Reference Value of Immunoglobulins in Healthy School Children of Bangladesh

Jasimuddin Ahmed, M Mostafa Zaman, Mian Abdur Rouf, M M Monzur Hassan and Salma Zareen

The reference value of immunoglobulins (Igs) should be known for a population concerned because it is influenced by many clinical and local conditions. As yet the reference value of the Igs have not been determined in Bangladeshi children. This study determined the reference value of Igs in apparently healthy 261 rural Bangladeshi primary school children (aged 5 to 14 years, mean 9.3 years). IgG, IgM and IgA were determined by an auto-analyzer. The mean (standard deviation) value of IgG was 1728 (344) mg/dl. The corresponding values for IgM and IgA were 200 (88) and 163 (63) mg/dl, respectively. The 95% reference value calculation in all subjects showed that the range for IgG was 1103 to 2524, IgM was 92 to 390, and IgA was 72 to 325 mg/dl. These values could be used to evaluate Ig status in children with a variety of clinical conditions.

J Epidemiol, 2001 ; 11 : 263-265

immunoglobulin, reference value, Bangladeshi children, developing country.

INTRODUCTION

Human body is equipped with a special system of defense mechanism. The chief armor of the defense mechanism is immunoglobulins (Ig), which are the effector products of differentiated B-cells and mediate the humoral arm of the immune response. Three main components of the Igs (G, M and A) are measured for many clinical conditions particularly in children. Interpretation of the results depends on the known reference values, and these values vary among populations. Therefore, it is necessary to determine the reference value in the population under question.

In Bangladesh, no report is available on normal level of Igs in children. This study was done to find out the normal level of IgG, IgM and IgA in healthy school children of Bangladesh.

MATERIALS AND METHODS

Primary education in Bangladesh consists of five years from grades I through V and is free of cost. Usually children enroll in to primary schools at 5 to 6 years of age, but there is no strict rule. This study was done, during February through May 1992, in Sanora Government Primary School located in Sanora village of Dhamrai upazilla (sub-district) in Dhaka district. Children of all socioeconomic status from the nearby area attend this school. It is run by a management committee, which consists of representatives of parents, teachers and government officers. A meeting was held between the investigators and management committee, which also included the local health authority. Consent was obtained from the management committee. Then class teachers explained the purpose of the study to the students and requested them to participate in the study. A total of 450 boys and girls of all grades participated in the study. We excluded those who suffered from fever and sore throat during the last four weeks, and those who had clinical evidence of tonsillo-pharyngitis on physical examination. None of them suffered from immunodeficiency diseases. Thus, 361 (80.2%) children were selected for laboratory investigation. Among them 261 (72.2%) subjects were finally selected for this study after excluding those with C-reactive protein more than 0.05 mg/dl and yielded bacteria on throat culture (mostly streptococci and staphylococci). Blood samples were collected in fasting condition and sera were separated within two hours of venepuncture and preserved in -80°C until mea-
measurement of total protein, albumin, C-reactive protein, IgG, IgM and IgA. Multipurpose Immunochemistry System Autoanalyzer Model LA-2000 (Eiken Chemical Company, Japan) using latex reagent was used to measure Igs. All reagents used in this study were from the same company.

**Statistical analysis:**

All statistical analyses were done by using SAS statistical package (Release 6.11, SAS Institute Inc., Cary, NC). The reference value for Igs were defined as the ranges that included 95% of values obtained from the percentile distributions. Results are presented according to age groups because there are some reports from developed countries \(^2\) that Ig levels in children are related to age.

**RESULTS**

Subjects are 5 to 14 years (mean 9.3 years) old, and boys and girls are similar in age. Age-specific levels of proteins are presented in Table 1. Percentile distributions with mean (standard deviation) according to age groups are presented in Table 2. There is no age related trend of immunoglobulin levels. The 95% reference value calculation in all subjects showed that the range for IgG was 1103 to 2524, IgM was 92 to 390, and IgA was 72 to 325 mg/dl.

