

COMPARISON OF LEVELS OF IgG, IgA, AND IgM IN DIABETIC PATIENTS WITH DIFFERENT GLYCEMIC CONTROLS

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ABSTRACT

Immunoglobulins G, A, and M have been reported to be present in statistically significant higher levels in diabetic patients compared to healthy controls. It may be conceived that the levels of immunoglobulins might be significantly higher in diabetics with long-lasting (months of) poor control than in peers with an equally long term period of good control. To assess this possibility, we measured and compared serum levels of IgG, IgA, and IgM in two diabetic populations; one consisting of 27 patients with mean values of at least monthly-measured fasting plasma sugars during the 3 months prior to the study of 140 mg/dL or less, and the second group consisting of 34 diabetics with mean levels of fasting plasma glucoses for each patient during the same interval in excess of 160 mg/dL. We found that, while the mean blood sugars were remarkably different between the groups ($P < 0.001$), the difference between mean values of serum immunoglobulins were not statistically significant (P -values more than 0.3, 0.8, and 0.8 for IgG, IgA, and IgM, respectively). We conclude that no relationship exists between long-lasting glycemic controls and serum immunoglobulin levels in diabetics.

Key Words: Diabetes mellitus, glycemic control, immunoglobulins

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INTRODUCTION

In an initial investigation, we found higher levels of IgG, IgA, and IgM in type 1 diabetics in comparison with those obtained from healthy controls.¹ We assumed that possible immuno-inflammatory abnormalities^{3,4} were the underlying cause for the elevated immunoglobulins in our patients with IDDM and its complications, and that these abnormalities might have either a role in the genesis of type 1 diabetes and its complications or may themselves be a complication thereof.¹ In a subsequent study in type 2 (non-insulin-

dependent) diabetes mellitus, a chronic hyperglycemic disorder in which autoimmunity does not play a role in pathogenesis, similar abnormalities were demonstrated.⁴

Our findings of hyperimmunoglobulinemia both in type 1 and type 2 diabetes mellitus suggested that the shared metabolic disturbance (i.e. chronic hyperglycemia) was the underlying cause for this finding and that hyperimmunoglobulinemia could also be looked upon as a possible complication of diabetes mellitus.⁴ With this consideration, we found it of interest to see if there is any difference in immunoglobulin levels in diabetic patients with long-term (months of) different glycemic controls.

PATIENTS AND METHODS

Twenty-seven consecutive diabetic patients with means

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of at least monthly-measured fasting plasma sugars during the preceding 3 months of 140 mg/dL or less, were selected as group A. Thirty-four consecutive diabetics with means of at least monthly-measured fasting plasma glucoses for each patient for 3 successive months prior to the study in excess of 160 mg/dL were selected as group B. Careful clinical as well as routine paraclinical studies had excluded any diabetic patients with evidence of recent infections or history of chronic infectious diseases. Furthermore, patients with a history of drug addiction,⁵ any accompanying pulmonary or hepatic disease, or any clinical problems unrelated to diabetes mellitus or its known complications were not included in the study. Serum immunoglobulin concentrations were measured by radial immunodiffusion technique⁶ with a modified standard procedure as described elsewhere.^{1,4} Student's *t* test was employed for statistical analysis.

RESULTS

In group A, there were 27 patients, 13 male and 14 female, with a mean age at diagnosis of 39.15 ± 16.12 years (mean \pm SD), with a range from 9 to 72 years. The duration of disease (mean \pm SD) for the same group was 5.13 ± 4.21 , with a range of 0-13 years.

In group B, there were 16 males and 18 females, making a total of 34 patients, with a mean age at diagnosis of 40.12 ± 12.85 years (mean \pm SD), with a range from 4 to 62 years. The duration of disease for the same group was 6.94 ± 4.67 years (mean \pm SD), with a range of 0-20 years.

