The Turkish Journal of Pediatrics 32: 175-182, 1990

SERUM IgD CONCENTRATIONS IN IMMUNODEFICIENCY DISEASES*

*Özden Sanal MD***, *Fügen Ersoy MD****, *İlhan Tezcan MD*****
İhsan Yeniay ******

Summary: Sanal Ö, Ersoy F, Tezcan İ, Yeniay İ. (Immunology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Serum IgD concentrations in immunodeficiency diseases. Turk J Pediatr 32: 175-182, 1990.

Serum IgD levels were determined in 66 patients with well-defined primary immunodeficiency diseases. The two major groups of patients consisted of those with ataxia-telangiectasia (38 patients) and those with selective IgA deficiency (11 patients). The ataxia-telangiectasia patients tended to have higher serum IgD levels while no significant difference was found in the serum IgD levels of the selective IgA deficiency patients when compared with the controls. No correlation was found between the IgD levels and the presence of frequent infections in both patient groups or the associated disorders present in the selective IgA deficiency patients. The percentage of low serum IgD phenotype in the normal subjects was similar to that described in the literature. *Key words: serum IgD, immunodeficiency diseases, low IgD phenotype.*

The role of serum IgD in the immune system is still unclear, and therefore cannot usually be determined routinely in clinical laboratories. There are few studies describing IgD concentrations in immunodeficiency diseases[1-3].

In this study we determined serum IgD concentrations in 66 patients with various primary immunodeficiency diseases.

Material and Methods

Venous blood samples were obtained from 66 patients with well-defined immunodeficiency diseases and from 33 healthy age-matched controls. The study population consisted of patients with immunodeficiency diseases. There were 38 patients with ataxia-telangiectasia (AT), 11 with selective IgA deficiency, five with

* From the Immunology Unit, the Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara.
** Professor of Pediatrics and Pediatric Immunologist, Hacettepe University Faculty of Medicine.
*** Professor of Pediatrics and Pediatric Immunologist, Hacettepe University Institute of Child Health.
**** Instructor in Pediatrics and Fellow in Immunology, Hacettepe University Faculty of Medicine.
***** Pharmacist, Hacettepe University Institute of Child Health.

Supported by the Hacettepe University Research Foundation, Ankara.

common variable immunodeficiency (CVID), five with Hyper-IgM syndrome (HIgM), three with X-linked hypogammaglobulinemia (XLA), one with selective IgM deficiency, one with Chèdiak-Higashi syndrome (CH), one with chronic mucocutaneous candidiasis (CMCC), and one with severe combined immunodeficiency (SCID).

Serum IgD concentrations were measured by the radial immunodiffusion technique using commercial plates (Behringwerke; Germany).

The Mann-Whitney *U* test was used for statistical analysis. Since it has been reported that 13-14 percent of normal individuals also have low serum IgD levels (low serum IgD phenotype)[4-6], the median and geometric mean values and the Mann-Whitney *U* test were calculated either with or without the zero IgD values.

Results

The serum IgD concentrations of the AT patients were found to be significantly higher than the controls ($p = 0.018$; Tables I-III; Fig. 1) by the Mann-Whitney *U* test. Serum IgD was undetectable in nine of 38 AT patients (23.6%) and in six of the 33 controls (18.1%). The difference between these two groups was not significant. Of the 38 patients with AT, 18 had low or undetectable serum IgA levels. Although the number of patients with undetectable IgD levels was higher in the IgA deficiency group than in the normal IgA group (33.3% vs. 15.0%), the difference between these two groups was not found to be significant. In ten families there were 24 AT patients, all siblings. Four of these families had three AT children each, and six families had two AT children each. Of these 24 patients, four patients from three families had undetectable serum IgD levels. Two of three affected siblings in one family had undetectable IgD levels while two patients with undetectable IgD levels had AT siblings with normal IgD levels.

AT patients with normal IgA levels had significantly elevated serum IgD levels when compared with the controls ($p = 0.0001$), while AT patients with IgA deficiency did not differ significantly ($p = 0.3$) when patients with zero IgD levels were included. But when the patients with zero IgD levels were excluded, AT patients with low IgA levels had significantly higher IgD levels than the controls, such as the patients with normal IgA levels ($p = 0.014$; $p = 0.0002$). No significant difference was found between AT patients with normal or decreased IgA levels when evaluated either with or without zero IgD levels. Serum IgD concentrations in AT patients did not show any correlation with the concentration of other Ig isotypes (IgG or IgM) or the presence of recurrent infections.

