**Normal Immunoglobulin (IgG, IgA, and IgM) Values In Healthy Children Without Newborn Period**

**AIM:** Immunoglobulins are an important element of the adaptive immune system produced against antigens in plasma cells and have a specific association with antigens. Determination of normal immunoglobulin values ​​will guide the diagnosis, treatment, and follow-up of immunodeficiency diseases. OurstudysOur studies determine the IgG, IgA, and IgM levels in healthy children and the reference values ​​specific to our region.

**METHODS:** Inclusion criteria for the study were 200 healthy children aged one month to 18 years, with no known history of chronic disease, no suspected infection, no drug use, no congenital disease or anomaly, and consent for the study. Venous blood samples from the patients were studied in the Medical Microbiology Laboratory by nephelometry method by the instructions.

**RESULTS:** The 200 children included in our study were divided into ten groups according to their age groups. Serum IgG values ​​increased gradually until the age of 6-8, then reached a plateau and approached the adult level. The serum IgA level started at very low values ​​in the first months, gradually increasing after age two and reaching the adult level at 18. Serum IgM level approaches the adult level 4-5 years after ıt was contacted at sımılar values.

**CONCLUSION:** Our study provided data for normal serum IgG, IgA, and IgM values ​​in healthy non-neonatal children. Immunoglobulin values ​​in healthy children have been studied in a small number of different places and clinics, and it is aimed to obtain data from our region. Our study is considered one of our country's original and reliable reference sources.

**Keywords:** Child, immunoglobulin, immune system

**1. Introduction** The immune system is the system that protects living beings against diseases, detects foreign structures such as tumor cells and pathogens, and eliminates them. The immune system scans all foreign substances that come into contact with and enter the body. Preventing the development of diseases such as cancer by distinguishing foreign substances is also a feature of the immune system (1).

In order for the immune system to fulfill its function, immune cells must recognize a foreign agent, amplify it, and regulate their response to foreign agents. This response provides protection through many different mechanisms. Protection includes mechanisms such as phagocytic cells and physical barriers. These mechanisms can be divided into two interrelated defense systems: the specific acquired immune system and the non-specific hereditary (innate) immune system (2).

Immunoglobulins are an important element of the adaptive immune system, which are produced against antigens in plasma cells and have specific association with antigens (3)

In order for immunoglobulins to show their functions in the immune response, their levels must be sufficient, and for this, their normal values ​​must first be known (4). Normal values ​​of serum immunoglobulins may vary depending on age, gender, patient population, place of residence, and the method of determining the values ​​(5).

Our aim in our study is to determine the numerical and percentage reference values ​​of serum normal immunoglobulin values ​​in children who are citizens of the Republic of Turkey and living in Sakarya.

**2. Materials and methods**

*2.1. Study population* Our study was conducted prospectively by evaluating 200 healthy children who came to Sakarya University Training and Research Hospital Child Health and Diseases Polyclinic between 01.01.2022 and 01.05.2022. Children included in the research; They are children between the ages of 1 month and 18 years, who are citizens of the Republic of Turkey, without a known history of chronic disease, suspicion of infection, medication use, congenital disease or anomaly. While evaluating the health status of the children, anamnesis was taken and physical examination was performed by the same physician. There are twenty children each in 10 groups created according to the age groups of the children participating in the study. In each group of twenty, there are 10 boys and 10 girls equally distributed. All children live in Sakarya province. Approval was received for the study from Sakarya University Clinical Research Ethics Committee (Ethical committee number: E-16214662-050.01.04-70471-178). This study was supported by SAU Scientific Research Projects Budget.

*2.2. Laboratory analysis* Venous blood samples taken from the patients included in the study in accordance with standard safety precautions were centrifuged at 5,000 rpm for 10 minutes in the Microbiology Laboratory, the serum portion of the blood was separated and stored at -80 °C until the day of study. On the day of the study, N antiserum human IgG, IgA, IgM kits (S. Healthineers, Germany) were used and the S. BNII (S. Diagnostics, Germany) device was used, in accordance with the company's recommendations. In order to evaluate the validity of the results before the study, an internal quality and external quality control (RIQAS International Quality Assessment Scheme, United Kingdom) study was carried out using control sera at normal, high and low levels. Serum immunoglobulin values ​​measured in the study were expressed as mg/dl.

*2.3. Statistical analysis* The Kolmogorov-Smirnov test was used to evaluate whether the distribution of continuous variables was normal. According to the normality test results, two independent sample t tests were used to compare IgG, IgA and IgM values ​​between genders. One-way ANOVA was used to compare IgG, IgA, and IgM values ​​between age groups. According to one-way ANOVA results, Tukey HSD test was used for pairwise comparisons between age groups. Since the distribution range of immunoglobulin values ​​is normal, **they are presented as arithmetic mean ± standard deviation.** **A p value of <0.05 was considered significant.** Analyzes were performed using off-the-shelf statistical software (IBM SPSS Statistics, Version 23.0. Armonk, NY: IBM Corp.).

