IgG versus IgG+ IgM anti-double stranded DNA measurement:

A comparative report for clinical practice

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Rheumatology key message:

Serum detection of anti-double stranded DNA antibodies using IgG ELiA assay is more specific in diagnosing serological activity compared to the classic IgM+IgG ELISA assay as it doesn't take into consideration the less pathogenic IgM antibodies.

Dear Editor,

Many different assays have been used to detect serum levels of anti-double stranded (ds) DNA antibodies (Ab) in patients with systemic lupus erythematosus (SLE). For over 30 years, University College Hospital has used an enzyme linked immunosorbent assay (ELISA) (*DIASTAT ELISA assay; FDNA 100*) that is about to become unavailable. It detects IgG and IgM anti-dsDNA Ab. We will now be using an IgG specific automated fluorescence immunoassay (ELiA) (*Phadia 2500 analyser; 14-5500-01*). The choice of the latter was mainly based on the findings that IgG anti-dsDNA Ab is the most pathogenic class in SLE patients (1). Studies even suggest that IgM Ab can have a protective role in lupus nephritis and are associated with lower cardiovascular events (2).

The aim of our work was to compare the clinical use of both assays in our SLE cohort. We therefore collected samples of patients who attended our SLE clinic between October 2020 and February 2021 and for whom both DIASTAT ELISA (assay A) and IgG specific ELiA (assay B) were run.

For efficient comparability, results were classified in 5 ranges: Range 0= Normal range (NR) that is <50 IU/ml for assay A and <10 IU/ml for assay B; Range 1 < 2 times NR; Range 2= [2-5 NR [; Range 3= [5 – 10 NR [; Range 4 ≥ 10 NR. Discrepancy was defined by a discrepancy of at least one level range of assay A versus assay B.

Overall**,** 265 samples, performed in 186 patients, were considered. The mean age was 45 years old [19 – 76]; sex ratio F/M of 11.4. Main ethnicities were Caucasian (42.5%), Afro-Caribbean (27.4%), South Asian (17.2%) and Chinese (5.4%). Disease activity was assessed using the British Isles Lupus Assessment Group (BILAG) 2004 index expressed as a global score (GS) and varied between 0 and 32; 17.5% had a GS ≥12.

Both assays were correlated to the GS ($p<0.0001$); the correlation coefficient was higher in assay B than assay A (34.1% versus 28%). The Correlation coefficient between assay A and B was 82.4%.

A discrepancy was found in 50 samples of 33 patients (18.9 %) (Table1). Among these samples, 11 (4.2%) had levels of assay A which exceeded those of assay B by more than one range, leading to a marked discrepancy (Table1). We assume the anti-dsDNA antibodies in these patients were virtually all IgM.

There was no statistical difference in patients' age, gender, ethnicity and disease activity between samples with and without discrepancy.

Furthermore, among 49 samples taken from patients in full remission (GS=0), 9 had high levels of anti-dsDNA antibodies (> 3 times NR) in either or both assays: Only positive assay A (n=7), only positive assay B (n=1), and both positive assays (n=2).

In light of our findings, we can assume that despite the lack of major added-value of IgG specific ELiA in reflecting SLE disease activity, this assay seems to help differentiating between patients in clinical and serological remission who have high IgM Ab and those serologically active. Hence, the use of this new assay in clinical routine should prevent over treating patients in clinical and serological remission by improving the diagnosis of serological activity.

References:

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2. Grönwall C, Akhter E, Oh C, Burlingame RW, Petri M, Silverman GJ. IgM autoantibodies to distinct apoptosis-associated antigens correlate with protection from cardiovascular events and renal disease in patients with SLE. Clin Immunol. 2012;142:390–8.

Table1: Samples with discrepant anti-dsDNA assays' values

Sample	GS	IgG+IgM (Assay A)		IgG (Assay B)	
		Absolute level	Range	Absolute level	Range
1. *	2	141	2	8.3	0
2. *	2	128	2	8.1	0
3. *	2	127	2	8.7	0
4. *	1	283	3	8.9	0
5. *	0	274	3	13	1
6. *	2	219	2	4.1	0
7. *	0	119	2	3.6	0
8. *	0	12520	4	12	1
9. *	0	5183	4	4.9	0
10. *	1	558	4	37	2
11. *	2	151	2	4.3	0
12.	5	385	3	45	2
13.	2	173	2	18	1
14.	2	204	2	11	1
15.	1	126	2	16	1
16.	0	65	1	6.5	0
17.	2	228	2	18	1
18.	16	464	3	35	2
19.	0	259	3	29	2
20.	17	259	3	26	2
21.	0	71	1	4.4	0
22.	21	461	3	43	2
23.	11	443	3	43	2
24.	23	390	3	30	2
25.	12	185	2	16	1
26.	5	166	2	11	1
27.	2	620	4	95	3
28.	10	58	1	3.2	0
29.	2	59	1	9.9	0
30.	0	67	1	8.9	0
31.	0	468	3	24	2
32.	1	644	4	95	3
33.	0	595	4	75	3
34.	0	101	2	11	1
35.	21	146	2	18	1
36.	14	168	2	13	1
37.	10	169	2	19	1
38.	0	177	2	12	1
39.	10	748	4	61	3
40.	3	559	4	54	3
41.	3	78	1	7.2	0
42.	8	253	3	24	2
43.	9	61	1	2.4	0

44.	3	54	1	4.2	0
45.	3	137	2	18	1
46.	0	73	1	7.1	0
47.	1	504	4	88	3
48.	1	518	4	98	3
49.	1	776	4	88	3
50.	1	53	1	7.4	0

GS: Global score, Assay A: DIASTAT ELISA, Assay B: IgG specific ELiA.
*samples with marked discrepancy

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