**DISCUSSION**

Estimation of Ig is now an established tool for the study of immune status or the immunologic response of an individual in a high-risk condition. The reference value of Igs should, therefore, be established by using data from a representative local healthy population. To the best of our knowledge, this is the first study of Igs in apparently healthy school children in Bangladesh. The school that we have selected for this study includes children from all socioeconomic background of the locality and may represent primary school children of rural Bangladesh, but not Bangladesh at large. More representative studies are necessary to validate our finding. It could be more informative to know the situation in other developing countries, particularly South Asian countries. Unfortunately, such data for children are not available from those countries.

Maturation of immune responses is a continuous process in childhood. Adult level of IgG reached in the child by the seventh year of life and remains relatively constant thereafter \(^3\). After birth, the rate of synthesis of IgM increases rapidly and adult level may be reached by the ninth month of age \(^4\). Some authors \(^5\) have shown that IgA synthesis begins during the first few weeks after birth and the concentration rises slowly during the first year and continued throughout early adulthood. However, we did not observe any age dependent change in Ig levels, which is similar to the study of Stiehm et al \(^6\) for IgG and IgM but not for IgA. Higher level of serum Igs in Ethiopian pre-school age children, as compared with the Swedish, has been reported by Johansson et al \(^7\) which is similar to our study. Repeated infection and malnutrition in early life remains the underlying cause of elevated Ig levels in children of developing countries \(^7,8\) including Bangladesh. Children in Bangladesh are often exposed to malnutrition and various type of respiratory and intestinal infections in the early

| Age group | Number | Total protein (mg/dl) | Albumin (mg/dl) | Globulin (mg/dl) | Albumin/Globulin ratio |
|-----------|--------|-----------------------|-----------------|------------------|-----------------------|
| 5 - 7     | 46     | 7.5 (0.5)             | 4.0 (0.2)       | 3.5 (0.5)        | 1.2 (0.2)             |
| 8         | 49     | 7.8 (0.5)             | 4.2 (0.3)       | 3.6 (0.5)        | 1.2 (0.3)             |
| 9         | 47     | 7.8 (0.7)             | 4.3 (0.4)       | 3.5 (0.7)        | 1.2 (0.3)             |
| 10        | 52     | 7.8 (0.6)             | 4.2 (0.3)       | 3.6 (0.7)        | 1.2 (0.3)             |
| 11        | 38     | 7.7 (0.5)             | 4.2 (0.3)       | 3.5 (0.4)        | 1.2 (0.2)             |
| 12 - 14   | 29     | 7.8 (0.5)             | 4.3 (0.3)       | 3.6 (0.5)        | 1.2 (0.2)             |
| Total     | 261    | 7.7 (0.5)             | 4.2 (0.3)       | 3.5 (0.6)        | 1.2 (0.2)             |

| Age group | Number | Immunoglobulin G Mean (SD) | 25th | 50th | 97.5th | Immunoglobulin M Mean (SD) | 25th | 50th | 97.5th | Immunoglobulin A Mean (SD) | 25th | 50th | 97.5th |
|-----------|--------|---------------------------|------|------|-------|---------------------------|------|------|-------|---------------------------|------|------|-------|
| 5 - 7     | 46     | 1679 (336)                | 1107 | 1643 | 2342  | 207 (98)                   | 72   | 202  | 462   | 155 (59)                   | 81   | 147  | 250   |
| 8         | 49     | 1755 (377)                | 1224 | 1660 | 2636  | 229 (131)                  | 108  | 214  | 721   | 161 (60)                   | 82   | 147  | 283   |
| 9         | 47     | 1775 (350)                | 1132 | 1755 | 2520  | 194 (72)                   | 103  | 193  | 390   | 165 (59)                   | 72   | 155  | 348   |
| 10        | 52     | 1736 (356)                | 1090 | 1714 | 2551  | 204 (67)                   | 116  | 188  | 339   | 157 (73)                   | 67   | 144  | 345   |
| 11        | 38     | 1683 (352)                | 930  | 1652 | 2426  | 173 (46)                   | 84   | 173  | 269   | 158 (53)                   | 72   | 158  | 297   |
| 12 - 14   | 29     | 1734 (319)                | 1165 | 1796 | 2228  | 182 (65)                   | 92   | 174  | 344   | 188 (71)                   | 57   | 191  | 340   |
| Total     | 261    | 1728 (344)                | 1103 | 1690 | 2524  | 200 (88)                   | 92   | 189  | 390   | 163 (63)                   | 72   | 153  | 325   |
childhood. Therefore, they attain adult level of Igs before adulthood, and age-dependent changes in childhood become masked.