The standards specified in the Clinical and Laboratory Standards Institute (CLSI) C28-A3 guide were used to determine reference ranges. Since the number of people was less than 120, the Robust method was used when determining 95% reference intervals. Reed method was used to remove outliers. MedCalc Statistical Software was used to calculate reference intervals according to the Robust method (MedCalc® Statistical Software version 20.114, MedCalc Software Ltd., Ostend, Belgium; https://www.medcalc.org; 2022) (6). Data for the 17-18 age group could not be used as data because they were used in confidence interval calculations (Table 2). The reason why the lower and upper limits are given as zero within the 90% confidence interval by taking the 95% reference interval is that very low values ​​approach negative values ​​when determining the lower and upper limits (Figure 1).

**3. Results** Among 200 children, IgG, IgA and IgM values ​​were divided into 100 children between the ages of 1 month and 18 years, and the **IgG result was found to be significantly higher in boys** (p<0.05). The arithmetic mean was found to be 943.58 mg/dl in boys and 828.38 mg/dl in girls. There was no statistically significant difference in IgA and IgM values ​​(Table 1).

According to age groups: 1-3 months, 4-6 months, 7-12 months, 13-24 months, 25-36 months, 4-5 years, 6-8 years, 9-11 years, 12-16 years IgG, IgA Lower and upper limits were determined according to the **arithmetic mean of IgM and IgM** values, minimum maximum values ​​and 90% confidence interval of the 95% reference interval (Table 2). The results that will be used primarily in clinical use, patient evaluation and comparison with other studies are included in this table. Considering the reference values ​​of our study, **serum IgG values ​​gradually increase until the age of 6-8, then reach a plateau and approach adult levels.** While higher values ​​were found for 1-3 months due to maternal IgG transmission, a decrease and a gradual increase were observed afterwards. Serum IgA level starts at very low levels in the first months, gradually increases after the age of 2 and reaches adult levels at the age of 18 (Table 2).

According to age groups, the arithmetic mean and minimum and maximum IgG values ​​in boys and girls were higher in boys at the age of 4-8 (p <0.001 and 0.017). The arithmetic mean of IgG was found to be 1175 (min.–max.: 849-1400) mg/dl in boys and 813 (min.–max.: 524-1020) mg/dl in girls at the age of 4-5 (p <0.001). The arithmetic mean of IgG was found to be 1279 (min.–max.: 884-1600) mg/dl in boys and 1046 (min.–max.: 858-1350) mg/dl in girls at the age of 6-8 (p= 0.017). The arithmetic mean of IgA was found to be 104 (min.–max.: 79-135) mg/dl in boys and 84 (min.–max.: 55-106) mg/dl in girls at the age of 4-5 (p= 0.033). There was no significant difference in IgM data (Table 3).

The arithmetic means of IgG, IgA and IgM values ​​were compared with two studies conducted in different locations in the same age groups and healthy children. These studies are two reference studies conducted at Konya Selçuk University and the United States of America (USA).

In our study, the arithmetic mean of IgG for ages 4-5 was 994.4 mg/dl; 6-8 years old 1162.75 mg/dl; According to the study conducted in Konya, 839.87 mg/dl for 4-5 years old; 1014.93 mg/dl was found to be statistically significantly higher in 6-8 years old (p1:0.009, p1:0.042). In our study, the IgG arithmetic mean was 1162.75 mg/dl for ages 6-8, 1213.95 mg/dl for ages 12-16; Compared to the study conducted in the USA, it was found to be statistically significantly higher for ages 6-8, 923 mg/dl, and ages 12-16, 946 mg/dl (p2=0.002, p2<0.001, p2=0.029). In our study, the arithmetic mean of IgA was 94.35 mg/dl for ages 4-5; 9-11 years 160.45 mg/dl; 12-16 years 163.6 mg/dl; According to the study conducted in Konya, 68.98 mg/dl for 4-5 years old; 9-11 years 115.99 mg/dl; It was found to be statistically significantly higher at 12-16 years old at 120.90 mg/dl (p1=0.005, p1=0.010 and p1=0.004).

In our study, the IgA arithmetic mean was 54.2 mg/dl for 25-36 months; 59.77 for 25-36 months was found to be lower than the study conducted in Konya (p1=0.001). In our study, the IgA arithmetic mean was found to be 37.35 mg/dl for 13-24 months, 50 mg/dl lower for 13-24 months than the study conducted in the USA (p2=0.035). In our study, the IgM arithmetic average was 50.15 mg/dl for 4-6 months; 7-12 months 57.95 mg/dl; 13-24 months 85.4 mg/dl; 25-36 months 100.45 mg/dl; According to the study conducted in Konya, 75.44 mg/dl for 4-6 months; 7-12 months 81.05 mg/dl; 13-24 months 122.57 mg/dl; It was found to be 111.31 mg/dl lower in 25-36 months (p1=0.003, p1=0.013, p1=0.002 and p1<0.001).

In our study, the IgM arithmetic mean was 85.4 mg/dl for 13-24 months; 25-36 months 100.45 mg/dl; 4-5 years old 121.1 mg/dl; 6-8 years old 118.15 mg/dl; 9-11 years 102.2 mg/dl; 12-16 years 143.6 mg/dl; 17-18 years old 128.5 mg/dl; From the study conducted in the USA, 58 mg/dl for 13-24 months; 25-36 months 61 mg/dl; 4-5 years old 56 mg/dl; 6-8 years 65 mg/dl; 9-11 years 79 mg/dl; 12-16 years 59 mg/dl; 99 mg/dl was found to be higher in 17-18 years of age (p2=0.004, p2 <0.001, p2 <0.001, p2 <0.001, p2=0.031, p2<0.001, p2=0.016) (Table 4) All these differences are between countries or regions It is thought that variables such as genetics, lifestyle, nutrition, infection, geographical location and altitude may make a difference on immunoglobulin levels (7,8).

