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Clinical features and treatment outcomes in children with IgG subclass deficiency: A retrospective study

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Abstract
Introduction: Immunoglobulin G (IgG) subclass deficiencies are among the most common primary immunodeficiencies in children and are associated with increased susceptibility to infections. This study aimed to investigate the clinical features, associated immunological conditions, and treatment outcomes in affected pediatric patients.
Methods: A retrospective analysis was conducted on 43 patients diagnosed with IgG subclass deficiency at the Allergy and Immunology Clinic of Fırat University between January 2019 and July 2024. Clinical records were reviewed for demographic data, immunoglobulin levels, and history of infections. The impact of prophylactic treatments—including intravenous immunoglobulin (IVIG), oral bacterial lysates, and antibiotics—on the frequency of infection was evaluated.
Results: Among the 43 patients, 32 (74.4%) were male and 11 (25.6%) were female, with a mean age at diagnosis of 6.77 ± 2.30 years. The most common clinical presentation was recurrent upper respiratory tract infections, reported in 23 patients (53.5%). Isolated IgG3 deficiency was identified in 34 patients (79.1%). During follow-up, normalization of IgG levels was achieved in 39 patients (90.7%), with a mean time to normalization of 2.1 ± 1.19 years. Prophylactic interventions significantly reduced the annual infection rate from 18.12 ± 10.37 to 3.09 ± 2.40 ($p < 0.001$).
Conclusion: IgG subclass deficiencies represent a significant health concern in children because of their association with recurrent infections. Early diagnosis and the implementation of appropriate prophylactic treatment strategies are crucial in reducing infection frequency and improving the quality of life. However, the retrospective nature of the study and the relatively small sample size may have limited the evaluation of clinical outcomes and treatment responses, potentially affecting the generalizability of the results. Despite these limitations, the findings highlight the potential benefits of prophylactic interventions in managing infections among children with IgG subclass deficiencies and emphasize the need for larger, prospective studies to inform evidence-based therapeutic strategies for this population.

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Introduction

Among primary immunodeficiencies, antibody deficiencies constitute by far the largest group. Immunoglobulin G (IgG) subclass deficiency is one of the four most common primary immunodeficiency disorders in children.[1] The earliest reports of IgG subclass deficiency date back to the late 1960s and was primarily focused on patients with well-characterized primary immunodeficiency disorders, such as ataxia-telangiectasia (AT) or common variable immunodeficiency (CVID).[2,3] Approximately a decade later, Schur et al.[4] described patients with isolated reductions in the levels of serum IgG subclass who experienced recurrent sinopulmonary infections. Interest in IgG subclass deficiencies increased significantly following a 1974 report by Oxelius, who described a mother and her two children with recurrent sinopulmonary infections, normal serum levels of IgG, IgA, and IgM but selectively low levels of IgG2 and IgG4.[5]

Although more than 60 years have passed since the initial reports, the biological and clinical significance of IgG subclasses and their deficiencies remains a subject of ongoing debate. These discussions often focus on individuals with persistently low serum IgG subclass levels but no apparent increase in susceptibility to infections.[6,7]

IgG subclass deficiency is defined as the presence of abnormally low levels of one or more IgG subclasses relative to age-specific reference ranges, despite normal total IgG concentrations. IgG is the most abundant immunoglobulin in the human immune system and plays a critical role in host defense against infections. In children, serum levels of IgG1 and IgG3 typically reach adult concentrations earlier than those of IgG2 and IgG4. Among these, IgG3 deficiency is more likely to normalize by approximately 6 years of age, whereas IgG2 deficiency often persists or tends to remain below age-specific reference levels. The underlying mechanism of IgG subclass deficiency is believed to involve delayed immunological maturation, resembling the transient hypogammaglobulinemia of infancy.[8-10]