TABLE I: Serum IgD Concentrations of Patients With Immunodeficiency Diseases

Group	n	Age (yrs)	Serum IgD (u/ml) Range	Median	Geometric mean
Ataxia-telangiectasia	38	4-23	0-440	84.5 (115)*	20.64 (107.8)*
a. normal IgA	20	4-16	0-440	95 (115)	39.44 (113.33)
b. IgA deficiency	18	5-23	0-410	51 (100)	10 (100.38)
Selective IgA deficiency	11	2-10	0-240	15 (47)	4.83 (44.36)
X-linked hypogammaglobulinemia	3	5-18	0-105	0	
Common variable immunodeficiency	5	6-15	0-10	0	
Hyper – IgM syndrome	5	2-17	0-147	0	
Controls	33	2-12	0-120	49 (53)	16.27 (50.3)

* Numbers in parenthesis are the values obtained when zero IgD values were excluded. *Statistical analysis* : AT (total) - control $p = 0.018$, AT (IgA normal) - control $p = 0.0001$, AT (IgA low) - control $p = 0.3$, AT (IgA normal) - AT (IgA low) $p = 0.11$

Since it has been reported that 13-14 percent of normal individuals have low serum IgD levels (low serum IgD phenotype), the Mann-Whitney *U* test was used with or without zero IgD values and the results did not differ statistically except for AT patients with low IgA and the controls.

In the selective IgA deficiency patient group, serum IgD levels and the number of patients with undetectable serum IgD levels did not differ significantly when compared with the controls (36.3% vs 18.1%). Again serum IgD levels did not seem to correlate with other Ig isotypes or associated disorders.

Serum IgD was undetectable in the patients with SCID, HIgM syndrome, CVID and XLA with the exception of one patient in each of the latter three disease groups. However, IgD levels were normal in patients with CH or selective IgM deficiency, and high in patients with CMCC.

TABLE II: Serum Immunglobulin Concentrations of AT Patients With Normal IgA Levels

	Age (yrs)	IgG (mg/dl)	IgM (mg/dl)	IgA (mg/dl)	IgD (u/ml)
MP	8	1130	200	118	0
EK	15	1130	414	162	440
AÖ	15	963	299	210	410
OÇ	5	1000	190	117	188
ÖK	13	1310	88	130	84
IY[a]*	4	1140	160	56	230
MY[a]	9	802	290	118	35
ED	11	1560	200	84	75
SŞ[b]	16	1250	402	135	190
OŞ[b]	15	1370	208	252	115
SY	14	1190	243	162	0
MT[c]	8	1900	290	162	18
ST[c]	7	1250	243	101	125
HT[c]	14	1250	200	144	137
BaB[d]	9	1170	113	110	160
BB[d]	2	1100	167	94	85
NB[d]	21	963	130	42	85
AA[e]	26	1100	110	84	0
KA[e]	6	1650	175	126	63
LÖ[f]		463	184	49	105

* Small letters indicate sibling pairs.

TABLE III: Serum Ig Concentrations of AT Patients With Low IgA Levels

	Age (yrs)	IgG (mg/dl)	IgM (mg/dl)	IgA (mg/dl)	IgD (u/ml)
AE	23	2110	252	0	0
AA[g]	5	1900	445	0	85
OA[g]	13	1250	343	< 42	410
MP	8	1130	200	0	0
DH[h]	11	1430	200	0	0
MH[h]	10	2260	252	0	251
EÇ	16	1690	370	< 42	19
SA	7	2340	448	0	35
IS	9	2260	448	0	199
KAG[k]	5	963	160	< 42	60
AG[k]	6	1500	170	< 42	315
OG	9	1560	243	0	42
GB	6	700	243	< 42	0
ÖT[l]	7	3770	145	< 42	160
ÖzT[l]	8	3770	90	0	0
RA[e]	18	1150	109	< 42	0
ZÖ[f]	10	1300	237	< 42	63
HÖ[f]	9	550	175	< 42	115

