

# The Role of Anti-DNA Antibodies & Their Circulating Immune Complexes in the Developments of Diabetes Mellitus Dependent or Non-Dependent on Insulin.

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## Summary:

**Background:** Anti-DNA antibodies (Abs) adversely affect the prognosis of various diabetes mellitus complications.

**Material and methods:** A total of 124 diabetic patients (77 females and 47 males), diabetic patients circulating immune complexes (CICs) were detected and analyzed by Platelets Aggregation test (P.L.A.test) and anti-DNA Abs were also detected by ELISA (MELISA™ Cambridge life sciences plc/ England).

**Results:** The results appeared that from a total of 124 patients the high prevalence of circulating immune complexes (CICs) in IDDM & NIDDM patients afflicted with angiopathy than those without angiopathy.

**Conclusion:** It was concluded that early detection of anti-DNA Abs in the sera of diabetics is important coupled with early treatment thereby avoid long term risks of diabetes macro & micro angiopathy.

**Keywords:** Anti-DNA antibodies (Abs) diabetes mellitus, CICs diabetes mellitus, CICs diabetic nephropathy.

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## Introduction

The pathogenesis of the late diabetic complications is multifactorial. In the last few years a number of studies have focused on the hypothesis that immune reaction are important in mediating vessel injuring in diabetes mellitus.

Circulating immune complexes (CICs) have been also detected frequently in the sera of diabetic patients in association with the presence of micro-angiopathy<sup>(1, 24)</sup>.

Since anti-DNA antibodies were observed to be significantly more frequent in the serum of patient with vascular complication and in particular in patients with overt nephropathy than those without complications which have been present before clinical evidence of vascular complications in patients with type 1 & type 2 diabetes that could be of importance in the pathogenesis or progression of angiopathy<sup>(2, 25)</sup>.

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## Subjects and Methods:

1- **subject:** This study was performed on 124 patients (they were categorized into eight main subdivision, with clear distinction between males and females, as IDDM, NIDDM patients, comparison groups and control group. Representing age group between (9-87) years those patients had been admitted to Al-Mansor and Baghdad Teaching hospitals.

2- **Methods:** five ml of venous blood was drawn from each individual involved in the study to detect anti-DNA-Abs by ELISA and CICs by platelets aggregation (P.L.A) test.

## Results :

The positive results of P.L.A.test in the present study are shown in figures (1) and (2), while figure (3) shows the intermediate results, and figure (4) shows the negative results of P.L.A. test.

The results were examined microscopically (at first) to insure that the degree of platelets aggregation as indicator for the presence of CICs. The results show also the high prevalence of CICs detected by P.L.A.test in IDDM and NIDDM patients with angiopathy than those without angiopathy respectively at in figure (5).

Table (1) summarized the higher level of anti-DNA-Abs (IU/ml) in IDDM and NIDDM patients with angiopathy than those without angiopathy.

The results show also that there was positive correlation of anti-DNA-Abs (IU/ml) and the titer of CICs detected by P.L.A.test in 8/9 of IDDM patients with angiopathy group afflicted with

nephropathy ( $r= 0.794$ ,  $P<0.05$ ) while negative correlation were found with two previous parameters (anti-DNA-Abs and CICs) in NIDDM patients with angiopathy ( $r= -0.282$ ,  $P>0.05$ ).

#### Discussion:

Platelets aggregation test (P.L.A.test) was used in the present study to measure and determine circulating immune complexes (CICs) in diabetics to look for association between immune complexes levels and the clinical course or prognosis of a given disease (e.g. late complications of D.M. that are presented)<sup>(3)</sup>.

The percent of low number with positive results of P.L.A.test in the present study agreed with that reported by<sup>(4)</sup>, who mentioned that equivalence state when both Antigen (Ag) and Antibody (Ab) ratios near equivalence will be uncommon and usually transient, result in larger complexes (precipitates) that reach undetectable levels.