IgG subclass deficiency should be considered in children presenting with recurrent infections, particularly sinopulmonary infections. IgG2 deficiency, in particular, has been associated with increased susceptibility to infections caused by encapsulated bacteria, as well as with impaired antibody responses to polysaccharide antigens. In such cases, respiratory tract infections are most commonly caused by *Streptococcus pneumoniae*, *Haemophilus influenzae* type B, and nontypeable bacterial strains. In IgG3 deficiency, recurrent upper or lower respiratory tract infections are often attributed to both viral and bacterial pathogens, particularly *Moraxella catarrhalis*. IgG subclass deficiency may also be associated with comorbid conditions such as asthma, allergic rhinitis, and various autoimmune diseases.[11-13] In addition, IgG subclass deficiencies may coexist with other primary immunodeficiencies or allergic disorders, further complicating both clinical presentation and treatment strategies. Each IgG subclass deficiency can occur either in isolation or in combination with deficiencies of other subclasses. For example, IgG3 deficiency is frequently associated with IgG1 deficiency, whereas IgG2 deficiency may coexist with IgG4 deficiency. Although IgG2 deficiency is generally reported as the most prevalent subclass deficiency in pediatric populations, some studies have identified IgG3 deficiency as the most common in children.[9,14,15] Moreover, IgG subclass deficiency may coexist with other primary immunodeficiencies, such as selective IgA deficiency or IgM deficiency. In addition to isolated subclass deficiencies, well-characterized immunodeficiency syndromes associated with IgG subclass abnormalities have also been reported. For instance, children with AT or Nijmegen breakage syndrome may present with IgG subclass deficiencies. Furthermore, IgG subclass deficiencies have been documented in individuals with inflammatory bowel disease and in patients receiving antiepileptic medications.[11-13] A comprehensive clinical history, physical examination, and quantification of IgG subclass levels, together with the evaluation of immune responses to specific immunizations (including protein and polysaccharide antigens), are essential components in the diagnostic assessment of IgG subclass deficiency. Nevertheless, low serum IgG subclass levels do not necessarily indicate an underlying pathological condition. Although IgG subclass deficiency may increase susceptibility to recurrent infections, a significant proportion of affected individuals remain asymptomatic and do not exhibit increased infection frequency. Therefore, assessing specific antibody responses to protein and polysaccharide antigens is considered more informative than IgG subclass quantification alone in the evaluation of patients with suspected immunodeficiency.[16]

The objective of this study is to investigate the clinical characteristics, associated immunological conditions, and treatment outcomes in pediatric patients with IgG subclass deficiency. In particular, the study aims to assess the impact of these deficiencies on infection frequency and to evaluate the efficacy of various prophylactic interventions. Ultimately, the goal is to contribute to the development of more effective diagnostic and management strategies for IgG subclass deficiencies in children.

Materials and Methods

Patients with severe combined immunodeficiencies, AT, other syndromic immunodeficiencies, CVID, hyper-IgM syndrome, or acquired immunodeficiency syndrome were not included in the study. Quantification of serum IgA, IgM, IgG, and IgG1, IgG2, IgG3 subclasses was performed using a nephelometric method with Behring nephelometer analyzer and commercially available kits from Dade Behring (Germany).

In this retrospective study, data were collected from the medical records of patients who presented at the Allergy and Immunology Clinic at Fırat University between January 2019 and July 2024. A total of 43 patients diagnosed with IgG subclass deficiency were included. IgG subclass deficiency was defined as having one or more IgG subclass levels more than two standard deviations (SDs) below the age-specific reference mean, in the presence of relevant clinical symptoms. Patients with IgG1 subclass deficiency were excluded, as they were evaluated in the context of hypogammaglobulinemia.[17] Recurrent infections were defined as the occurrence of at least six febrile episodes requiring antibiotic treatment within a 1-year period. “Normalization” was defined as the return of IgG subclass

levels to age-appropriate reference ranges. "Improvement" was defined as a ≥50% reduction in the annual frequency of infections compared to the pretreatment period. Patients with severe combined immunodeficiency, AT, other syndromic immunodeficiencies, CVID, hyper-IgM syndrome, or acquired immunodeficiency syndrome were excluded. Quantification of serum IgA, IgM, total IgG, and IgG subclasses (IgG1, IgG2, and IgG3) was performed using a nephelometric method with the Behring Nephelometer Analyzer and commercially available kits (Dade Behring, Germany).