In a study conducted in 3 different centers, IgG values ​​were detected at equal levels in the first months, then gradually increased and remained close to 4-5 years of age, after which our study reached a higher and early adult level (Figure 2).

IgA remained at similar levels in the first months, and our study showed higher levels after the age of 4-5, and the results of 3 different centers reached similar/close values ​​in the 17-18 age group (Figure 3).

In the study conducted in Konya, IgM values ​​reached higher levels in 4-6 months and then plateaued. In our study, it increased gradually and approached the adult level after 4-5 years of age. In the study conducted in the USA, it remained constant at lower levels. The fact that its level is higher in our country compared to the USA suggests that it may be caused by acute infection, migration and crowded population (Figure 4).

**4. Discussion** Many different studies have been conducted to determine reference ranges for serum immunoglobulins. As a result of the studies, it was determined that the values ​​may vary depending on the method used for measurement, age, gender and patient population (5). Therefore, when selecting the study group, factors that could affect IgG, IgA and IgM levels were tried to be minimized with the determined criteria.

It is known that medical reference values ​​are close to accurate and reliable in order to diagnose and monitor a disease and to accurately evaluate laboratory results during the treatment process (9). In our study, it was aimed to determine reference values ​​specific to our country and partly to our region in IgG, IgA and IgM levels in healthy children.

The advantage of nephelometric measurements is that they have higher sensitivity at low concentrations. The disadvantages of nephelometric systems are that the potent and optically clear antisera used for antigen detection are expensive, samples containing lipid and hemoglobin change the results, and the sample must be diluted at high antigen concentrations. The method used in our study is also nephelometric, and the results can be said to be more reliable as stated.

It has been thought that the immunoglobulin reference values ​​determined by WHO may be affected by environmental variables in several different studies (10). Variables were evaluated as age, gender, ethnicity, nutrition, infection, geographical location and altitude. The effects of ethnicity on immunoglobulin have been observed in studies conducted in healthy Caucasian children, the Indian community and West Africa (11-13). In some studies, IgG and IgM levels were found to be higher and IgA levels to be lower in girls (14). There are also studies indicating that gender differences do not have a significant effect on the immunoglobulin level (12). In our study, factors such as age, gender, and ethnicity were taken into consideration and included as criteria for participation in the study. In this study, according to age groups, the arithmetic mean and minimum and maximum IgG values ​​in boys and girls were higher in boys at the age of 4-8 (p <0.001 and 0.017). At the age of 4-5, the arithmetic mean of IgA in boys was found to be 104 (min.–max.: 79-135) mg/dl, and the arithmetic mean in girls was 84 (min.–max.: 55-106) mg/dl (p= 0.033). No significant difference was found in IgM data (Table 3).

In another study, IgG, IgA and IgM were studied in 447 healthy children to investigate differences depending on age and gender; The childhood period between the ages of 2 and 16 is divided into 1-year groups. Geometric means and 95% confidence intervals were determined. Significantly higher gender-related values ​​for the IgM class were observed in girls across all age groups examined. IgG approached adult levels after 8 years of age, IgM after 5 years of age, and IgA after 16 years of age. A transiently significant decrease in IgM was observed in males at age 11 years. Regression analysis with age was performed separately for boys and girls, and it was observed that the three main immunoglobulin values ​​increased linearly with age (15). In our study, IgM was higher in girls in all age groups compared to the 95% reference interval. This suggests that IgM is at higher levels in girls. In our study, IgG 6-8, IgA 9-11 and IgM approached adult levels after the age of 4-5. Similarly, there was a decrease in IgM levels in the 9-11 age group, which suggests that IgM is low in this age group. It was found that the arithmetic average of IgG, IgA and IgM values ​​in boys and girls separately in age groups, IgG values ​​were higher in 4-8 years of age, and IgA was higher in boys at 4-5 years of age.

In a study conducted in our country, serum IgG, IgA and IgM age-related geometric mean, minimum and maximum values ​​and 95% confidence intervals were studied. IgG levels were found to be high in the neonatal period due to maternal IgG transmission. Afterwards, it was observed that it was at a low level for 1-5 months and then all values ​​gradually increased. IgA and IgM levels were found to be very low in the newborn and then started to increase gradually.

IgG levels reach a plateau after the age of 9-10 (4). In our study, IgG and IgA gradually increased in age groups within the 95% reference range, while IgM remained more stable after 4-5 years of age.

In our country, when we look at the gender-based evaluation of children whose immunoglobulin levels are measured by the Ankara Child Health and Diseases Unit of the University of Health Sciences, the female sex ratio is higher in patients with low IgA levels. It is noteworthy that the frequency of low IgG and IgM levels is higher in the male gender (16). In our study, IgA and IgM were higher in girls compared to the 95% reference interval.

