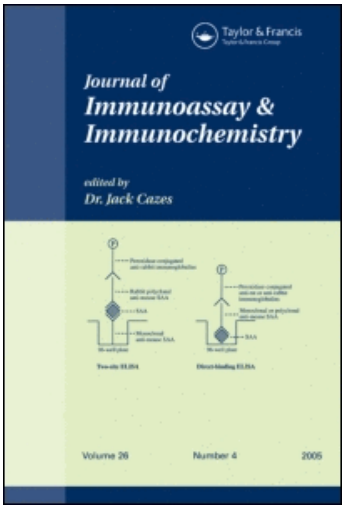

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ABSTRACT

Local reference ranges of immunoglobulins are required for studies and clinical interpretation. In this study, serum levels of IgA, IgG, and IgM in 914 Iranian healthy adult blood donor volunteers, aged 18–55 years, were measured by nephelometry. Our data showed that serum reference intervals of IgA, IgG, and IgM in subjects were 72–375, 636–1518, and 39–283 mg/dL, respectively. Data analysis showed a significant difference between the male and female subjects only for IgM; thus, the means of IgM in females were higher than for

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males ($p < 0.05$). Correlation coefficient r for paired samples showed no statistically significant relationship between age and each Ig ($p > 0.05$). Comparison of this study with others demonstrated that results are similar; some differences are probably related to ethnic differences. Therefore, our results can be considered as a source of reliable local reference for use in laboratories.

Key Words: Normal values; Immunoglobulins; Iranian; Nephelometry.

INTRODUCTION

Normal values of immunoglobulins always have been required for research studies and clinical interpretations in every population. One of the wonders of the immune system is its ability to produce antibodies of essentially similar structure, but with enormous diversity to react with antigens. To know normal levels of these effectors is important, especially for local reference. In 1998, Ritchie et al., in a cohort study among 109 publications presenting immunoglobulin reference data in healthy individuals (1961–1997), that Iranian population studies were not involved, with about 17 acceptable studies being selected and compared.[1] Levels of immunoglobulins may vary by gender and race, although these differences are generally not clinically significant; but, a knowledge of local reference values is important.[2–5] In Iran, there was no complete study in this area until now; only two small studies were done, first in 1973 on 102 healthy adults and next in 1987 on 252 healthy males between ages 15–60 years, by means of the RID Mancini method.[6,7] In recent decades, the determination of a reference range for serum proteins such as immunoglobulins has been done using nephelometry in most studies.[8–19] Aims of these determinations was to study preparation of immunoglobulins references by nephelometric methods.

EXPERIMENTAL

Sample Collection

Among blood donor volunteers, after laboratory test for infection disease and completing a questionnaire which included health status, age, sex, and a physicial examination, 1056 healthy adults were selected. After

sampling 3 mL peripheral blood, sterile serum was separated and divided to several aliquots and frozen at $-80^{\circ}C$ immediately.

Immunoglobulin Measurement

Serum immunoglobulin concentrations, determined by means of nephlometry methods, were measured (Minineph^{TM} Human Ig Kit, The Binding Site Ltd., Birmingham, UK). Highly lipaemic, contaminated, turbid, or hemolysed samples (142 samples) were not suitable for nephelometric measurements and were excluded from the study. Therefore, 914 serum samples were measured.

Statistical Analysis

Kolmogorov-Smirnov tests were done for normal distribution. Differences in immunoglobulin concentrations between the male and female were analyzed with the Mann-Whitney *U*-test. *P*-values of less than 0.05 were considered significant. Correlation between age and each immunoglobulin was also calculated by means of the correlation coefficient, *r*, by a correlation Pearson test.[20]

Ethics

The ethical committee of the Iran Blood Banking and Transfusion Organization approved this study.

RESULTS

Nine hundred and fourteen selected subjects, aged 18–55 years (33.3 ± 9), comprising 825 males and 89 females, (most blood donor volunteers in Iran are male), was entered into this study. Raw data of IgA and IgM concentrations weren't normal distribution ($p < 0.05$); for this reason, these data were transformed into natural logarithm ($\ln[x]$) for analysis. Therefore, data approached normal distribution ($p > 0.05$). Normal range for Ig calculated by mean $\pm$ 1.96 $\times$ SD, on IgA and IgM natural logarithm of mean and standard deviation were put into the formula. Results showed serum reference intervals of IgA, IgG, and IgM in subjects were 72–375, 636–1518, and 39–283 mg/dL, respectively; also, there was no significant

Table 1. Normal ranges of immunoglobulin levels in Iranian adults (mg/dL).

		IgA		IgG		IgM	
Group	*n*	Range	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD
Male	825	72–374	165 ± 70	631–1516	1074 ± 226	39–282	105 ± 61
Female	89	69–388	164 ± 74	703–1503	1103 ± 204	48–289	117 ± 58
p-value			0.947		0.24		0.038[a]
Total	914	72–375	165 ± 71	636–1518	1077 ± 224	40–283	106 ± 60

[a]p-value < 0.05 is statistically significant.

difference between the male and female subjects only with IgM, so that means of IgM in females were higher than in males ($p = 0.038$). Ig concentration means and 95% reference ranges are shown in Table 1. As reported in Fig. 1, the result of correlation coefficient r for paired samples showed no statistically significant correlation between these age ranges and each immunoglobulin concentration ($p > 0.05$). Comparison of immunoglobulin reference intervals between international medical references and this study are shown in Table 2.