Clinical data were extracted from patients' medical records, laboratory findings, and treatment protocols. Documented variables included demographic and clinical characteristics such as age, sex, age at the onset of symptoms, time to diagnosis, family history of primary immunodeficiency, and history of sibling death. In addition, serum immunoglobulin levels (IgG, IgA, IgM, and IgE), IgG subclass concentrations (IgG1, IgG2, IgG3, and IgG4), and coexisting immunological conditions (e.g., hypogammaglobulinemia, atopy, and allergic disorders) were evaluated.

Isolated IgG subclass deficiencies and accompanying immunological conditions were identified based on immunological findings and diagnostic criteria at the time of diagnosis. The treatment course and prophylactic strategies were subsequently analyzed. Prophylactic interventions—including intravenous immunoglobulin (IVIG), oral bacterial lysates, and antibiotic therapy—were evaluated. Infection frequencies before and after treatment were compared by calculating patients' annual infection rates. The infection rate was defined as the mean number of infections per year prior to the initiation of prophylaxis and following its implementation. Vaccine responses were evaluated based on serum antibody levels against vaccines administered as part of the routine childhood immunization schedule, rather than through post-vaccination challenge.

Individualized prophylactic treatment strategies were implemented based on each patient's infection history and clinical presentation. For patients with fewer than 10 infections per year, typically mild and viral upper respiratory tract infections that did not require antibiotic therapy, prophylaxis with an oral bacterial lysate (OM-85, Vaxoral®, Switzerland) was initiated. In patients experiencing 8 to 10 infections annually, particularly mild to moderate infections such as tonsillitis and sinusitis requiring antibiotic treatment, trimethoprim-sulfamethoxazole (Bactrim®) was administered prophylactically at a dose of 5 mg/kg, three times per week.

For patients with more than 10 infections per year and a history of recurrent moderate to severe tonsillitis, sinusitis, or pneumonia, IVIG (0.5 g/kg per dose) was initiated. During follow-up, if IVIG alone failed to achieve a significant reduction in the frequency of infection or severity, adjunct prophylactic therapy was tailored according to the infection type. In cases of persistent upper respiratory tract infections (e.g., tonsillitis or sinusitis), trimethoprim-sulfamethoxazole was added to IVIG. In contrast, for patients with lower respiratory tract infections, defined as ≥2 episodes of pneumonia per year or radiologic evidence of bronchiectasis, azithromycin prophylaxis was added. Azithromycin was administered at a dose of 5 mg/kg, thrice a week.

Statistical analysis

Statistical analyses were performed using SPSS software, version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were reported as frequencies and percentages. The Student's *t*-test was used to compare patients with isolated IgG3 deficiency to those with other IgG subclass deficiencies. For normally distributed continuous variables, results were expressed as mean ± SD. Paired *t*-tests were conducted to compare infection of frequencies before and after prophylactic treatment. A p-value < 0.05 was considered statistically significant.

Results

In this study, IgG subclass deficiency was identified in 11 female (25.6%) and 32 male (74.4%) patients. The mean age at diagnosis was 6.77 ± 2.30 years, and the mean age at the onset of symptoms was 3.74 ± 2.57 years. The average duration between the onset of symptoms and diagnosis was 3.02 ± 2.05 years. Parental consanguinity was documented in nine patients (20.9%), a family history of primary immunodeficiency in eight patients (18.6%), and a history of sibling death in six patients (14.0%). At diagnosis, the mean annual frequency of recurrent infections was 18.12 ± 10.37, which significantly decreased to 3.09 ± 2.40 following prophylactic treatment (p <0.001). The levels of serum immunoglobulin at diagnosis and at the final follow-up visit are summarized in Table 1.

IgA deficiency was identified in two patients (4.7%) with IgG subclass deficiency, and IgM deficiency was observed in seven patients (16.3%). No cases of isolated IgG2 deficiency were noted. The most frequently observed subclass abnormality was isolated IgG3 deficiency (Table 2). Specifically, isolated IgG3 deficiency was detected in 34 patients (79.1%), isolated IgG4 deficiency in 2 patients (4.7%), combined IgG2 and IgG4 deficiencies in 1 patient (2.3%), combined IgG2 and IgG3 deficiencies in 1 patient (2.3%), and combined IgG3 and IgG4 deficiencies in 5 patients (11.6%).

