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LETTER TO THE EDITOR

Comparison of the Prevalence of Antinuclear Antibody and Subserology in Urban and Rural Settings

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Arguably one of the most commonly ordered autoantibody tests, the antinuclear antibody (ANA) test is frequently used in a variety of medical disciplines including rheumatology.[1] ANA has become a general marker of autoimmunity in clinical practice and is measured in titres and fluorescent patterns.

Although previous studies have investigated the prevalence of ANA positivity in regional/rural areas,[2,3] very limited number of studies have directly compared ANA positivity in rural and urban areas. Hence, we decided to evaluate ANA and its subserologies [anti-extractable nuclear antigens (anti-ENA) and anti-double stranded deoxyribonucleic acid (anti-dsDNA)] in both an urban and rural population of Tasmania, Australia.

The study included a total of 32,600 first-episode ANA tests with any concurrent anti-ENA and-dsDNA tests which were requested for urban and rural patients 10,577 males (32.4%), 22,005 females (67.5%); mean age 49.2 years; range 0 to 99 years) in the north-west rural district and southern urban district laboratories between January 2004 and December 2014. These included both general practice (community) and hospital requests. Duplicate testing were excluded. All ANA tests, performed on the HEp-2000® substrate (Immuno Concepts Inc., Sacramento, CA, USA), were conducted by the same master laboratory and a positive result was deemed at a titre of ≥1:80. The HEp-2000 substrate is similar to the standard HEp-2 substrate but has Sjögren's syndrome A (Ro/SSA) complementary DNA transfected into it to create a unique 'SSA/speckled' pattern on immunofluorescence microscopy. Anti-ENA testing was performed by enzyme-linked immunosorbent assay (Immuno Concepts) and anti-dsDNA testing via EIA (Immuno Concepts) and Farr radioimmunoassay (Siemens Healthcare Diagnostics, Erlangen, Germany). Tests were extracted anonymously and ethics approval to conduct the investigation was granted by the Tasmanian Health and Medical Human Research Ethics Committee.

Approximately two-thirds of the tests originated from the urban center (n=20,765, 63.7%). Though there was slightly higher ANA positivity from the rural center (Table 1), there were no differences when broken down according to patterns. There was, however, a trend for higher-titred ANA being more prevalent in rural areas. Finally, whilst there was no difference in

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Table 1. Comparison of antinuclear antibody and subserologies in an urban versus rural center

	Urban center			Rural center			Value for differences in proportions
	n	%	Mean±SD	n	%	Mean±SD	*p*
ANA cases	20765			11835			
Females*	14274	68.8		7731	65.3		<0.001
Age (years)			49.0±17.6			49.4±18.1	0.051
General practitioner requests	3383	16.3		1988	16.8		0.242
Positive ANA cases	4457	21.5		2662	22.5		0.036
ANA patterns:							
Speckled	1647	36.9		937	35.2		0.149
Homogeneous	1294	29.0		770	28.9		0.928
Nucleolar	99	2.2		560	21.0		0.362
Centromeric	151	3.4		57	2.1		0.779
SSA pattern	151	3.4		115	4.3		0.053
Mixed/miscellaneous	369	8.3		223	8.4		0.883
ANA titres‡							
Low (1:80, 1:160)	2516	57.2		1416	54.0		0.009
Medium (1:320, 1:640)	1362	31.0		857	32.7		0.138
High (>1:1280)	522	11.9		350	13.3		0.085
Anti-ENA requests (concurrent)	3003	14.5		1186	10.0		<0.001
Positive anti-ENA result	139	4.6		65	5.5		0.222
Anti-dsDNA requests (concurrent)	1275	6.1		951	8.0		<0.001
Positive anti-dsDNA result	84	6.6		86	9.0		0.035

SD: Standard deviation; * 18 cases excluded due to unknown sex (newborns with unregistered sex); ANA: Antinuclear antibody; ‡ 96 cases excluded due to equivocal titres; ENA: Extractable nuclear antigen.

anti-ENA positivity, there was higher anti-dsDNA positivity in the rural center (Table 1).

Our results demonstrate that autoantibody positivity tends to be higher in rural areas compared to urban areas. This is in line with one study in a Polish rural community that demonstrated that ANA, anti-ENA, and -dsDNA are proportionally more positive compared to an urban area.[4] Another study of systemic lupus erythematosus patients, however, found no significant difference in ANA and anti-dsDNA positivity between urban and rural patients.[5]

Our results are paradoxical given that epidemiological studies find decreased autoimmune diagnoses in regional areas.[6,7] This indicates that autoantibodies may not be the best surrogate marker for autoimmunity and is congruent with the fact that autoantibodies may be raised in many non-autoimmune states including chronic inflammation. Unfortunately, the epidemiology of autoimmune conditions in Tasmania (Australia) is not available to correlate our results to. This information would be useful in understanding the relationship between autoimmune serology and epidemiology. Certainly, further epidemiological studies of autoimmunity would be of great benefit.

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