DM) can be defined as a disease that results from an increase in the level of glucose in the blood (Hyperglycemia) over the normal level as a result of lack or reduction of insulin hormone secretion (from the beta cells of islets of Langerhans located within the pancreas) of most vertebrates. Also, it occurs if there is a weakness of insulin mechanism of action, or both together. In addition, the defect in the Insulin receptors as a result of epidemiological genetic disorders (Crespilho et al., 2011).

The first type of diabetes is caused by a lack of insulin secretion, due to the loss and destruction of beta cells in the pancreas. It is considered a disease that requires lifelong treatment with external insulin, because without insulin production, the body will lose its ability to use carbohydrates as an energy source (Abu-Lebdeh and Mair, 1996).

A recent statistical analysis indicated that the number of people with diabetes might exceed 347 million people all over the world, and the data indicated that in the year 2004, about 3.4 million people died of diabetes, and more than 80% of the deaths of people with this disease occur in low-lying countries.

Many studies have shown that type 1 diabetes mellitus (T1DM) is a pattern that affects children and adolescents, and it affects four million people annually in the world with a material cost of up to 160 million US dollars, all spent on treatment and medical care. The high prevalence of this disease affects a certain percentage of the income and health of society (Achenbach et al, 2009).

Diabetes mellitus is caused as a result of the deficiency of β cells in the pancreas, so the production of insulin by these cells is either little or no, and this is known as Type 1 diabetes mellitus insulin-dependent diabetes mellitus (IDDM 1). The body's use of insulin correctly (insulin resistance) is known as type 2 diabetes mellitus noninsulin-dependent diabetes mellitus (NIDDM 2). The function of the insulin hormone is to work on regulating the concentration of sugar in the blood. Diabetes mellitus It results from lack of control or lack of use of insulin in an organized manner, which affects the blood sugar level, and over time, major complications occur that affect the functions and components of body tissues (Abdella and Moussa, 1998).

MATERIALS AND METHODS:

The study samples included 300 patients who visited Yarmouk Teaching Hospital and some external laboratories in Baghdad governorate, during the period from 1/12/2021 to 1/4/2022, and the

studied samples were divided as indicated in (Table 1)

Table 1: List of sub-groups of the three main study groups

ITEM	IDDM 1	IDDM 2	CONTROL
Age	Number		
< 20	20	20	20
20:40	25	25	25
40:65	30	30	30
> 65	25	25	25
Weight	Number		
< 50	10	15	15
50:59	15	10	10
60:69	20	25	25
70:79	25	25	25
> 80	30	25	25

Five mL of a blood sample was drawn by a medical syringe from the venous blood of the subjects under study and serum was separated by centrifugation at 3000 rpm for 5 minutes. Sera were kept under freezing at -20^{o}C until used (Lewise et al., 2001).

All analyses of immunoglobulins were done based on single radial immunodiffusion using the appropriate kits for accurate and reproducible results (LTA s.r.l. company, Via Milano 15/F 20041, Bussero MI, Italy). The standard method was followed according to the instructions provided by the kits-producing company as follows:

1. The cover was removed from the plate and left at room temperature for a few minutes to allow the condensed water droplets in the Wells etching to evaporate.
2. Add 5µl of serum using a micropipette to each hole of the plate (of the sample or the control sample) after it was thawed under room temperature as well and left for a short time to complete absorption and reaction before carrying the plate to another place.
3. The plate was tightly covered with a lid and placed in a damp place at a temperature of about 8^{o}C for a period of 72 hours. To speed up the decomposition time, these plates were placed at a temperature of 30^{o}C.
4. The results were read after 72 hours of incubation using the Jewelers viewer to determine the diameter of the ring formed around each well. Through the diameter of the ring, we infer the concentration of antibodies and immune complements by the presence of an attachment to each plate containing concentrations that correspond to those diameters.

The statistical analysis was performed to determine the analysis of variance using the one-way ANOVA to measure the significance of variation among and between means of the groups.

RESULTS:

The measurements of the immunoglobulins concentration indicated a significant increase in immunoglobulin G (IgG) in patients with IDDM 1 and NIDDM 2 of mean values 626.99 and 158.05 mg/dl respectively. While the control group showed a mean value of 483.79 mg/dl (Table 2).

