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Diagnostic Accuracy of Anti-dsDNA Antibody Tests for the Diagnosis of Systemic Lupus Erythematosus – Systematic Literature Review

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INTRODUCTION AND AIM

Anti-dsDNA antibodies play an important role in the diagnosis and classification of Systemic Lupus Erythematosus (SLE). It forms part of the 1997 American College of Rheumatology (ACR) revised classification criteria(1) and the 2012 revised criteria for the diagnosis of Systemic Lupus Erythematosus from the Systemic Lupus International Collaborating Clinics (SLICC)(2). However, the diagnostic accuracy of anti-dsDNA may be dependent on the method and commercial test used.

Depending on the detection method used, anti-dsDNA antibodies of low, intermediate or high avidity can be measured. There is evidence that anti-dsDNA antibodies of high avidity are more specific for lupus(3).

The objective was to provide an overview of the diagnostic accuracy of anti-dsDNA antibodies tests for diagnosis of SLE.

MATERIALS AND METHODS

A systematic literature review was conducted to identify any studies that provided information on the diagnostic accuracy of dsDNA tests for the diagnosis of systemic lupus erythematosus (SLE). The search strategies were designed and performed by an experienced medical librarian. Electronic database searches (Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE®, Embase, Cochrane Library (Wiley) were supplemented by hand searching of reference lists of studies identified as eligible for inclusion as well as several identified systematic reviews.

For all outcomes the population of interest was patients with suspected or known SLE. The search was limited to published English abstracts between 2004 and June 2015 with no restrictions regarding the study country where studied.

Retrieved citations were screened and the selection reviewed. Outcome data were extracted from the included studies by two review authors and recorded in predefined data extraction forms. Methodological quality of included studies was assessed using the QUADAS-2 tool.

Following the systematic review, a qualitative assessment was performed to compare the diagnostic accuracy of the dsDNA tests for the diagnosis of SLE.

Table 1: Inclusion criteria

Inclusion Criteria.
Studies included: ▪ Subjects with suspected or known systemic lupus erythematosus ▪ Diagnostic Tests for double stranded-DNA (dsDNA) ▪ Tests have to be attributed to a named manufacturer ▪ ACR Diagnosis of SLE only ▪ Sensitivity and specificity reported (data to construct 2x2 table) using the manufacturer's recommended cut-off values ▪ Case-control, cohort and cross-sectional studies (retrospective and prospective) with at least 10 patients enrolled.
Studies omitted: ▪ Reviews, discussion papers, non-research letter and editorials ▪ Qualitative studies ▪ Case studies

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RESULTS

A total of 23 studies out of 1798 papers identified met the criteria for inclusion (table 1) and reported the diagnostic accuracy of 29 anti-dsDNA tests from 24 manufacturers.

Although dsDNA tests were identified from a number of different manufacturers the number of studies reporting the diagnostic accuracy of each test was limited, generally only one data set was available for each dsDNA test. Only nine dsDNA tests had more than one study published.

The diagnostic accuracy of each of the tests using weighted average sensitivity and specificity is outlined in table 2:

- Point estimates of weighted average sensitivity ranged from 36.9 % (QUANTA Lite dsDNA) to 77.1% (Diastat dsDNA).
- Point estimates of weighted average specificity of anti-dsDNA tests ranged from 85.5 % (Orgentec dsDNA) to 97.0% (Euroimmun dsDNA).

The quality assessment showed that the domains “patient selection” and “index test” were considered to be at high risk of bias.

Table 2: Weighted average sensitivity and specificity values of anti-dsDNA antibody tests for which more than one study was published.

Test	Assay	Studies evaluated (n)	Weighted Average Sensitivity	Range	Weighted Average Specificity	Range
Novalite dsDNA	CLIFT	5	60.1	8 – 83	86.9	44 – 100
Immunoconcepts dsDNA	CLIFT	3	42.7	28 – 31	96.9	97 – 100
IIFT Euroimmun dsDNA	CLIFT	2	51.9	32 – 56	97.0	97
Amerlex dsDNA	FARR-RIA	3	65.9	38 – 80	92.8	79 – 98
EliA dsDNA	ELISA	5	61.7	27 – 81	95.2	92 – 97
QUANTA Lite dsDNA	ELISA	3	36.9	30 – 54	96.7	93 –100
Farrzyme dsDNA	ELISA	3	51.0	36 – 70	95.5	95 – 97
Diastat dsDNA	ELISA	3	77.1	71 – 85	94.3	94 – 99
ORG 604 dsDNA	ELISA	2	74.5	63 – 90	85.5	83 – 88

CONCLUSIONS

- **The diagnostic accuracy was found to vary markedly between the anti-dsDNA tests evaluated. Particularly, the sensitivity displayed wide inter- and intra-test variability. This could be an effect of the high risk of bias identified in the “patient selection” domain of the quality assessment.**
- **EliA dsDNA demonstrated a weighted average sensitivity of 61.7% and a weighted average specificity of 95.2%, and it was the only fully-automated test of those evaluated.**

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