The Prevalence of Antinuclear Antibodies in the General Population of China: A Cross-Sectional Study

Ya-Ping Guo, BS[1,†], Chun-Guang Wang, MD[1,†], Xin Liu, MSc[1], Yi-Qian Huang, BS[1], De-Li Guo, BS[1], Xing-Zhuo Jing, BS[2], Chun-Gang Yuan, PhD[3], Song Yang, BS[1], Jin-Mei Liu, BS[1], Meng-Si Han, BS[1], Hong-Xing Li, PhD[1],*

[1] The First Center Hospital of Bao Ding, Baoding, Hebei, China
[2] The Fifth Hospital of Baoding, Baoding, Hebei, China
[3] School of Environmental Science and Engineering, North China Electric Power University, Baoding, Hebei, China

ABSTRACT

Background: The incidence of autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, and primary biliary cirrhosis has increased significantly in China. Information about the susceptibility or potential of autoimmune diseases in the general population is lacking.
Objective: To explore the prevalence of antinuclear antibody (ANA) and its specificities in the general population in China.
Methods: Twenty thousand nine hundred seventy sera samples were taken from the physical examination center in Baoding, China. Indirect immunofluorescence and line immunoassays were used to detect ANA and its specificities, respectively.
Results: Samples from females had a higher prevalence of ANA than samples from males ($\chi^2 = 278.55$; $P < 0.01$). For both sexes, the prevalence of ANA positively correlated with age and there were significant differences among different age groups at 10-year intervals, except the 80 years group ($P < 0.05$). One thousand two hundred forty-three ANA-positive samples were further analyzed with line immunoassays. There was a significant difference among age groups and between sex groups in terms of the specific autoantibodies ($P < 0.01$). The autoantibodies with the top-3 positive frequencies were anti-Ro-52, anti-M2, and anti-SSA.
Conclusions: There was a high prevalence of ANA positivity in the general Chinese population that seemed to be influenced by sex and age and correlated with specific autoantibodies.
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Introduction

The incidence of autoimmune diseases (AIDs) such as systemic lupus erythematosus (SLE), rheumatoid arthritis, and primary biliary cirrhosis (PBC) has been increasing in China.[1,2] Until now, the antinuclear antibody (ANA) test, wherein antibodies are detected by indirect immunofluorescence assay on HEp-2 cells, is commonly used as an initial screening method. The presence of ANA is nonspecific and can be associated with many nonautoimmune factors, such as carcinoma, infection, pharmaceuticals, and environmental factors. As a result, an ANA positive frequency in healthy individuals > 20% has been reported.[3] On the other hand,

ANA may exist several years before an AID can be diagnosed,[4] with higher titer of ANA being correlated closely with a higher risk of the onset of AIDs during adolescence and adulthood.[5–8] The epidemiologic characteristics of AID in different countries and districts varies.[9] To our knowledge, information about the ANA prevalence and the susceptibility or potential of AIDs in the general population of China is lacking. We aimed to evaluate the ANA prevalence in a wide range of the general Chinese population (aged 2–88 years).

Materials and Methods

Study population

To assess the ANA positive rate among the general population of China, we conducted a cross-sectional study. Twenty

* Address correspondence to: Hong-Xing Li, The First Center Hospital of Bao Ding, North Great Wall St 320, Baoding, Hebei 071000 China.
  E-mail address: bdsdyzxyyjyk@163.com (H.-X. Li).
  † These authors contributed equally to this work.

thousand nine hundred seventy sera were taken from the physical examination center in Baoding, Hebei, China, from July 2011 to September 2013 (**Figure 1**). The sample size and male to female ratio conform to the standard of the sixth National Census of China in 2010–2011 (http://www.stats.gov.cn/tjsj/pcsj/rkpc/6rp/indexch.htm). A total of 6800 children (including 3300 girls and 3200 boys) aged from 2 to 18 years were recruited from 3 public kindergartens, 5 middle schools, and 2 high schools. The other participants consisted of 14,170 individuals (7220 women and 6950 men) obtained by random sampling. Participants with established AID were excluded from this study. Informed consent was obtained from all participants. The study complied with the World Medical Association Declaration of Helsinki and was approved by the Ethics Committee of the First Center Hospital of Bao Ding. All data were dealt with in an anonymous way.