The results also recorded a significant increase (P< 0.05) in the level of immunoglobulin M (IgM) concentration in patients with NIDDM 2, as its concentration mean value was 144.50 mg/dl while the control group showed 120.71 mg/dl. On the other hand, the concentration recorded in patients with IDDM 1 showed a significant decrease (P<0.05), as it reached (81.38) mg/dl compared with the control group as indicated in Table 2.

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Table 2: Levels of immunoglobulins in patients with IDDM 1 and IDDM 2 mellitus and the control individuals

GROUPS	IMMUNOGLOBULINS CONCENTRATION (mg/dl, Mean ± Standard Error)		
	IgG	IgM	IgA
IDDM 1	280.09 ± 27.57	81.38 ± 6.73	280.09 ± 27.57
NIDDM 2	220.09 ± 21.00	144.50 ± 7.40	220.09 ± 21.00
Control	188.38 ± 11.82	120.7 ± 19.60	188.38 ± 11.82

* Significant difference at P<0.05

At the same time, the IgA concentration rose to its highest level in patients with IDDM 1, and this rise was significant (P<0.05), as it reached 280.09 mg/dl, compared with each of the patients with NIDDM 2 and the control individuals, as its value reached 220.09 and 188.83 mg/dl. while its level increased significantly in patients with NIDDM 2 compared with the control group (Table 2).

Regarding IgG concentration in patients of IDDM 1 in the third (≥ 40-65 years) and fourth (≥ 65 years) age groups only, its concentration reached 584.87 and 277.80 mg/dl respectively. The level of IgG concentration in IDDM 1 patients also recorded a significant increase compared

to the control group and for all age groups, except for the fourth age group (≥ 65 years).

The results (Table 4) showed a direct increase in the levels of immunoglobulin IgM in patients with IDDM 1 and NIDDM 2 with advancing age. 104.90, 140.63, and 140.72 mg/dl compared to the control group (90.65), (130.26), (132.80) mg/dl, at the time when its concentration levels in type 1 patients recorded a significant decrease compared to patients with the second type and control group for all age groups.

Results also showed that there is a decrease in the levels of total IgA concentration with advancing age in patients with type 1 and type 2 diabetes and for all age groups. 262.2, 231.23, and 173.02 mg/dl compared with the control group 197.80, 168.23 and 160.63 mg/dl respectively. As for patients with IDDM 1, the mean concentrations of IgA were significantly higher compared with the control group in the first and third age groups (506.20 and 220.00 mg/dl) respectively, while the fourth and third age groups recorded a mean IgA concentration in each of them (143.30) mg/dl decreased with the control group.

The results in table (Table 4) for measuring the levels of immunoglobulins showed that the concentrations of IgG, IgM and IgA in uninfected people decreased, significantly in the male group, as their concentration rates reached 464.94, 109.37, 179.46 mg/dl, respectively. Compared with uninfected females, whose average concentrations were 503.00, 130.63, and 197.30 mg/dl. The results came with non-significant decreases in the concentration of the studied globulins in males compared to females.

The results in Table 4, indicate the level of immunoglobulins IgG, IgM, and IgA in patients with IDDM 1, males and females, showed low levels of concentrations of these globulins in males, as they amounted to 512.01, 80.86, and 21.56 mg/dl compared to In females with type 1 diabetes, which reached 758.40, 81.90 and 232.68 mg/dl, this decrease was significant at $P<0.05$ in condition of level of IgG in males only.

When measuring the concentration levels of immunoglobulins IgG, IgM, and IgA in males with NIDDM 2, a significant decrease appeared, as they reached 1089.76, 136.84, and 229.64 mg/dl respectively, compared with the

concentrations recorded in females with diabetes. In the NIDDM 2, which reached

Table 3: Relationship of immunoglobulins with age levels in patients with IDDM 1, NIDDM 2, and the control individuals