In a study where IgG, IgA and IgM serum levels were studied in 270 healthy children between the ages of 4 and 12 by the radial immunodiffusion method, nine different age groups, each consisting of 30 children (15 boys and 15 girls), were created. IgG and IgA concentrations gradually increased with increasing age. The IgM concentration remained constant at a lower level. IgA levels were almost the same in both genders. Significantly higher IgM and IgG levels were found in girls than in boys. A consistent seasonal effect on the three serum immunoglobulin concentrations could not be demonstrated (11). In our study, IgG and IgA concentrations increased gradually with increasing age, compared to the 95% reference interval. IgM concentration remained constant at a lower level at 4-5 years of age. In girls, IgA and IgM were higher and IgG varied.

In a study conducted in Nigeria consisting of 43 children (20 boys, 23 girls), it was thought that age and gender affected the serum levels of IgG, IgA and IgM. It was found that girls had significantly lower IgA values ​​than boys (p<0.05) (17). In our study, IgA values ​​were found to be higher in girls.

It is thought that the reason why our study and other studies conducted in Turkey found higher levels of IgM compared to the study conducted in America is due to more acute infections in our country due to frequent infection, contamination and migration (8,18).

Although approximately 400 genetic diseases that cause primary immune deficiencies have been identified, it is thought to be rare because the true frequency of the disease is unknown in the world. While it is assumed that there are 638,000 PID cases in Europe, only 15,052 cases are registered (2.27%). The most common antibody deficiencies in Turkey (73.5%) are followed by other autoinflammatory diseases (13.3%), identified immune deficiencies (5.5%), phagocyte dysfunctions (3.5%), combined immune deficiencies (2%), and natural immune deficiencies (13.3%). 1%), followed by immune system regulation disorders (0.7%). The average age of 94% of the patients is 9.2±6 years. The rate of consanguineous marriage is 14.3%. Based on records, the frequency of PID was found to be 30.5/100,000. It would not be a wrong interpretation to assume that this rate will increase considerably if all patients are entered into the patient registration system in Turkey and clinical immunology centers become widespread (19,20). Studies conducted in recent years have shown that hereditary immunodeficiencies are more common, especially in countries with high rates of consanguineous marriages and high fertility rates. Considering that consanguineous marriages in our country are higher than in other countries, the expected immunodeficiency rate is expected to be higher. This should also be taken into consideration in the evaluation of genetic diseases and immunodeficiencies (16). We hope that the results of this study will be useful in the evaluation of immunodeficiency in our country.

The most common primary immunodeficiency in our country is selective IgA deficiency. When studies on selective IgA deficiency were examined, no significant differences were found in terms of age, gender and geographical characteristics. However, when the patients with low IgA in our country were examined in terms of gender, the female sex ratio was seen to be higher. It is noteworthy that the incidence of low IgG and IgM levels is higher for the male gender (16).

Considering the nutritional habits of countries and all these variables, it may be expected that reference ranges will change in different regions. In the results from the same region, it was stated that the family's lifestyle may affect the results (21,22).

It is thought that variables such as genetic differences, geography, quality and type of life between countries may make a difference on immunoglobulin levels (8). We hope that our study will be a reference for the values ​​of children in this age group and help in the diagnosis and treatment of diseases.