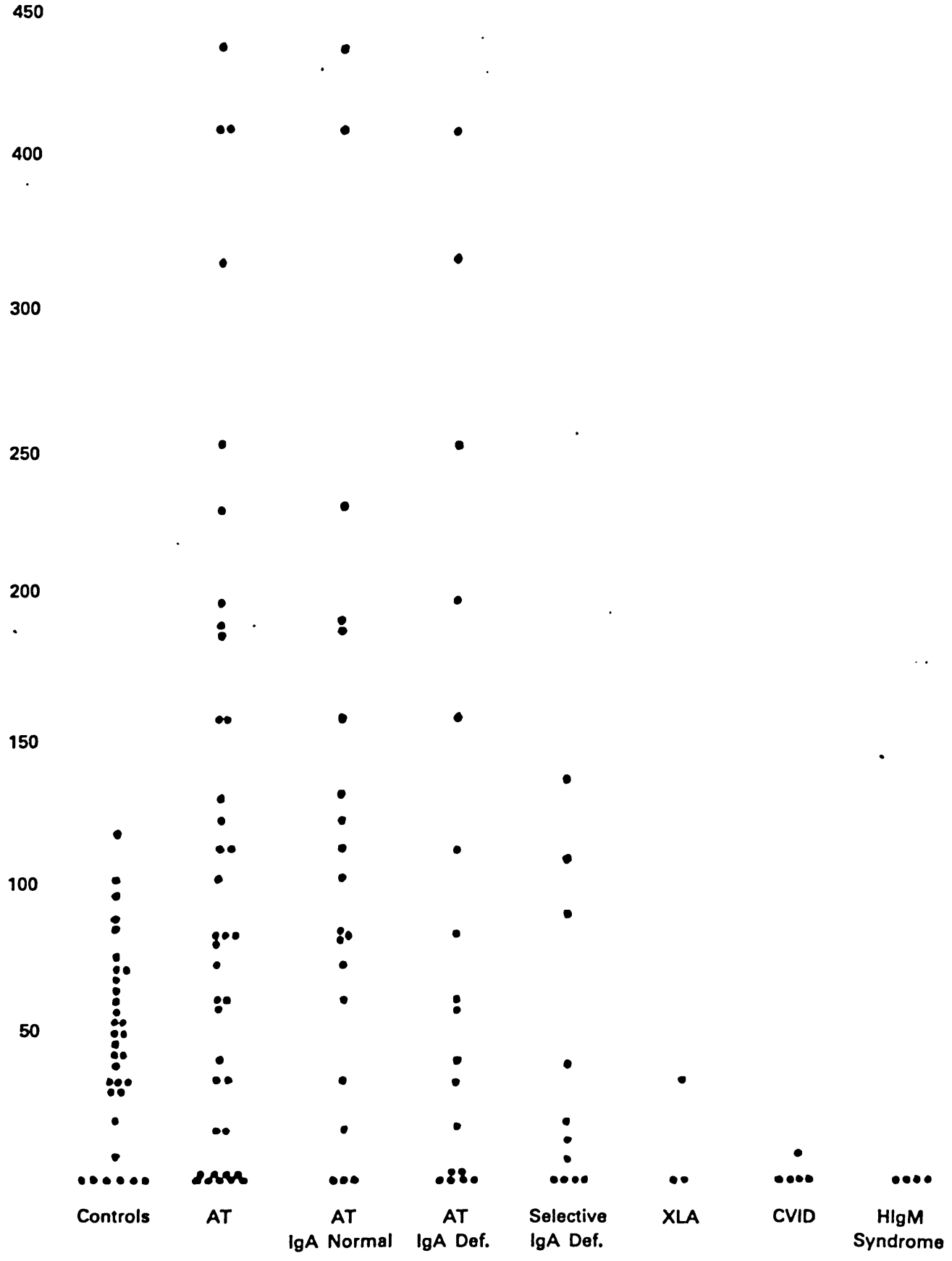

Fig. 1: Serum IgD concentrations (u/ml) in various immunodeficient patients and controls.

