Diagnostic Significance of Reduced IgA in Children

Jasmina Nurkić1, Fatima Numanovic1, Lejla Arnautalic2, Nijaz Tihic1, Dzenan Halilovic3, Mahira Jahic1

Polyclinic for laboratory diagnostic. University Clinical Centre Tuzla, Bosnia and Herzegovina 1
Clinic for Radiology. University Clinical Centre Tuzla, Bosnia and Herzegovina 2
Clinic for Pulmonary Disease. University Clinical Centre Tuzla, Bosnia and Herzegovina 3

Corresponding author: Jasmina Nurkić, MD PhD. Specialist in Clinical Immunology University Clinical Centre Tuzla. Tuzla, Bosnia and Herzegovina. E-mail: jnurki@yahoo.com

ABSTRACT

Introduction: The finding of reduced value of immunoglobulin A (IgA) in children is frequent in daily medical practice. It is important to correctly interpret the findings as adequate further diagnostic evaluation of the patient in order to make the determination on the significance of such findings. In children younger than 4 years always consider the transient impairment of immunoglobulins, maturation of child and his immune system can lead to an improvement in the clinical picture. In older children decreased IgA may lead to serious illnesses that need to be recognize and acknowledge through the appropriate diagnostic methods. Material and methods: Research was realized at the University Clinical Center Tuzla. Children with suspected deficient immune response due to reduced values of IgA observed and , goes through further diagnostic evaluation at the Polyclinic for Laboratory Medicine, Department of Immunology and Department of Microbiology, as well as the Clinic of Radiology. In the period of year 2013, there were a total of 91 patients with reduced values of IgA, age up to 13 years, of which 55 boys and 36 girls. Results: Our study followed 91 patients, for the year 2013, through their medical charts and made evaluation of diagnostic and screening tests. The significance of this paper is to draw attention to the importance of diagnostic approach to IgA deficient pediatric patient and relevance of knowledge of individual diagnostic methods as well as to the proper interpretation of the results thereof.

Key words: IgA deficiency, children, diagnostic evaluation.

1. INTRODUCTION

Understanding of the advantages and limitations of laboratory tests and their correct interpretation prerequsites rational diagnosis of any disease. In pediatrics that interpretation is even more complex due to the need to understand child development especially in the first few years of life. In practice, often in the evaluation of children with frequent infections are done numerous serological tests which attempts to prove the etiology of infection by measuring specific immunoglobulins. In addition to infections, serum immunoglobulins should be determined in each child with unclear elevated erythrocyte sedimentation rate, paraproteinemia in electrophoresis and suspected chronic inflammatory disease of any organic system (post infectious, autoimmune and/or auto inflammatory).

Immunoglobulin (Ig) A deficiency is defined as decreased or absent level of serum IgA in the presence of normal serum levels of IgG and IgM in a patient older than 4 years of age, in whom other causes of hypogammaglobulinemia have been excluded (1). The threshold of 4 years of age issued to avoid premature diagnosis of IgA deficiency which may be transient in younger children due to delayed ontogeny of IgA system after birth. Most individuals are present with recurrent infections of the respiratory and gastrointestinal tracts, allergic disor- ders, and autoimmune manifestations. Subclass IgA1 in monomeric form is mainly found in the blood circulation, whereas subclass IgA2 in dimeric form is the dominant immunoglobulin in mucosal secretions. Monomeric IgA in the circulation may have a role in activation of phagocytic system by means of the FcRα receptors (2, 3, 4). More than 95% of secretory IgA is produced locally. In the gastrointestinal system, organized Payer’s patches or isolated lymphoid follicles as well as non-organized lamina propria can be sites for local IgA production by T cell-dependent as well as T cell-independent mechanisms (5). Secretory IgA level is not determined; therefore, it is possible that the individuals diagnosed with selective IgA deficiency may still have some IgA in the mucosal systems enough to provide some protective functions. In IgA-deficient patients, the common finding is a maturation defect in B cells to produce IgA (6). The defect appears to involve the stem cells since IgA deficiency can be transferred by bone marrow transplantation (7). An intrinsic B cell defect, T helper cell dysfunction, and suppressor T cells have all been reported in IgA deficiency. Abnormalities in the cytokine network such as lack of IL-4, IL-6, IL-7, IL-
10, TGF-β, and most recently IL-21 have also been proposed to play a role in IgA deficiency (6, 8).

The aim was to make an insight into the analysis conducted on immunoglobulins at Department of Immunology, Polyclinic of Laboratory Medicine, University Clinical Centre Tuzla and other diagnostic tests in patients with reduced values of immunoglobulin A.

2. PATIENTS AND METHODS

In the period of year 2013, there were a total of 91 patients with reduced values of IgA, age up to 13 years, of which 55 boys and 36 girls. The average age was 2.6 for boys and 2.4 years for girls. Of the total number of patients, 27 boys and 24 girls were hospitalized, the rest were outpatients or patients treated on an outpatient basis. With Nephelometry method (BN II analyzer, Siemens) were determined immunoglobulin-A, M, G and E. The results are interpreted according to the age of patients (Table 1).

3. RESULTS AND DISCUSSION

The standard 1:20 dilution of samples that takes place in the process of automated BN II nephelometry means that immunoglobulin A values less than 0.24 g/L are automatically displayed as a result of <0.24 g/L. Because IgA deficiency is covered only if the values are reduced or absent with normal serum levels of IgG and IgM in patients older than 4 years with the exclusion of other causes of hypogammaglobulinemia, in our study population, nine boys and five girls meets the above criteria. Mean values of immunoglobulin G, M and E are shown in Table 2.