**References**

1. Ekinci, A. (2006). Sağlıklı Çocuklarda İnvitro Lenfosit Fonksiyonunun İki Farklı Yöntemle Araştırılıp Karşılaştırılması. A. Ü Biyoteknoloji Enstitüsü, Yüksek Lisans Tezi, Ankara (Danışman Prof. Dr. E Babacan).
2. Songu, M., Katılmış, H. (2012). Enfeksiyondan korunma ve immün sistem. Journal of Medical Updates, 2, 31-42.
3. (Düzgün, 2015)(<http://avys.omu.edu.tr>, Erişim tarihi: 10.10.2022).
4. Aksu, G., Genel, F., Koturoğlu, G., Kurugöl, Z., & Kütükçüler, N. (2006). Serum immunoglobulin IgG, IgM, IgA and IgG subclass concentrations in healthy children: a study using nephelometric technique. Turk J Pediatr, 48(1), 19-24.
5. Plebani, A., Ugazio, A. G., Avanzini, M. A., Massimi, P., Zonta, L., Monafo, V., & Burgio, G. R. (1989). Serum IgG subclass concentrations in healthy subjects at different age: age normal percentile charts. Eur J Pediatr, 149(3), 164-7.
6. Gary, L. H. (2008). CLSI. Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline Third Edition. CLSI document Wayne, PA: Clinical and Laboratory Standards Institute, C28-A3.
7. Bayram, R. O., Özdemir, H., Emsen, A., Türkdağı, H., & Artaç, H. (2019). Reference ranges for serum immunoglobulin (IgG, IgA, and IgM) and IgG subclass levels in healthy children. Turk J Med Sci, 497-505.
8. Stiehm, E. R., Fudenberg, H. H. (1966). Serum levels of immune globulins in health and disease: a survey. Pediatrics, p:715-727.
9. Enli, Y., Aslan, D., Akalın, N., Aydın, Y., Yılmaztürk, G. C., Göçhan, İ., Tekintürk, S., & Demir, S. (2003). Determination of Reference Intervals for 18-40 Years Old People Living in Denizli by Using Different Methods. Turk J Biochem, 28(4), 228-245.
10. Madison, S. E., Stewart, C. C., Farshy, C. E., & Rejmer, C. B. (2005). The relationship of race, sex and age to concentrations of serum ımmunoglobulins expressed in international units in healthy adults in the USA. Bull World Health Organ, 52, 2, 179-185.
11. Stoop, J. W., Zegers, B. J. M., Sander, P. C., & Ballieux, R. E. (1967). Serum immunoglobulin levels in healthy children and adults. Clin exp Immunol, 4(1), 101-112.
12. Bhat, G. A., Mubarik, M., & Bhat, M. Y. (1995). Serum immunoglobulin profile in normal Kashmiri adults. J Postgrad Med, 41(3), 66-69
13. Rowe, D. S., McGregor, I. A., Sylvia, S. J., Hall, P., & Williams, K. (1968). Plasma immunoglobulin concentrations in African community and in a group of healthy British adults. Clin exp Immunol, 3(1), 63-79
14. Cassidy, J. T., Nordby, G. L., & Dodge, H. J. (1974). Biologic variations of human serum immunoglobulin concentrations sex-age specific effects. J Chron Dis, 27(11), 507-516
15. Wiedermann, D., Wiedermannová, D. (1982). The development of three major immunoglobulin serum levels in healthy children between 2 and 16 years of age with regard to sex. Physiol Bohemoslov, 30(4), 315-22.
16. Altan, A. (2017). İmmünglobulin Ölçümü Yapılan Hastalarda Yaşa Göre Düşüklük Sıklığının Belirlenmesi Sağlık Bilimleri Üniversitesi, Tıpta Uzmanlık Tezi, Ankara (Danışman:Doç. Dr. Ersoy CİVELEK)
17. Obiandu, C., Okerengwo, A.A., & Dapper, D.V. (2013). J. Physiol. Sci. Levels of serum immunoglobulins in apparently healthy children and adults in Port Harcourt, Nigeria. Niger J Physiol Sci, 28, 023 -027.
18. Keyt, B. A., Baliga, R., Sinclair, A. M., Carroll, S. F., & Peterson, M. S. (2020). Structure, Function, and Therapeutic Use of IgM Antibodies. Antibodies Basel, 13, 9(4), 53.
19. Bousfiha AA, Jeddane L, Ailal F, Benhsaien I, Mahlaoui N, Casanova JL, Abel L. (2013). Primary immunodeficiency diseases worldwide: more common than generally thought.J Clin Immunol. 33(1):1-7.
20. Kilic SS, Ozel M, Hafizoglu D, Karaca NE, Aksu G, Kutukculer N. (2013) The prevalences [correction] and patient characteristics of primary immunodeficiency diseases in Turkey--two centers study. J Clin Immunol. 33(1):74-83.
21. Childs, C.E., Calder, P.C., and Miles, E.A. (2019). Diet and immune function. Nutrients, 11(8).
22. Türkiye Beslenme Rehberi TÜBER 2015, T.C. Sağlık Bakanlığı Yayın No: 1031, Ankara

**TABLES**

**Table 1.** Distribution of serum immunoglobulin levels in children between 1 month and 18 years of age according to their gender.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Cinsiyet** | **n** | 1. **Ort ± SS** | **Min.-Max.** | **p** |
| **IgG** | **Erkek** | 100 | 943,58±413,98 | 141-1830 | **0,039** |
| **Kız** | 100 | 828,38±370,17 | 145-1760 |
| **IgA** | **Erkek** | 100 | 94,87±82,35 | 6-359 | 0,580 |
| **Kız** | 100 | 88,76±73,43 | 7-350 |
| **IgM** | **Erkek** | 100 | 92,8±49,75 | 18-256 | 0,688 |
| **Kız** | 100 | 95,64±50,16 | 18-285 |

(Abbreviations n: Number of patients, A. Mean: Arithmetic mean, Min: Minimum, Max: Maximum)