Antibody assays

Sera were tested by indirect fluorescence on HEp-2 cells according to the manufacturer's instructions (Euroimmun AG, Lubeck, Germany). Titer $\geq 1:320$ was considered to be positive. As a result, 243 positive samples were further tested by line immunoassay (LIA) (Euroimmun AG) for 15 specific autoantibodies (ie, anti-nRNP, anti-Sm, anti-SSA, anti-Ro52, anti-SSB, anti-Jo-1, anti-Scl-70, anti-CNEPB, anti-dsDNA, anti-His, anti-PCNA, anti-Nuk, anti-Rib, anti-M2, and anti-PMScl-70). The sera for LIA test

were diluted 1:100. EUROBlotMaster (Euroimmun AG) and EURO-LineScan (Euroimmun AG) were used to complete the operation and for test result interpretation, respectively.

Statistical analysis

SPSS for Windows version 17.0 (IBM-SPSS, Inc, Armonk, New York) was used for statistical calculations. Nonparametric analysis with the Wilcoxon signed-rank test was used for matched pairs. Categorical variables were compared using χ^2 test as appropriate. $P < 0.05$ was considered to be statistically significant.

Results

The age and sex distribution of 20,970 participants are summarized in **Table I**. The ages ranged from 2 to 88 years, with mean age 32 (19.7) years for both sexes.

The prevalence of ANA in male and female participants by age groups are shown in **Table I**. The overall prevalence of ANA was 5.92% and correlated positively with age. There were significant differences among each age group except age older than 80 years, as shown in **Table I** ($P < 0.01$). In the female group, there are 2 sharp peaks in ANA positivity at the 20-year and 40-year age groups.

In 1243 ANA-positive sera tested by LIA, 44.2% were positive for at least 1 of 15 specific ANA antibodies. In terms of the effect of age and sex on ANA positivity, there were significant differences among the 3 groups (ie, ≤ 20 years, 21–49 years, and ≥ 50 years;
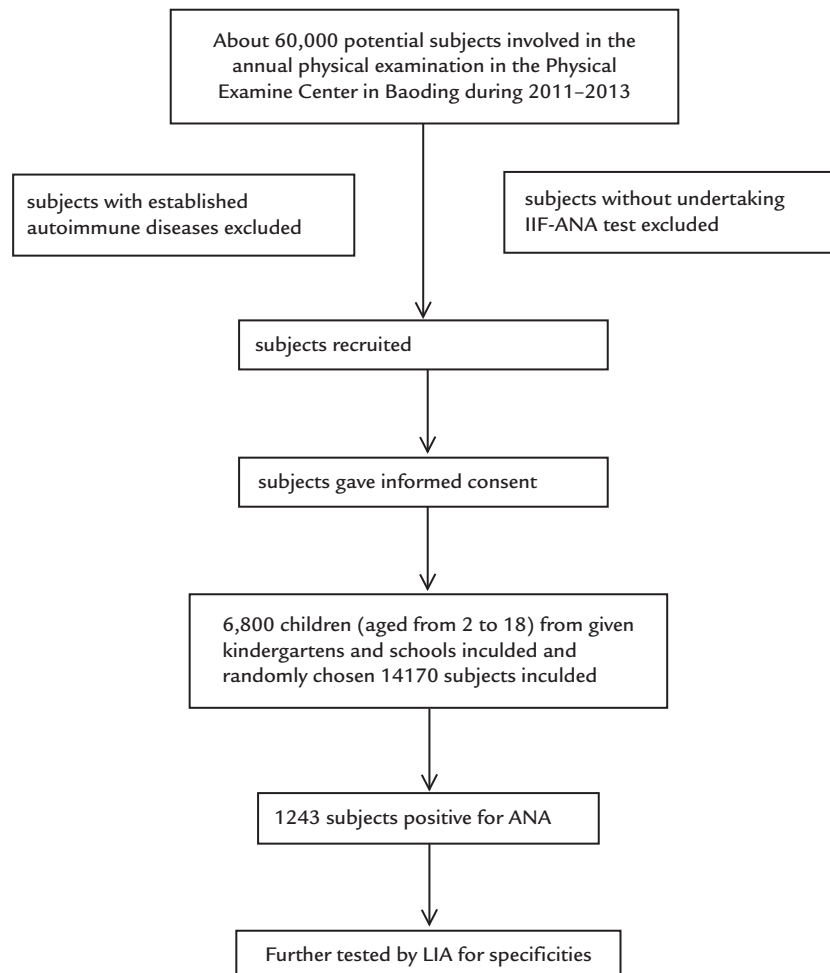

Figure 1. Flowchart for the involvement of potential participants in the study. ANA = antinuclear antibodies; IIF = indirect immunofluorescence; LIA = line immunoassay.