![Table 1. Reference values of immunoglobulins are interpreted in relation to the age of the patient.](image)

| Table 2. Mean values of immunoglobulin in the total population of analyzed patients |
|-------------------------------------------------|
| Immunoglobulins | Mean value (males) | Mean value (females) |
|------------------|-------------------|-------------------|
| IgG              | 5.98 g/L          | 7.57 g/L          |
| IgM              | 0.8 g/L           | 0.84 g/L          |
| IgE              | 150.5 IU/ml       | 46.6 IU/ml        |

![Table 3. Relation of number of recusted microbiology analysis to the gender of patients](image)

| Table 3. Relation of number of recusted microbiology analysis to the gender of patients |
|-------------------------------------------------|
| Mycrobiology analyses | Males (n=25) | Females (n=25) |
|------------------------|--------------|---------------|
| TORCH                  | 5 (20%)      | 1 (4%)        |
| ASTO                   | 6 (24%)      | 2 (8%)        |
| Urine culture          | 11 (44%)     | 14 (56%)      |
| Coproculture           | 5 (20%)      | 7 (28%)       |
| Swab of nose and throat| 4 (16%)      | 1 (4%)        |

At Clinic for Radiology, University Clinical Centre Tuzla was processed 30 (32.9%) patients, 15 males and 15 females with chest X ray, paranasal sinuses x ray, Magnetic Resonance Imaging (MRI) of head, stomach or sinuses (Table 4).

| Table 4. Relation of number of radiology exam’s to the gender of patients |
|-------------------------------------------------|
| Radiology exams | Male (n=15) | Female (n=15) |
|------------------|-------------|--------------|
| Chest X ray      | 10 pulmonary infiltration (66.7%) | 9 pulmonary infiltration (60%) |
| Sinuses X ray    | 1 sinusitis (6.7%) | 2 heterotopy of gray mass (13.3%) |
| MRI head         | 1 normal findings (6.7%) | 1 intra ventricular hemorrhage (6.7%) |
| MRI stomach      | 1 multicistic renal displasia (6.7%) |
and cause infection (11). Malabsorption may ensue sec-
ondary to structural damage to the intestinal villi. Even
in the absence of infection, some molecules may enter
the subepidermal and submucosal tissue because of the
impaired mucosal clearance of macromolecules and pro-
teins. This process may facilitate antibody production
against certain antigens and intolerance to certain foods
(12). For instance, patients with IgA deficiency have a
higher chance of developing celiac disease (13). Patients
with IgA deficiency are not expected to develop IgA iso-
type antibodies against gliadin and tissue transglutaminase
or endomysium; however, they may have IgG isotype an-
tibodies against those antigens. Inflammatory bowel dis-
eses, mostly ulcerative colitis, have also been reported
in association with selective IgA deficiency (6). At Immu-
nology laboratory tests

| Table 5. Immunology laboratory tests | Males (n=21) | Females (n=19) |
|-------------------------------------|-------------|---------------|
| Tissue transglutaminase (TTg) IgA antibody | 7 (33.3%) | 8 (42.10%) |
| Anti Nuclear Antibodies | 4 (19.04%) | 2 (10.5%) |
| Autoimmune liver profile (anti-
mitochondrial antibody, smooth
muscle antibody, liver/kidney/
microsomal antibody) | 2 (9.5%) | 0 |
| Circulating Immune Complexes (CIC) | 4 (19.04%) | 1 (5.3%) |
| Anti gliadin antibodies IgG | 7 (33.3%) | 6 (31.6%) |
| Anti Myeloperoxidase and Anti-
Proteinase 3 antibodies (MPO,
PR3) | 1 (4.8%) | 1 (5.3%) |
| Rheuma factor | 1 (4.8%) | 0 |
| Nose smear for eosinophiles | 4 (19.04%) | 3 (15.8%) |
| Specific antigen IgE (egg, milk, wheat) | 4 (19.04%) | 5 (26.3%) |

were detected in 19% of patients. This figure varies from
20% to 30% based on the age range of studied populations
(14). Celiac disease screening should include IgG isotype
antibodies against gliadin and tissue transglutaminase
since IgA isotype antibodies may not be detected because
of the IgA deficiency.

In our study from the total of 91 patients with reduced
IgA, 9 (9.9%) boys and 5 (5.5%) girls suit age criteria for
the diagnosis of true IgA deficiency. Radiological methods
in the four boys demonstrated pulmonary infiltration and
in one infiltration of the paranasal sinuses. Microbiologi-
cal tests were processed for all males but results indicated
only high ASTO levels for one male and culture of nasal
swab of one male indicated H. Influenzae. Immunology
tests for this true IgA deficiency group were same as for
other patients in study but only one male was positive for
anti gliadine IgG antibodies. Of the five girls diagnosed
with true IgA deficiency, two showed heterotopy gray
mass on head MRI, one inflammation of the paranasal si-
nuses and the only one microbiologically treated was with
normal titers of ASTO and anti DNase.

4. CONCLUSION
Repeated infections are undoubtedly the most frequent
indication for determination of serum immunoglobulins in
children. Such an approach is rational because most of
the primary disorder of the immune system in children
occurs as a result of impaired development or function of B lymphocytes (about 50%). Evaluation of a suspect-
ed IgA deficiency would generally include a diversity of
diagnostic procedures. In addition, pertinent laboratory
testing for the associated conditions, e.g., recurrent in-
flections, allergies, or celiac disease, should be performed.
Therefore, a patient with IgA deficiency, once identified,
would deserve a regular follow-up of clinical and immu-
nological findings.

CONFLICT OF INTEREST: NONE DECLARED.

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