As seen in Table I, while the mean of monthly plasma glucoses was remarkably different between the groups (117.50 ± 24 versus 221.50 ± 42 mg/dL, $P < 0.001$), the difference between mean values of serum immunoglobulins were not statistically significant. As demonstrated, for IgG, the mean value for group A was 16.50 ± 4.50 gm/L (mean \pm SD) as compared with 16 ± 4 gm/L for group B ($P > 0.6$). IgA had a value of 3.5 ± 1.5 gm/L (mean \pm SD) in group A and 3.5 ± 5 gm/L in group B ($P > 0.9$). IgM values were 3 ± 0.5 gm/L and 2.5 ± 3.5 gm/L (mean \pm SD) for groups A and B, respectively ($P > 0.5$). Furthermore, correlation studies did not reveal any relationship between plasma sugars and immunoglobulin levels in either group.

The comparison of the frequencies of serum levels of IgG in the two diabetic groups is depicted in Fig. 1-A; as seen, the proportions are almost identical for both.

Fig. 1-B illustrates that, in the case of IgA, while group A had higher frequencies for levels up to 3.55 gm/L, group B exceeded in proportions at higher serum levels.

The comparison of the frequencies of serum levels of IgM between the two groups is demonstrated in Fig. 1-C. As seen, both groups share almost similar frequencies.

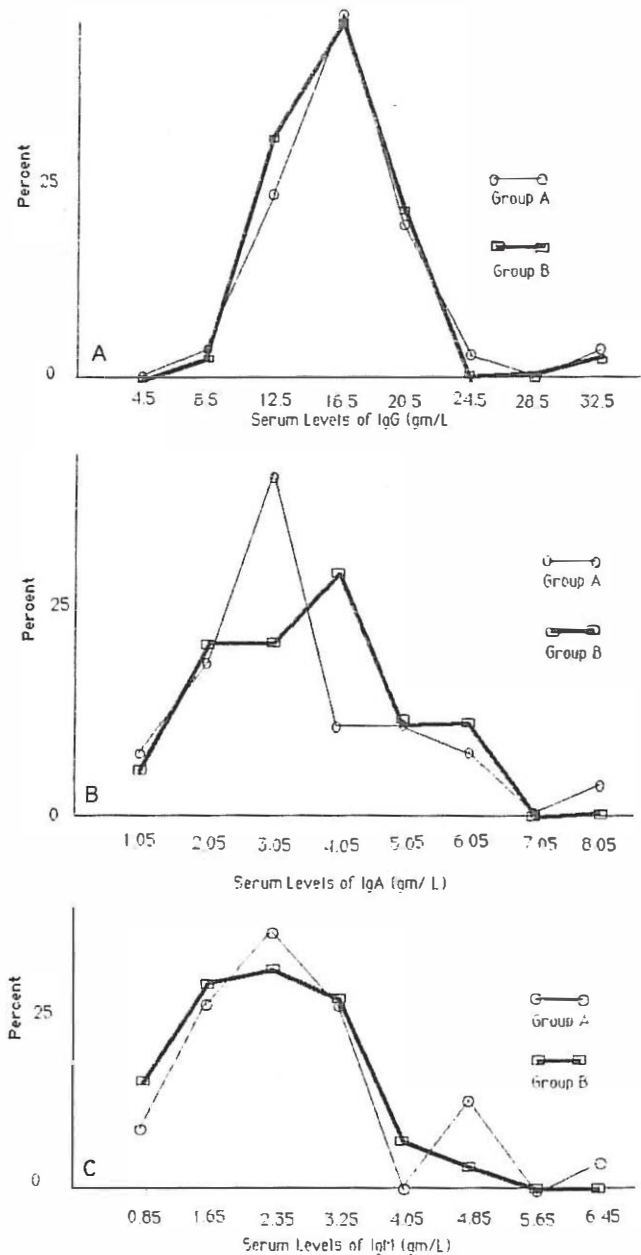


Fig 1. Comparison of the frequencies of serum levels of IgG (A), IgA (B), and IgM (C) in the two diabetic groups.

DISCUSSION

Our previous studies on immunoglobulin levels in diabetics have revealed higher levels of IgG, IgA, and IgM in patients compared to healthy controls.^{1,4}

This study was designed to compare immunoglobulin levels in two groups of long-lasting well- and long-lasting poorly-controlled diabetics.

Rodriguez-Segade, et al. in their investigation of the

Table I. Serum immunoglobulin concentrations and mean of fasting plasma glucoses in the two diabetic populations.