**Table 2.** Distribution of serum immunoglobulin levels according to age groups in children between 1 month and 18 years of age.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Yaş** | **n** | **A. Ort ± SS** | **Min-Max** | **%95 Referans Aralığı**  **Alt Sınır (%90 GA)** | **%95 Referans Aralığı**  **Üst Sınır (%90 GA)** |
|  | **1-3 Ay** | 20 | 433,55±137,11 | 227-770 | 45,72 (0- 113,97) | 677,11 (606,64 - 773,06) |
|  | **4-6 Ay** | 20 | 382,15±173,18 | 141-885 | 141,42 (81,17 - 191,10) | 825,520 (764,34 - 904,92) |
|  | **7-12 Ay** | 20 | 618,1±200,78 | 350-1010 | 236,02 (189,43 - 272,36) | 972,82 (916,73 - 1044,81) |
|  | **13-24 Ay** | 20 | 671,1±177,86 | 432-990 | 328,97 (284,73 - 363,04) | 1118,46 (1061,27 - 1186,48) |
| **IgG** | **25-36 Ay** | 20 | 834,75±193,52 | 437-1320 | 419,70 (369,16 - 457,53) | 1261,89 (1204,99 - 1330,59) |
|  | **4-5 Yaş** | 20 | 994,4±236,68 | 524-1400 | 507,68 (449,67 - 553,68) | 1402,57 (1346,03 - 1471,82) |
|  | **6-8 Yaş** | 20 | 1162,75±227,85 | 858-1600 | 592,34 (523,167 - 646,42) | 1539,92 (1483,07 - 1608,34) |
|  | **9-11 Yaş** | 20 | 1177,1±248,22 | 645-1520 | 673,13 (592,73 - 738,39) | 1673,42 (1614,20- 1744,370) |
|  | **12-16 Yaş** | 20 | 1213,95±229,63 | 877-1620 | 749,51 (648,78 - 831,55) | 1802,49 (1729,70 - 1888,42) |
|  | **1-3 Ay** | 20 | 15,95±12,02 | 6-47 | 0 (0 - 1,64) | 36,36 (26,17 - 49,61) |
|  | **4-6 Ay** | 20 | 19,95±12,7 | 7-63 | 0 (0 - 0) | 53,39 (45,93 - 63,11) |
|  | **7-12 Ay** | 20 | 35,75±23,29 | 12-114 | 0 (0 - 0) | 72,26 (64,86 - 80,54) |
|  | **13-24 Ay** | 20 | 37,35±10,95 | 15-52 | 0 (0 - 0,36) | 93,9 (84,75 - 103,12) |
| **IgA** | **25-36 Ay** | 20 | 54,2±16,04 | 24-84 | 2,29 (0 - 8,17) | 119,23(107,38 - 130,39) |
|  | **4-5 Yaş** | 20 | 94,35±20,9 | 55-135 | 13,24 (0 - 20,52) | 149,16 (134,47 - 162,7) |
|  | **6-8 Yaş** | 20 | 130,25±47,41 | 81-264 | 29,73 (14,8 - 38,98) | 184,63(167,07 - 200,93) |
|  | **9-11 Yaş** | 20 | 160,45±70,56 | 78-334 | 52,67 (35,85 - 65,42) | 226,55 (205,78 - 246,3) |
|  | **12-16 Yaş** | 20 | 163,6±49,58 | 87-234 | 82,99 (63,8 - 101,53) | 275,84(251,43 - 301,84) |
|  | **1-3 Ay** | 20 | 34,7±16,48 | 18-87 | 2,78 (0 - 9,42) | 63,58 (52,78 - 81,39) |
|  | **4-6 Ay** | 20 | 50,15±25,71 | 18-136 | 11,56 (4,05 - 16,6) | 89,45 (80,41 - 104,21) |
|  | **7-12 Ay** | 20 | 57,95±21,25 | 28-115 | 19,59 (13 - 24,84) | 114,57(106,56 - 126,48) |
|  | **13-24 Ay** | 20 | 85,4±36,53 | 32-148 | 26,48 (19,4 - 32,93) | 138,56 (130,8 - 149,28) |
| **IgM** | **25-36 Ay** | 20 | 100,45±25,58 | 47-144 | 31,87 (23,65 - 39,25) | 161,04(152,96 - 172,08) |
|  | **4-5 Yaş** | 20 | 121,1±37,33 | 65-205 | 35,37 (25,93 - 43,33) | 181,64(173,02 - 193,92) |
|  | **6-8 Yaş** | 20 | 118,15±39,49 | 47-198 | 36,61 (26,3 - 45,45) | 199,98(189,86 - 212,96) |
|  | **9-11 Yaş** | 20 | 102,2±36,58 | 38-163 | 35,21 (23,54 - 45,21) | 215,67 (203,3 - 231,12) |
|  | **12-16 Yaş** | 20 | 143,6±57,71 | 47-285 | 30,79 (16,79 - 43,41) | 228,35 (211,84 - 247,5) |