The most common presenting symptom at the time of diagnosis was recurrent upper respiratory tract infections, reported in 23 patients (53.5%) (Table 3). This was followed by a combination of upper respiratory tract infections and

Table 1 Immunoglobulin levels at diagnosis and at last follow-up.

Immunoglobulin	At Diagnosis (mean age: 6.70 ± 2.34 years) (mg/dL)	At Last Follow-up (mean age: 8.30 ± 1.45 years) (mg/dL)
IgM	105.8 ± 38.6	110.2 ± 45.7
IgG	790.5 ± 260.3	870.9 ± 210.1
IgA	75.3 ± 48.9	93.2 ± 56.5
IgG1	470.4 ± 290.0	495.8 ± 270.2
IgG2	160.1 ± 185.4	220.6 ± 235.7
IgG3	125.7 ± 65.4	180.2 ± 112.3
IgG4	42.5 ± 28.3	52.7 ± 34.1

pneumonia in 12 patients (27.9%). In addition, four patients (9.3%) presented with pneumonia alone, while two patients (4.7%) had upper respiratory tract infections accompanied by diarrhea.

Comorbid atopic conditions included asthma in 13 patients (30.2%), allergic rhinitis in 5 patients (11.6%), and atopic dermatitis in 2 patients (4.7%) (Table 4). In addition, food allergies were identified in five patients (11.6%), epilepsy in three patients (7.0%), familial Mediterranean fever in one patient (2.3%), and hypertension in one patient (2.3%).

When patients with isolated IgG3 deficiency were compared to those with other IgG subclass deficiencies, the mean annual frequency of infection at the time of diagnosis was similar between groups. No statistically significant difference was observed in post-prophylaxis infection frequency (Table 5).

Of the 43 patients, 39 (90.7%) reached age-appropriate IgG subclass levels during follow-up, whereas no improvement was observed in 4 patients. Among those who attained normal levels, the mean time to recovery was 2.1 ± 1.19 years. All patients received at least one form of prophylactic treatment for infections, including IVIG, oral bacterial lysates, or antibiotics. The mean duration of prophylaxis was 17.44 ± 8.33 months. The most frequently preferred prophylactic method was IVIG monotherapy, administered to 23 patients (53.5%, Table 6). Oral bacterial lysates were used alone in six patients (14.0%), while four patients (9.3%) received antibiotic prophylaxis alone. In addition, 10 patients (23.3%) received a combination of IVIG and antibiotics. Among the various prophylactic strategies, the group receiving combined IVIG and antibiotics exhibited a higher mean annual infection frequency; however, this difference was not statistically significant (p = 0.05).

Isohemagglutinin positivity was detected in 53.5% of the patients included in the study. The highest vaccine-specific IgG response was observed for the rubella vaccine, with 37 patients (86%) demonstrating a positive response. In contrast, the lowest response was noted for the pneumococcal vaccine, with only 12 patients (27.9%) showing a positive result. Serological responses were positive in 35 patients (81.4%) for tetanus, 33 (76.7%) for measles, 30 (69.8%) for mumps, 28 (65.1%) for varicella, and 26 (60.4%) for hepatitis B.

Table 2 Distribution of IgG subclass deficiency diagnoses (n = 43).

Diagnosis	n (%)
Isolated IgG3 deficiency	34 (79.1)
Combined IgG3 and IgG4 deficiency	5 (11.6)
Isolated IgG4 deficiency	2 (4.7)
Combined IgG2 and IgG3 deficiency	1 (2.3)
Combined IgG2 and IgG4 deficiency	1 (2.3)

Table 3 Clinical presentations in patients with IgG subclass deficiency (n = 43).

Presentation	n (%)
Recurrent upper respiratory tract infections (URTI)	23 (53.5)
URTI + pneumonia	12 (27.9)
Pneumonia only	4 (9.3)
URTI + diarrhea	2 (4.7)

Discussion

IgG consists of four subclasses: IgG1, IgG2, IgG3, and IgG4. Each subclass contributes uniquely to the immune response[18] IgG1 and IgG3 are primarily involved in antibody responses to protein antigens, whereas IgG2 is more effective against polysaccharide antigens.[19] In pediatric populations, serum levels of IgG subclasses increase with age and

Table 4 Comorbid conditions in patients with IgG subclass deficiency (n = 43).