	Study Group*	Mean \pm SD**	Range**	P- value
IgG	Group A	16.50 \pm 4.5	1.25 - 30.5	NS
	Group B	16 \pm 4	9 - 30.5	
IgA	Group A	3.5 \pm 1.5	1.5 - 8	NS
	Group B	3.5 \pm 5.00	1.50 - 6.50	
IgM	Group A	3 \pm 0.50	1 - 6	NS
	Group B	2.5 \pm 3.50	1 - 4.50	
FBS**	Group A	117.5 \pm 24	72 - 133.50	< 0.001
	Group B	221.50 \pm 42	158.5 - 330.5	

* Group A = fairly well-controlled diabetic patients.
Group B = diabetic patients in relatively poor control.
** Mean of at least monthly fasting plasma glucoses from 3 months prior to study.
Figures have been rounded to the nearest digits or their fifth tenths.
NS = not significant.

effect

fructosamine demonstrated significant correlations between the concentration of fructosamine and IgG, IgA, and IgM.⁷ But partial correlation studies between fructosamine and various serum proteins revealed that, concerning the relationship between fructosamine and each of the three immunoglobulins, only IgA demonstrated significant correlation.⁷ Singh and Kulig also demonstrated a significant correlation between fructosamine and IgA in diabetic patients.⁸

While there are numerous studies in regard to the levels of glycosylated immunoglobulins and their relationships with either fructosamine (two week average glycemia⁹) or glycosylated hemoglobin (six to eight week average glycemia¹⁰), to our knowledge there has, as of yet, been no investigation regarding the levels of total immunoglobulins in diabetic patients in relation to long-term (months of) glycemic control. In this work we measured total immunoglobulins G, A, and M by radial immunodiffusion technique (the simplest

and most direct method for quantitation of total immunoglobulins⁶) and demonstrated that, contrary to expectation, serum levels of immunoglobulins were not significantly different in diabetics with long-term (months of) poor control when compared with well-controlled peers. In a subsequent study on still a larger group of diabetics, when means of blood sugars were replaced by HgA_{1c} levels, similar results were demonstrated (Pishdad et al, unpublished). We therefore conclude that although hyperimmunoglobulinemia may be seen in both types of idiopathic diabetes mellitus,^{1,4} the magnitude of chronic (months of) hyperglycemia probably does not influence its degree.

REFERENCES

1. Pishdad GR, Hosseini Jaddae H, Ghalambor MA: Determination of the immunoglobulins in the sera of insulin-dependent diabetic patients. *Iranian Journal of Medical Sciences* 16: 156-161, 1991.
2. Drell DW, Notkins AL: Multiple immunological abnormalities in patients with type 1 (insulin-dependent) diabetes mellitus. *Diabetologia* 30: 132-143, 1987.
3. Eisenbarth GS: Type I diabetes mellitus: a chronic autoimmune disease. *New Eng J Med* 314: 1360-7, 1986.
4. Pishdad GR, Hosseini Jaddae H, Ghalambor MA: Hyperimmunoglobulinemia as a possible consequence of hyperglycemia. *Iranian Journal of Medical Sciences* 17: 32-38, 1992.
5. Cushman P, Grieco MH: Hyperimmunoglobulinemia associated with narcotic. *Am J Med* 54: 320, 1973.
6. Fahey JL, McKelvey EM: Quantitative determination of serum immunoglobulins in antibody-agar plates. *J Immun* 94: 84-94, 1965.
7. Rodriguez-Segade S, Lojo S, Camina MF, et al: Effects of various serum proteins on quantification of fructosamine. *Clin Chem* 35: 134-138, 1989.
8. Singh J, Kulig KA: Effects of albumin and immunoglobulin A on fructosamine assay. *Clin Chem* 38: 824-830, 1992.
9. Armbruster DA: Fructosamine: structure, analysis, and clinical usefulness. *Clin Chem* 33: 2153-63, 1987.
10. Goldstein DE, Little RR, Wiedmeyer HM, et al: Glycosylated hemoglobin: methodologies and clinical applications. *Clin Chem* 32 (Suppl B): 64-70, 1986.