In this case these deposited CICs can not also be detected by P.L.A.test if only when they are found in soluble form in cases of Ag excess.

While the presence of negative results of P.L.A.test suggests the possible existence of locally deposited IC<sup>(5)</sup>.

Consequently, the presence of false positive results in P.L.A.test was not excluded in apparent work suggests that patients with auto-immune disease (D.M.) may had auto-Abs to components of the test system itself, likewise P.L.A. can be induced by anti-platelet-Abs in the absence of ICs or non specifically aggregated IgG producing false positive results<sup>(6,7,8)</sup>.

Results in figure (6) show that human vascular disease may act via immunological pathways suggesting a possible role of CICs in the pathogenesis of development complications of D.M.<sup>(9,10,11,12,13)</sup>. While the presence of CICs in control group in the present study is in agreement with that reported by<sup>(14, 24)</sup>, the prevalence of Ag Ab complex that have been found in normal subjects vary according to the test used and reflect in part the criteria chosen for limit of positivity.

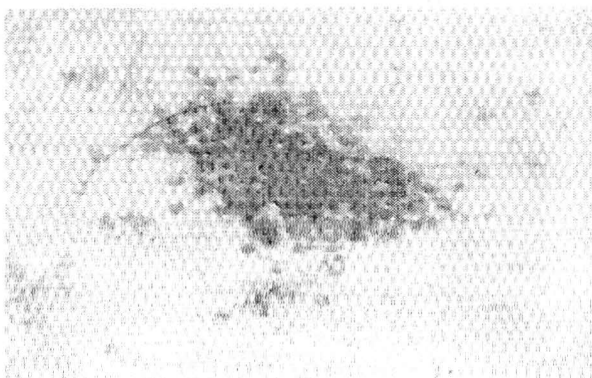
Results shown in table (1) agreed with that reported by<sup>(15)</sup>, that titer of anti-DNA-Abs was higher in patients with longer duration of D.M who tended to posses diabetic compliations that may formed as result of tissue destruction induced by diabetic angiopathy. Such tissue destruction may be directly caused by high blood glucose or other metabolic abnormalities.

Also, results showed that positive correlation between concentration of angiopathy and the titre of CICs, suggested with that reported by<sup>(12,16,17)</sup>, that CICs and auto-Abs were statistically associated in IDDM and its developments especially in diabetic nephropathy that are present in diverse auto-immune etiology of type I diabetes<sup>(10,18,19,26)</sup>.

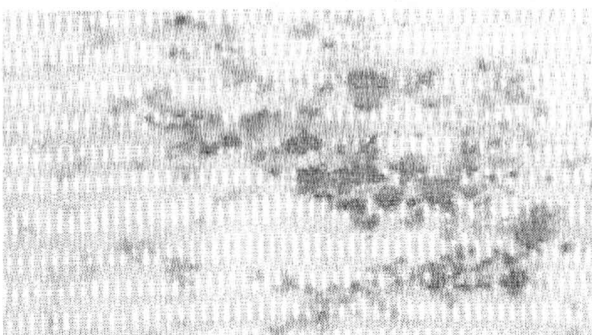
While negative correlations of such previous parameters, suggested that metabolic abnormalities may be associated with the development of diabetic complications rather than auto-immune abnormalities these results agreed with that reported by some researchers that most NIDDM patients are obese, hypertensive, and with metabolic abnormalities are likely to increase their risk of development macro and micro-vascular complications<sup>(20,21,22,23)</sup>.