Possible bias:
To recruit healthy children we have excluded those who had fever during last month, and tested positive for throat swabs and C-reactive protein. This definition for healthy children does not necessarily ensure inclusion of healthy children (and exclusion of sick children).

Implication:
In absence of a recognized reference range of Ig, determination of immune status would vary among physicians. We believe that the reference values suggested here would reduce such variations and may help in diagnosis and therapeutic decision making. On the other hand, the cut-off points for the reference value on a continuous test result is an arbitrary decision. Physicians should use their clinical judgement for decision making. As the immunoglobulin distributions are heterogeneous among the population, it is necessary to determine the distribution of Igs for the population concerned. However, in absence of data for the population under question, present data may provide some information for developing countries especially South Asian countries.

ACKNOWLEDGMENTS

This analysis is based on the routine work done by many other investigators of the National Center for Control of Rheumatic Fever and Heart Diseases. We are indebted to them. We extend special thanks to JICA (Japan International Cooperation Agency) experts who worked as counterpart in this Center during the study period. We are grateful to the teachers, parents and students of Sanora Primary School for their cooperation.

REFERENCES

1. Claus DR, Osmand AP, Gewurz H. Radioimmunoassay of human C-reactive protein and levels in normal sera. J Lab Clin Med, 1976; 87: 120-128.
2. Kawai T, et al. eds. Reference values among Japanese children. Japan Public Health Association, Tokyo, 1997: 263-270, 275-278.
3. Manuel JR, Russell HT. Humoral immunity: antibodies and immunoglobulins. In: Henry JB, ed. Clinical diagnosis and management by laboratory methods, 18th ed. WB Saunders, Philadelphia, 1991: 809-829.
4. Prasad LS, Sinha KP, Sen DK, Mallick H. Study on immunoglobulins in Indian children. Indian J Med Res, 1971; 59: 107-114.
5. Haworth JC, Norris M, Dilling L. A study of the immunoglobulins in premature infants. Arch Dis Child, 1965; 40: 243-250.
6. Stiehm ER, Fudenberg HH. Serum levels of immunoglobulins in health and disease: a survey. Pediatrics, 1966; 37: 715-727
7. Johanssan SG, Mellbin T, Vahlquist B. Immunoglobulin levels in Ethiopian preschool children with special references to high concentrations of immunoglobulin E (IgND). Lancet, 1968; 1: 1118-1121.
8. Neumann CG, Lawlor GJ Jr, Stiehm ER, Swenseid ME, Newton C, Herbert J, Ammann AJ, Jacob M. Immunologic responses in malnourished children. Am J Clin Nutr 1975; 28: 89-104.
9. Zaman MM, Yoshiike N, Faruq QO, Ahmed J, Zareen S, Rouf MA, Haque KM, Tanaka H. Erythrocyte sedimentation rate in healthy school children of Bangladesh. J Epidemiol, 2000; 10: 124-126.
10. Fletcher RH, Fletcher SW, Wagner EH, 3rd eds. Clinical Baltimore, epidemiology: The essentials. Williams and Wilkins, 1996: 43-74.