DISCUSSION

Most basic researches in the medical sciences involve determination of reference ranges of important body elements, such as serum proteins. In clinical immunology, known immune system components and their normal values are very critical. In this field, enormous studies have been conducted.[1–19,21,22] However, some of those surveys have been cited as sources in international medical books.[8,21,22] In most sciences, such as immunology, an approved, authoritative, global standard reference interval has been prepared which is profitable in laboratory and clinical tests. But, in reference books, theses normal values are different; for example, Kratz and Lewandrowski reported a lower range of IgG in adults, i.e., 800 mg/dL. However, the National Institute of Health reported 500 mg/dL, and now, an Iranian case with 650 mg/dL serum IgG concentration, is this healthy or deficient? Generally, human subjects throughout the world show differences, though small, in serum immunoglobulin levels; this is due, presumably, to environmental, nutritional, health, and ethnic variations.[24,25] All of the above reasons prove the importance and necessity of normal values preparation in any population. In our country, studies upon which we can rely do not exist.[6,7]

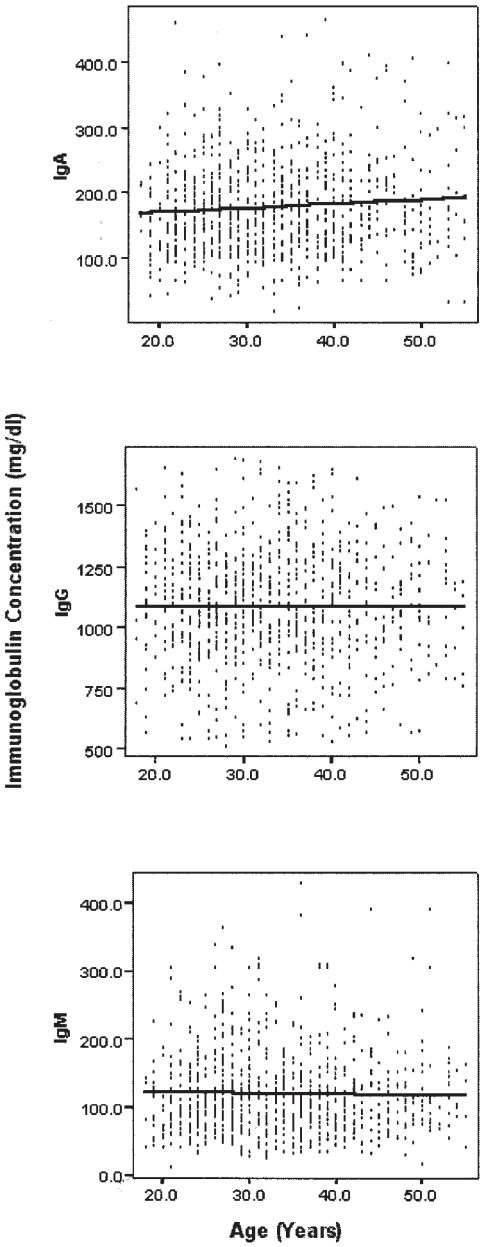

Figure 1. Relationship between age and Ig concentration. Correlation coefficients, *r*, for IgA, IgG, and IgM were 0.082, 0.003, and 0.017, respectively.

Table 2. Comparison immunoglobulin references intervals between area references and this study (mg/dL).

Study	*n*	Area	IgA (mg/dL)	IgG (mg/dL)	IgM (mg/dL)
Jolliff et al.[8]	120	America	70–312	639–1,349	56–352
Shido et al.[9]	88[a]	Africa	60–580	500–2,300	50–460
	100[b]	Euro	70–320	710–1,520	30–120
White et al.[15]	100	Asia	67–478	960–2,160	32–304
Lau et al.[18]	80	Asia	134–453	900–2,080	66–366
NIH reports[32]	–	America	51–375	523–1,422	37–200
This study	914	Asia	72–375	636–1,518	40–283

[a]Somali residents.
[b]Swedish residents.

Results for IgA and IgG levels are similar in both sexes, but for IgM levels, it has been observed that, in females, the IgM level is higher than in male subjects,[23,26] and some studies found a relationship between number of X chromosomes and IgM concentration.[27] Also, it was reported that immune response is regulated by sex hormones.[28,29] However, this hypothesis was not proved by other studies.[30,31] In this study, the number of female subjects was lower than for males; perhaps, by making subject ratio equal, differences of IgM would be lower or higher. In the age range of 18–55 years, we did not observe any correlation between increased age and level of immunoglobulins; therefore, this age range can be considered to be a group as adults with the same immunoglobulin levels.

Finally, as demonstrated in Table 2, this study's results are similar to other reliable references, except for some differences which are probably related to ethnic factors. Although, sampling from both Pesian populations, such as Fars, Turk, Kurd, and Baluchy throughout Iran may lead to different results. In conclusion, these results can be considered as a source of a reliable local reference for use in laboratories. In the future, the authors will determine normal values of immunoglobulins and complement component in all age groups from newborn to 18 years in the Iranian population.

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