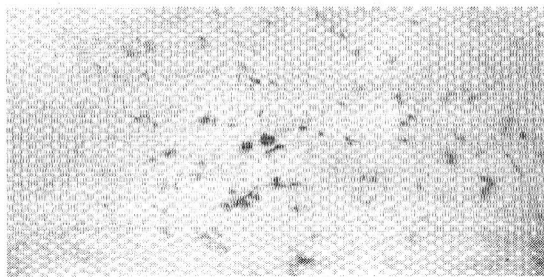
**Fig. (1) The positive result of PL.A. test (+++) under power 40x objective.**



**Fig. (2) The positive result of PL.A. test (++) under power 40x objective.**



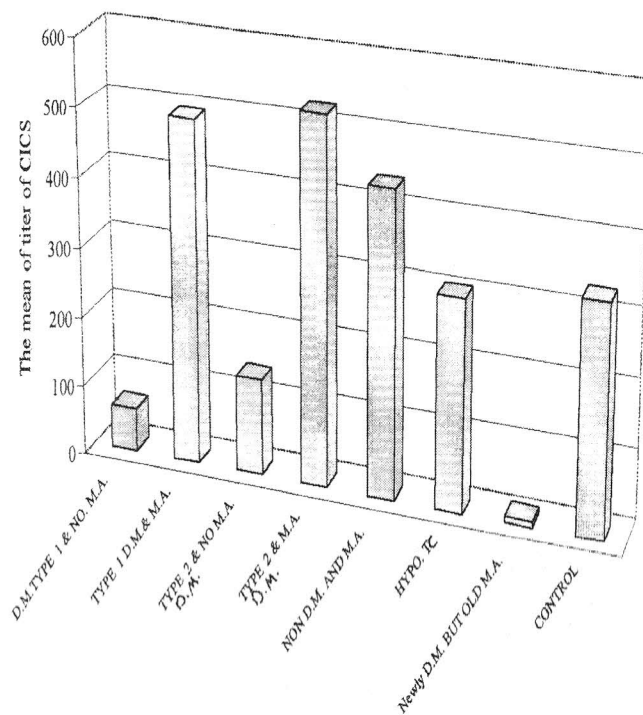
**Fig. (3) The intermediate result of PL.A. test (±) under power 40x objective**



**Fig. (4) The negative result of PL.A. test (-) under power 40x objective**

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**Fig. (4) The prevalence of CICs detected by PL.A test among different study groups**

No.	Group	No	Age (yr.) mean ± sd	FBG (mg/dl)	F.H. of D.M.	Duration of D.M. days	Anti-DNA-Abs IU/ml	Range of anti DNA Abs IU/ml	Pervalence of anti-DNA Abs	p
1.	IDDM +no-angiopathy	13	19.61 ± 8.42	362.15 ±175.5	6/13	300 ± 529.8	53.646± 13.20	35.5-88.6	1/13	>0.05
2.	IDDM + angiopathy	9	34 ±21.66	365.77±156.77	5/9	3177.7±1982	114.12±88	33.6-193.6	5/9	>0.05
3.	NIDDM+No-angiopathy	8	48.5±13.72	300.6±123.67	5/8	687.28±798.8	37.38±12.2	28.2-48.9	1/8	>0.05
4.	NIDDM+ angiopathy	27	58.44±8.08	281.2±90.56	13/27	4840.98±2853	50.96±24.82	22.7-123.8	3/27	>0.05
5.	Non diabetic+angiopathy	18	52.38±16.84	_____	10/18	_____	66.25±48.36	30.2-235.8	4/18	>0.05
6.	Hypocholesterolemic	27	55.59±12.8	195.69±119.94	8/27	1236.7±2100	82.07±104	28-235.8	7/27	>0.05
7.	Newly diagnosed diabetes type 2 with old angiopathy	11	59.81±12.7	252.27±69.9	6/11	49.63±105.98	40.59±10.76	22.7-59.4	0/11	>0.05
8.	Control	11	38.72±11.63	_____	5/11	_____	68.93±47.35	37.7-204.3	2/11	>0.05

Data are means ± Sd.

F.H.: Family History.

F.B.G.: Fasting blood Glucose.

**Table (1) The prevalence of anti-DNA Antibodies IU/ml in different study groups**