GROUP	AGE (years)	IMMUNOGLOBULINS ONCERNTRNTRATION (mg/dl, Mean ± Standard Error)		
		IgG	IgM	IgA
IDDM 1	**≤ 20**	261.50 ± 86.63	51.50 ±13.23	206.20 ± 10.85
NIDDM 2		191.9 ± 71.2	43.11 ± 16.71	211.0 ± 30.9
Control		366.3 ± 69.25	89.75 ± 16.33	223.80 ± 12.74
IDDM 1	**≥ 20-40**	121.20 ± 14.5	58.10 ± 11.28	180.77 ± 0.21
NIDDM 2		105.66 ± 12.89	43.4 ± 12.90	123.9 ± 22.5
Control		122.0 ± 20.11	63.1 ± 10.9	120.11 ± 0.11
IDDM 1	**≥ 40-65**	321.20 ± 63.20	74.50 ± 7.60	221.01 ± 22.00
NIDDM 2		519.00 ± 76.97	104.90 ± 11.5	262.2 ± 44.93
Control		446.60 ± 56.35	90.65 ± 17.38	197.80 ± 24.37
IDDM 1	**≥ 65**	2778.80 ± 81.5	109.40 ± 22.27	143.30 ± 24.21
NIDDM 2		564.95 ± 160.52	140.72 ± 22.07	173.02 ± 36.54
Control		411.50 ± 163.0	132.80 ± 12.41	160.63 ± 8.66

* Significant difference at P<0.05

Table 4: Relationship of levels of immunoglobulins with gender of patients with IDDM 1, and IDDM 1 and control individuals

GROUPS	GENDER	COMPLEMENT COMPONANT CONCENTRATION (mg/dl, Mean ± Standard Error)		
		IgG	IgM	IgA
IDDM 1	Male	512.01 ± 47.09	411.00 ± 31.0 12.57 ±80.8±	321.56 ± 45.48
	Female	758.40 ± 67.22	81.90 ± 2.45	232.68 ± 24.15
NIDDM 2	Male	508.9 ± 59.68	136.84 ± 10.18	229.64 ± 31.90
	Female	149.10 ± 125.80	151.21 ± 10.67	211.72 ± 28.60
Control	Male	464.94 ± 44.67	109.37 ± 13.95	179.46 ± 19.95
	Female	503.00 ± 32.92	130.63 ± 13.13	197.30 ± 13.03

* Significant difference at P<0.05

Table 5: Relationship of the weight with levels of immunoglobulins in patients with type 1 and type 2 diabetes mellitus and the control individuals

GROUPS	WEIGHT (Kg)	IMMUNOGLOBULINS CONCERNTRNTRATION (mg/dl, Mean ± Standard Error)		
		IgG	**IgM**	**IgA**
IDDM 1	**≤ 50**	721.20 ± 8.11	30.90 ± 0.98	475.25 ± 128.72
NIDDM 2		623.20 ± 9.00	21.90 ± 0.53	305.25 ± 108.72
Control		397.33 ± 8.92	80.33 ± 0.23	143.3 ± 104.00
IDDM 1	**≥ 50-59**	721.2 ± 10.11	58.90 ± 0.43	314.20 ± 110.0
NIDDM 2		692.11 ± 7.33	51.12 ± 0.11	311.12 ± 102.1
Control		759.0 ± 8.09	50.89 ± 0.90	305.34 ± 101.0
IDDM 1	**≥ 60-69**	656.70± 124.95	81.10 ± 0.12	285.78 ± 38,77
NIDDM 2		1090.72± 52.68	158.63 ± 0.16	153.65 ± 15.47
Control		411.50 ± 41.00	112.70 ± 6.92	157.66 ± 7.52]
IDDM 1	**≥ 70--79**	603.30 ±48.74	88.34 ± 88.34	275.17±44.18
NIDDM 2		196.15 ± 86.26	128.65 ± 40.03	239.90 ± 54.68
Control		503.30 ± 2.92	121.71 ± 11.83	233.30 ± 9.50
IDDM 1	**≥80**	514.87 ± 65.24	89.70± 7.60	170.55 ± 17.83
NIDDM 2		192.23 ± 21.72	126.34 ± 8.75	316.70 ± 24.34
Control		721.20 ± 24.9	126.98 ± 15.39	252.30 ± 20.1

DISCUSSION:

The results of this study indicate that the averages of each of the IgG and IgA antibodies are higher in patients with both types of diabetes_and the level of IgM, which confirms the existence of a relationship between diabetes mellitus and levels of immunoglobulins. The results of the current study agree with the findings of Akinlade et al. 2004, IgM concentrations in patients with type 2 diabetes mellitus compared with control people. IgM concentrations increased significantly in patients with type 2 diabetes. Type 2 patients compared to patients with type 1 DM.