Comorbid condition	n (%)
Asthma	13 (30.2)
Allergic rhinitis	5 (11.6)
Atopic dermatitis	2 (4.7)
Food allergy	5 (11.6)
Epilepsy	3 (7.0)
Familial mediterranean fever (FMF)	1 (2.3)
Hypertension	1 (2.3)

Table 5 Comparison of clinical characteristics between patients with isolated IgG3 deficiency and other IgG subclass deficiencies.

Clinical Feature	Isolated IgG3 Deficiency (n = 34)	Other Subclass Deficiencies[a] (n = 9)	p-value
Age at diagnosis (years)	6.56 ± 1.94	7.56 ± 3.36	0.252
Age at symptom onset (years)	3.41 ± 1.97	5.00 ± 4.06	0.100
Infection frequency at diagnosis	17.94 ± 10.69	18.78 ± 9.62	0.833
Infection frequency during prophylaxis	3.12 ± 2.60	3.00 ± 1.32	0.898
Age at IgG subclass normalization (years)	8.53 ± 2.18	9.22 ± 3.23	0.449

[a]Other subclass deficiencies include IgG3 and IgG4 deficiency, isolated IgG4 deficiency, IgG2 and IgG3 deficiency, and IgG2 and IgG4 deficiency.

Table 6 Effect of prophylactic interventions on infection frequency in patients with IgG subclass deficiency.

Prophylaxis Type	n (%)	Before Prophylaxis (mean ± SD)	After Prophylaxis (mean ± SD)	t	95% CI	p-value
IVIG	23 (53.5)	16.61 ± 10.17	2.52 ± 1.34	7.01	9.92–18.26	<0.001
Bacterial lysate	6 (14.0)	6.67 ± 0.52	2.83 ± 1.17	6.38	2.29–5.38	0.001
Antibiotic	4 (9.3)	8.50 ± 0.58	2.25 ± 1.26	13.06	4.73–7.78	0.003
IVIG + Antibiotic	10 (23.3)	23.60 ± 12.68	4.90 ± 4.04	5.42	10.90–26.50	<0.001

*p-values were calculated using paired samples *t*-tests. CI: confidence interval; SD: standard deviation; IVIG: intravenous immunoglobulin.

typically reach adult reference levels by around 5 years. In the present study, isolated IgG3 deficiency was the most frequently observed abnormality, consistent with previous findings.[9,14] However, some studies have reported IgG2 as the most commonly deficient subclass.[20] Given the key role of IgG3 in antiviral immunity, its deficiency may help explain the high rate of recurrent respiratory tract infections observed in our cohort.

In the present study, approximately 20% of children with IgG subclass deficiency had a history of parental consanguinity, and 14% had a history of sibling death. A male predominance (74.4%) was observed, consistent with prior reports in the literature.[9,14,20,21] IgG subclass deficiency is typically diagnosed between 5 and 10 years of age,[14] and the mean age at diagnosis in our cohort was 6.77 ± 2.30 years. The notable predominance of male patients raises the possibility that undiagnosed X-linked primary immunodeficiency disorders may underlie some cases, as previously suggested.[1,9]

Diagnosing IgG subclass deficiencies in childhood can be challenging because of the wide variability in clinical manifestations and the often nonspecific nature of the presenting symptoms. Affected children are at increased risk for recurrent respiratory tract infections, including sinusitis, pneumonia, and other infectious complications. Commonly observed respiratory infections in these patients include recurrent otitis media, sinusitis, tonsillitis, pneumonia, bronchitis, and, in more severe cases, bronchiectasis. Previous studies on IgG subclass deficiency in children have identified recurrent sinusitis as the most common clinical presentation, as reported by Visitsunthorn et al.,[14] and recurrent upper respiratory tract infections, as described by Karaca et al.[9,20] In our study, the most frequent clinical manifestation was recurrent upper respiratory tract infections. Atopy was observed in 46.5% of our patients, which is markedly higher than the 15% reported by Karaca et al.[9] The absence of a tetanus-specific antibody response was identified in 18.6% of our cohort, a finding consistent with the 18% reported in the same study.[9]