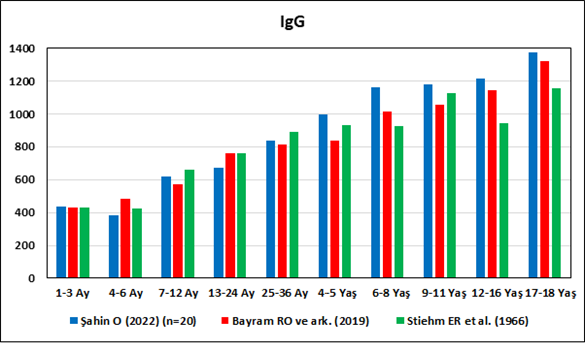
**Table 3.** Distribution of serum immunoglobulin levels in children between 1 month and 18 years of age according to age groups and gender.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Yaş** | **Cinsiyet** | **n** | **A.Ort ± SS** | **Min-Max** | **p** |
| **IgG** | **1-3 Ay** | **Erkek** | 10 | 491,2±156,57 | 227-770 | 0,058 |
| **Kız** | 10 | 375,9±88,25 | 236-505 |
| **4-6 Ay** | **Erkek** | 10 | 354,7±147,93 | 141-691 | 0,493 |
| **Kız** | 10 | 409,6±199,39 | 145-885 |
| **7-12 Ay** | **Erkek** | 10 | 626,6±197,47 | 379-1010 | 0,856 |
| **Kız** | 10 | 609,6±214,36 | 350-951 |
| **13-24 Ay** | **Erkek** | 10 | 688,4±179,88 | 475-959 | 0,676 |
| **Kız** | 10 | 653,8±183,74 | 432-990 |
| **25-36 Ay** | **Erkek** | 10 | 908,8±185,3 | 726-1320 | 0,087 |
| **Kız** | 10 | 760,7±180,39 | 437-1130 |
| **4-5 Yaş** | **Erkek** | 10 | 1175±159,98 | 849-1400 | **<0,001** |
| **Kız** | 10 | 813,8±142,09 | 524-1020 |
| **6-8 Yaş** | **Erkek** | 10 | 1279,4±234,59 | 884-1600 | **0,017** |
| **Kız** | 10 | 1046,1±155,95 | 858-1350 |
| **9-11 Yaş** | **Erkek** | 10 | 1219,7±216,05 | 763-1490 | 0,458 |
| **Kız** | 10 | 1134,5±281,72 | 645-1520 |
| **12-16 Yaş** | **Erkek** | 10 | 1278,7±205,3 | 924-1620 | 0,216 |
| **Kız** | 10 | 1149,2±244,65 | 877-1560 |
| **17-18 Yaş** | **Erkek** | 10 | 1413,3±355,14 | 863-1830 | 0,587 |
| **Kız** | 10 | 1330,6±312,43 | 758-1760 |
| **IgA** | **1-3 Ay** | **Erkek** | 10 | 12,1±8,44 | 6-33 | 0,161 |
| **Kız** | 10 | 19,8±14,17 | 7-47 |
| **4-6 Ay** | **Erkek** | 10 | 16,4±8,59 | 7-28 | 0,220 |
| **Kız** | 10 | 23,5±15,45 | 8-63 |
| **7-12 Ay** | **Erkek** | 10 | 41,7±30,73 | 14-114 | 0,273 |
| **Kız** | 10 | 29,8±11,03 | 12-52 |
| **13-24 Ay** | **Erkek** | 10 | 36,2±11,82 | 15-52 | 0,651 |
| **Kız** | 10 | 38,5±10,5 | 21-52 |
| **25-36 Ay** | **Erkek** | 10 | 56,5±10,19 | 43-71 | 0,536 |
| **Kız** | 10 | 51,9±20,68 | 24-84 |
| **4-5 Yaş** | **Erkek** | 10 | 104,1±19,34 | 79-135 | **0,033** |
| **Kız** | 10 | 84,6±18,37 | 55-106 |
| **6-8 Yaş** | **Erkek** | 10 | 148,4±57,34 | 82-264 | 0,087 |
| **Kız** | 10 | 112,1±26,94 | 81-150 |
|  | **9-11 Yaş** | **Erkek** | 10 | 176,7±87,17 | 82-334 | 0,316 |
| **Kız** | 10 | 144,2±48,22 | 78-233 |
| **12-16 Yaş** | **Erkek** | 10 | 163,7±55,77 | 88-234 | 0,993 |
| **Kız** | 10 | 163,5±45,61 | 87-230 |
| **17-18 Yaş** | **Erkek** | 10 | 192,9±95,77 | 6-359 | 0,489 |
| **Kız** | 10 | 219,7±72,48 | 111-350 |
| **IgM** | **1-3 Ay** | **Erkek** | 10 | 38,5±21,51 | 19-87 | 0,315 |
| **Kız** | 10 | 30,9±8,88 | 18-46 |
| **4-6 Ay** | **Erkek** | 10 | 39,1±12,8 | 18-61 | 0,052 |
| **Kız** | 10 | 61,2±30,99 | 32-136 |
| **7-12 Ay** | **Erkek** | 10 | 58,2±20,37 | 29-95 | 0,960 |
| **Kız** | 10 | 57,7±23,2 | 28-115 |
| **13-24 Ay** | **Erkek** | 10 | 75,1±33,2 | 42-148 | 0,216 |
| **Kız** | 10 | 95,7±38,47 | 32-146 |
| **25-36 Ay** | **Erkek** | 10 | 105±24,77 | 64-144 | 0,441 |
| **Kız** | 10 | 95,9±26,86 | 47-137 |
| **4-5 Yaş** | **Erkek** | 10 | 119,7±33,79 | 65-179 | 0,872 |
| **Kız** | 10 | 122,5±42,38 | 68-205 |
| **6-8 Yaş** | **Erkek** | 10 | 121,9±44,24 | 47-198 | 0,683 |
| **Kız** | 10 | 114,4±36,1 | 53-175 |
| **9-11 Yaş** | **Erkek** | 10 | 107,8±42,15 | 54-163 | 0,508 |
| **Kız** | 10 | 96,6±31,3 | 38-150 |
| **12-16 Yaş** | **Erkek** | 10 | 124,4±49,3 | 47-180 | 0,141 |
| **Kız** | 10 | 162,8±61,48 | 57-285 |
| **17-18 Yaş** | **Erkek** | 10 | 138,3±58,63 | 64-256 | 0,397 |
| **Kız** | 10 | 118,7±40,86 | 61-180 |