This study also agreed with the findings of, Plevova et al. (1998), as the results of their studies showed an increase in the concentrations of both IgG and IgA in patients with diabetes in general and an increase in the concentration of IgM. Shanatram et al. (1991) pointed out that the reason for the high level of immunoglobulins IgG, IgM, and IgA in some patients with type 2 diabetes is due to the formation of antibodies that compete with or hinder the action of insulin in the early stages of life.

The level of total immunoglobulin IgG in groups with type 2 diabetes showed a positive relationship with increasing age, as the average of this immunoglobulin was recorded in the third, fourth, and fifth groups, with a significant increase ($P<0.05$).

Type 2 patients. The second is diabetes, as its levels increased compared with the control group, and this increase was significant. Compared with patients with type 1 diabetes in the fourth and fifth age groups only. The level of IgG concentration in type 1 patients recorded a significant increase compared to the control group and for all age groups. Except for the fifth age group, as it recorded a clear decrease Compared with patients with type 1 diabetes in the third and fourth age groups, The level of IgG concentration in type 1 patients also recorded a significant increase compared to the control group and for all age groups. Except for the fourth age group, as it recorded a clear decrease.

The results of the current study showed an increase in the concentrations of IgG, IgM, and IgA antibodies in patients with type 2 diabetes with advancing age, and an increase in the average immunoglobulin IgM (IgM) only in patients with type 1 with advancing age, which confirms the existence of a relationship between diabetes and age.

The results of this study were consistent with the findings of Islam(2006)

who confirmed that the immunoglobulins IgG, IgM in patients with type 2 diabetes are higher than those in the first type and the group of control people, and their concentrations rise at the beginning of the infection from the early stages of life, and this rise continues to decrease with age due to the instability of the sugar level and repeated exposure to the closeness of the levels of immunoglobulins in type 1 patients with control people, which decreases with age, is due to the fact that type 1 patients can control their sugar level within the normal range, and this slight rise is caused by non-compliance with taking insulin on time, or due to the wrong diagnosis of the disease. Or the poor quality of the insulin produced or its poor storage. Borzy (1988) also indicated that the level of total IgM concentration rises with age for both types, and its level is higher in patients with type 2 compared to patients with type 1 and the group of uninfected people, and this is consistent with what was mentioned by Gonzales-Qnintela and others (2008) who indicated There is a difference in the levels of immunoglobulins according to the difference in age, sex, and body mass index (BMI). The level of these globulins is affected by the increase in chronic infections in elderly people. These globulins may be affected by liver disease, smoking, or metabolic disorders as a result of diabetes, so the production of these proteins decreases Van de Wiel and others (1988) showed that the level of concentration of IgG and IgA decreases in patients with type II compared with non-infected people, while the concentration of immunoglobulin IgM does not change significantly compared with the healthy group, indicating the reasons for these changes in people with diabetes due to the long period of high-level Blood sugar, which negatively affects white blood cells and phagocytic cells, and reduces the body's resistance to bacterial infections that weaken the immune system in general. A significant decrease in the concentration of IgM in people with diabetes may be due to hardening of the capillary blood vessels or cases of increased blood viscosity, which reduces blood flow in the vessels. The lack of activity of white blood cells, ultimately leads to a lack of production of antibodies, as the relationship between vascular disease and infection is intertwined.

As Saleh (2011) pointed out, the decrease in the levels of immunoglobulins IgG, IgM, and IgA significantly compared with healthy people is caused by a weak immune system in people with type 2

diabetes due to the large number of infections resulting from repeated infection of the body with bacterial attacks, which causes depletion of the ability of the immune system with age and the length of the infection period.

Conclusion:

Through the results of this study, the following was concluded :

1-rise in levels of immunoglobulins, especially IgG, and the integral part concentration of C3 and C4 in type 2 diabetes patients.

2- There is a direct relationship between diabetes and the age of the infected person, with the rise of IgG and IgM with age, while rates of levels of the integral part C3 and C4

3- IgM levels recorded a decrease in the weight of insulin-dependent diabetes, while the levels of IgG and IgA increased in these patients, and this was evident in the third and fourth age groups, as well as the concentration of C3 and C4 decreased by weight gain Diabetes patients, the decrease was limited to type I patients in the concentration level of the third part of the

4. The level of immune variables in females is higher than that of males

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