Prophylactic antibiotics are considered as the first-line therapeutic option for patients with IgG subclass deficiency who experience recurrent infections. Additional treatment modalities include conjugate vaccines and oral bacterial lysates. Immunoglobulin replacement therapy is generally reserved for patients with severe or recurrent bacterial infections that do not adequately respond to antibiotic prophylaxis, those with poor antibody responses to polysaccharide vaccines, or cases in which other treatment strategies have proven ineffective. Following prophylactic treatment, the annual infection rate in our cohort decreased markedly from 18.12 ± 10.37 to 3.09 ± 2.40. Similarly, Karaca et al.[9]reported a reduction from 13.4 ± 7.4 to 5.7 ± 3.9. Among the treatment subgroups, patients who received both IVIG and prophylactic antibiotics exhibited a higher mean annual infection rate. This difference was at the threshold of statistical significance (p = 0.05), which may be attributable to the fact that this combination was more frequently administered to patients with more severe clinical manifestations. No statistically significant differences were observed among the remaining treatment groups.

This study has several limitations. First, its retrospective design restricted the assessment of clinical progression and treatment response to data documented in medical records. Second, the relatively small sample size limits the generalizability of the findings. Despite these constraints, the study emphasizes the role of prophylactic interventions in reducing the frequency of infection among children with IgG subclass deficiencies. To address these limitations, future studies should adopt a prospective design to facilitate systematic and real-time collection of clinical and immunological data. This would enhance the precision of outcome measurements and provide a more detailed understanding of disease trajectories. Moreover, multicenter studies with larger cohorts are needed to improve statistical power and external validity. Such efforts are crucial for establishing evidence-based guidelines for clinical management and prophylactic treatment of patients with IgG subclass deficiencies.

In conclusion, IgG subclass deficiencies constitute a clinically significant immunological disorder in the pediatric population, often manifesting as recurrent infections. Early diagnosis and the implementation of targeted prophylactic strategies are critical for mitigating infection risk and improving patient outcomes. The present study contributes to the existing literature by highlighting the clinical utility of prophylactic interventions in reducing the frequency of infection.

Ethics Approval

Ethical approval was obtained from the Non-Interventional Research Ethics Committee of Fırat University (Approval No. 2024/12-59).

Author's Contributions

Conceived and designed the analysis: MK, FDŞ; Collected the data: OK; Performed the analysis: FDŞ; Wrote the paper: FDŞ.

Conflicts of Interest

The authors declare that they have no conflicts of interest to disclose.