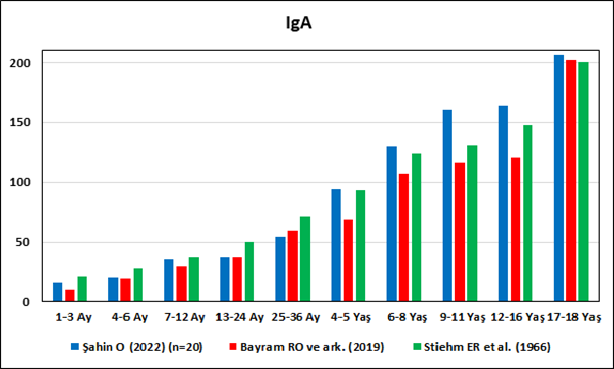
|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Yaş** | **Şahin O (2022) (n=20)** | **Bayram RO ve ark, (2019)**  **(n=30)** | | **Stiehm ER et al, (1966)**  **(n=25)** | |
| **A.Ort±SS** | **A.Ort±SS** | **p1** | **A.Ort±SS** | **p2** |
| **IgG** | **1-3 Ay** | 433,55±137,11 | 429,5±145,59 | 0,922 | 430±119 | 0,926 |
| **4-6 Ay** | 382,15±173,18 | 482,43±236,8 | 0,111 | 427±186 | 0,412 |
| **7-12 Ay** | 618,1±200,78 | 568,97±186,62 | 0,381 | 661±219 | 0,502 |
| **13-24 Ay** | 671,1±177,86 | 761,7±238,61 | 0,154 | 762±209 | 0,129 |
| **25-36 Ay** | 834,75±193,52 | 811,5±249,14 | 0,726 | 892±183 | 0,315 |
| **4-5 Yaş** | 994,4±236,68 | 839,87±164,19 | **0,009** | 929±228 | 0,352 |
| **6-8 Yaş** | 1162,75±227,85 | 1014,93±255,53 | **0,042** | 923±256 | **0,002** |
| **9-11 Yaş** | 1177,1±248,22 | 1055,43±322,27 | 0,160 | 1124±235 | 0,467 |
| **12-16 Yaş** | 1213,95±229,63 | 1142,07±203,83 | 0,251 | 946±124 | **<0,001** |
| **17-18 Yaş** | 1371,95±328,3 | 1322,77±361,89 | 0,628 | 1158±305 | **0,029** |
| **IgA** | **1-3 Ay** | 15,95±12,02 | 10,53±5,16 | 0,033 | 21±13 | 0,188 |
| **4-6 Ay** | 19,95±12,7 | 19,86±9,77 | 0,978 | 28±18 | 0,684 |
| **7-12 Ay** | 35,75±23,29 | 29,41±12,37 | 0,216 | 37±18 | 0,840 |
| **13-24 Ay** | 37,35±10,95 | 37,62±17,1 | 0,950 | 50±24 | **0,035** |
| **25-36 Ay** | 54,2±16,04 | 59,77±24,52 | **0,001** | 71±37 | 0,066 |
| **4-5 Yaş** | 94,35±20,9 | 68,98±34,05 | **0,005** | 93±27 | 0,855 |
| **6-8 Yaş** | 130,25±47,41 | 106,9±49,66 | 0,104 | 124±45 | 0,654 |
| **9-11 Yaş** | 160,45±70,56 | 115,99±47,05 | **0,010** | 131±60 | 0,138 |
| **12-16 Yaş** | 163,6±49,58 | 120,90±47,51 | **0,004** | 148±63 | 0,371 |
| **17-18 Yaş** | 206,3±83,8 | 201,84±89,92 | 0,861 | 200±61 | 0,771 |
| **IgM** | **1-3 Ay** | 34,7±16,48 | 36,66±13,55 | 0,648 | 30±11 | 0,259 |
| **4-6 Ay** | 50,15±25,71 | 75,44±29,73 | **0,003** | 43±17 | 0,269 |
| **7-12 Ay** | 57,95±21,25 | 81,05±35,76 | **0,013** | 54±23 | 0,557 |
| **13-24 Ay** | 85,4±36,53 | 122,57±41,63 | **0,002** | 58±23 | **0,004** |
|  | **25-36 Ay** | 100,45±25,58 | 111,31±40,55 | **<0,001** | 61±19 | **<0,001** |
| **4-5 Yaş** | 121,1±37,33 | 121,79±39,24 | 0,951 | 56±18 | **<0,001** |
| **6-8 Yaş** | 118,15±39,49 | 114,73±41,27 | 0,772 | 65±25 | **<0,001** |
| **9-11 Yaş** | 102,2±36,58 | 113,18±43,68 | 0,358 | 79±33 | **0,031** |
| **12-16 Yaş** | 143,6±57,71 | 125,78±39,31 | 0,200 | 59±20 | **<0,001** |
| **17-18 Yaş** | 128,5±50,2 | 142,54±64,32 | 0,428 | 99±27 | **0,016** |

**Table 4.** Comparative distribution and statistics of serum immunoglobulin levels according to age groups in children between 1 month and 18 years of age.

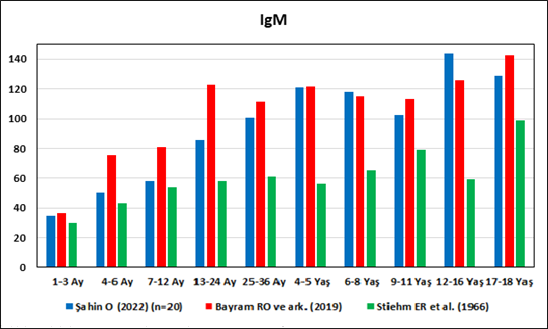
**FIGURES**



**Figure 2.** Graphical comparison of IgG made in three different centers.



**Figure 3.** Graphical comparison of IgA made in three different centers.



**Figure 4.** Graphical comparison of IgM made in three different centers.