Discussion

Since the exact role of serum IgD in the immune system is still unclear, this Ig isotype has been studied less thoroughly than others in various disorders. In this study, we determined IgD levels in 66 primary immunodeficiency patients (38 AT patients) and in 33 healthy age-matched controls. Serum IgD was undetectable in 18.1 percent of normal children, and the percentage of low IgD sera was similar to the values earlier reported[4-6]. Nine of 38 AT patients (23.6%) also had undetectable serum IgD. The difference between the control and patient groups was not significant in this respect. The pattern of segregation of low serum IgD in AT sibling pairs was compatible with a mode of autosomal recessive inheritance of low serum IgD phenotype and with crossing-over. AT patients tended to have higher IgD concentrations, and the difference between controls and AT patients was found to be significant ($p = 0.018$). When AT patients were evaluated according to their serum IgA levels, the number of patients with undetectable serum IgD was higher in the IgA deficient group than in the patients with normal IgA levels (33.3% vs 15%), but the difference was not significant. In contrast to AT patients with normal IgA levels, the IgD values in patients with IgA deficiency did not differ significantly when compared with the controls, but the difference was significant when zero IgD values were excluded. Since low IgD values (low IgD phenotype) have been reported in 13-14 percent of normal individuals, it is impossible to ascertain, without knowing the IgD values of other family members, whether patients have low IgD or come from families with low IgD phenotype. Buckley and Fiscus[1] have reported elevated median IgD values in patients with AT but the difference was not significant. McFarlin et al[2] found high IgD levels in some of their AT patients. Since no difference has been found between patients with high and normal IgD values in respect to frequent infections and levels of IgG or IgM, chronic antigenic stimulation alone does not seem to be responsible for high IgD values. In addition some immunodeficient patients who had recurrent infections did not have high IgD values. Production of specific IgD antibody has been reported infrequently in infection[4]. Increases in serum IgD are not common. Hodgkin's disease and AIDS are among the diseases in which IgD has been found to be high[7-9]. In patients with bacterial and fungal infections (e.g. tuberculosis, leprosy, aspergillosis) IgD may be elevated but no consistent correlation exists between increased IgD and chronic infection[1].

Conflicting results have been reported regarding serum IgD concentrations in patients with selective IgA deficiency. While Buckley and Fiscus[1] found depressed levels, Plebani et al[3] found normal values in this patient group. In the present study, the difference between the patients and control groups was found to be insignificant. Again serum IgD concentrations did not show any correlation with the associated diseases in IgA deficiency patients. Thus our data did not reveal a compensatory increase in serum IgD in patients with IgA deficiency.

REFERENCES

1. Buckley RH, Fiscus SA. Serum IgD and IgE concentrations in immunodeficiency diseases. *J Clin Invest* 55:157, 1975.
2. McFarlin DE, Strober W, Waldmann TA. Ataxia-telangiectasia. *Medicine* (Baltimore) 51:281, 1972.
3. Plebani A, Mira E, Mevio E, et al. IgM and IgD concentrations in the serum and secretions of children with selective IgA deficiency. *Clin Exp Immunol* 53:689, 1983.
4. Dunnette SL, Gleich GJ, Weinshilboum RM. Inheritance of low serum immunoglobulin D. *J Clin Invest* 62:248, 1978.
5. Fraser PA, Schur PH. Hypoimmunoglobulinemia D: frequency, family studies, and association with HLA. *Clin Immunol Immunopathol* 19:67, 1981.
6. Litwin SD, Tse-Eng D, Butler VP Jr, Pernis E. Studies on human low serum IgD phenotype and Gm markers. *Clin Genet* 27:134, 1985.
7. Corte G, Ferraris AM, Rees JK, et al. Correlation of serum IgD level with clinical and histologic parameters in Hodgkin's disease. *Blood* 52:905, 1978.
8. Mizuma H, Zolla-Pazner S, Litwin S, et al. Serum IgD elevation is an early marker of B cell activation during infection with the human immunodeficiency viruses. *Clin Exp Immunol* 68:5, 1987.
9. Papadopoulos NM, Frieri M. The presence of immunoglobulin D in endocrine disorders and diseases of immunoregulation, including the acquired immunodeficiency syndrome. *Clin Immunol Immunopathol* 32:248, 1984.