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References

1. Schatorjé EJH, Gathmann B, van Hout RWNM, de Vries E, Alsina L, Baumann U, et al. The PedPAD study: boys predominate in the hypogammaglobulinaemia registry of the ESID online database. Clin. Exp. Immunol. 2014 Jun;176(3):387–93. https://doi.org/10.1111/cei
2. Skvaril F, Morell A, Perret B, editors. Clinical Aspects of IgG Subclasses and Therapeutic Implications. 1988; Basel: Karger.
3. Yount WJ, Hong R, Seligmann M, Good RA, Kunkel HG. Imbalances of gamma globulin subgroups and gene defects in patients with primary hypogammaglobulinemia. J. Clin. Invest. 1970 Nov;49(11):1957–66. https://doi.org/1172/JCI106441
4. Schur PH, Borel H, Gelfand EW, Alper CA, Rosen FS. Selective gamma-G globulin deficiencies in patients with recurrent pyogenic infections. N. Engl. J. Med. 1970 Sep 17;283(12):631–4. https://doi.org/10.1056/NEJM197009172831205
5. Oxelius VA. Chronic infections in a family with hereditary deficiency of IgG2 and IgG4. Clin. Exp. Immunol. 1974 May;17(1):19–27. https://doi.org/10.1111/j.1365-2249.1974.tb00269.x
6. Plebani A, Carbonara A, Bottaro A, Gallina R, Boccazzi C, Crispino P, et al. Two siblings with deficiency of IgA1, IgG2, IgG4 and IgE due to deletion of immunoglobulin heavy chain constant region genes. Clin. Exp. Immunol. 1993;93(2):231–5. https://doi.org/10.1111/j.1365-2249.1993.tb05512.x
7. Shackelford PG, Granoff DM, Madassery JV, Scott MG, Nahm MH. Clinical and immunologic characteristics of healthy children with subnormal serum concentrations of IgG2. Pediatr Res. 1990 Jan;27(1):16–21. https://doi.org/10.1203/00006450-199001000-00004
8. Wahn V and von Bernuth H. IgG subclass deficiencies in children: facts and fiction. Pediatr. Allergy Immunol. 2017 Sep;28(6):521–4. https://doi.org/10.1111/pai.12746
9. Karaca NE, Karadeniz C, Aksu G, Kutukculer N. Clinical and laboratory evaluation of periodically monitored Turkish children with IgG subclass deficiencies. Asian Pac. J. Allergy Immunol. 2009 Mar;27(1):43–51.
10. Atkinson AR and Roifman CM. Low serum immunoglobulin G2 levels in infancy can be transient. Pediatrics. 2007 Sep;120(3):e543–7. https://doi.org/10.1542/peds.2006-3466
11. Buckley RH. Immunoglobulin G subclass deficiency: fact or fancy? Curr. Allergy Asthma Rep. 2002 Oct;2(5):356–60. https://doi.org/10.1007/s11882-002-0059-3
12. Horton N, Wu X, Philpott J, Garber A, Achkar JP, Brzezinski A, et al. Impact of low immunoglobulin G levels on disease outcomes in patients with inflammatory bowel diseases. Clin. Gastroenterol. Hepatol. 2016 Dec;14(12):3270–7. https://doi.org/10.1016/j.cgh.2016.06.013
13. Go T. Carbamazepine-induced IgG1 and IgG2 deficiency associated with B cell maturation defect. J. Clin. Immunol. 2004 May;24(3):187–90. https://doi.org/10.1023/B:JOCI.0000024992.54445.1c
14. Visitsunthorn N, Hengcrawit W, Jirapongsananuruk O, Luangwedchakarn V. Immunoglobulin G (IgG) subclass deficiency in Thai children. Asian Pac. J. Allergy Immunol. 2011 Dec;29(4):332–8.
15. Kutukculer N, Karaca NE, Demircioglu O, Aksu G. Increases in serum immunoglobulins to age-related normal levels in children with IgA and/or IgG subclass deficiency. Pediatr. Allergy Immunol. 2007 May;18(2):167–73. https://doi.org/10.1111/j.1399-3038.2006.00404.x
16. Read G and Williams P. Evaluation of assays of serum IgG subclasses and IgG antigen-specific antibodies in the investigation of recurrent infection. Ann. Clin. Biochem. 2000 May;37(3):326–9. https://doi.org/10.1258/0004563001899432
17. European Society for Immunodeficiencies. IgG subclass diagnostic criteria. 2024. Available from: https://esid.org/Education/Diagnostic-Criteria-PID.
18. Schur PH. IgG subclasses: a historical perspective. Monogr. Allergy. 1988;23:1–11.
19. Vidarsson G, Dekkers G, Rispens T. IgG subclasses and allotypes: from structure to effector functions. Front. Immunol. 2014; 5:520. https://doi.org/10.3389/fimmu.2014.00520
20. Schatorjé EJ, de Jong E, van Hout RW, Driessen GJ, van der Burg M, Wulffraat NM, et al. The challenge of immunoglobulin-G subclass deficiency and specific polysaccharide antibody deficiency: a Dutch pediatric cohort study. Clin. Exp. Immunol. 2016;184(2):226–34. https://doi.org/10.1111/cei.12751
21. Kocaoğlu M, Kocaoğlu BE, Aytekin SE, Karabulut E, Karakaya G, Kalyoncu AF. Clinical and laboratory evaluation of Turkish children with IgG subclass deficiency. Turk J Pediatr. 2022;64(1):38–45. https://doi.org/10.24953/turkjped.2021.06.006