Alergia, Asma e Inmunología
Pediátricas

Artículo original

Vol. 25, Núm. 2 • Mayo-Agosto 2016
pp 38-45

Basal serum levels of immunoglobulins G, A, M, and E in the group of patients with cystic fibrosis at Hospital Infantil Universitario de San José Bogotá DC, in 2014

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ABSTRACT

Background: Patients with cystic fibrosis have poor lung function and chronic infections which impair the quality of life and are the leading cause of death. Hypogammaglobulinemia is associated with less severe lung disease; hypergammaglobulinemia with major lung impairment, presumably due to a hyperimmune response. **Objective:** Determine G, A, M, and E immunoglobulins serum levels in patients diagnosed with cystic fibrosis at Hospital Infantil Universitario de San José de Bogotá in 2014. **Material and Methods:** Case series of patients diagnosed with cystic fibrosis. Fifty three patients were included. Forty one samples of serum IgG, IgA, IgM, and IgE immunoglobulins were taken from patients without acute infectious disease, and who had not received gamma-globulin therapy or immunosuppressive therapy. Body mass index, lung function, bronchiectasis, and *Pseudomonas aeruginosa* colonization were assessed. **Results:** 51.2% of participants were male. The median age was 17.7 years; 58.5% of the patients had a normal BMI; the median FEV_1 was 67.9%. The frequency of bronchiectasis was 39%, 31.7% were colonized with *Pseudomona aeruginosa*. Most of the patients had normal immunoglobulin levels; low levels of IgG were present in less than 5% of the patients. Patients with high IgG had bronchiectasis in 85.7%. High IgA was mainly present in male between 10 and 20 years old, who also had the worst respiratory impairment. They also had a greater colonization for more than three months. Bronchiectasis was found in 85% of the cases and was colonized by *Pseudomonas aeruginosa*. **Conclusion:** Increase in immunoglobulins levels correlate with bronchiectasis and inversely with FEV_1.

Key words: Cystic fibrosis, immunoglobulins, inflammation, malnutrition, bronchiectasis, *Pseudomona aeruginosa*, FEV_1.

Abbreviations:
CF = Cyst fibrosis.
CFTR = Cystic fibrosis transmembrane regulator.
TNF = Tumor necrosis factor.
IRA = Instituto de referencia andino.
BMI = Body mass index.
CDC = Centers for Disease Control and Prevention.
FEV_1 = Volume in 1 second was determined.

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RESUMEN

Antecedentes: *Los pacientes con fibrosis quística tienen una mala función pulmonar e infecciones crónicas que deterioran su calidad de vida, y son la principal causa de muerte. La hipogammaglobulinemia se asocia con enfermedad pulmonar menos severa; mientras que la hipergammaglobulinemia se asocia con insuficiencia pulmonar importante, presumiblemente debido a una respuesta hiperinmune.* ***Objetivo:*** *Determinar los niveles de inmunoglobulinas séricas G, A, M y E en pacientes con diagnóstico de fibrosis quística del Hospital Infantil Universitario de San José de Bogotá en 2014.* ***Material y métodos:*** *Serie de casos de pacientes diagnosticados con fibrosis quística. Se incluyeron cincuenta y tres pacientes. Cuarenta y un muestras de inmunoglobulinas del suero IgG, IgA, IgM e IgE fueron tomadas de pacientes sin enfermedad infecciosa aguda y que no habían recibido tratamiento con gammaglobulina o terapia inmunosupresora. Se evaluó el índice de masa corporal, la función pulmonar, bronquiectasias, y la colonización de* Pseudomonas aeruginosa*.* ***Resultados:*** *El 51.2% de los participantes eran hombres. La edad promedio fue de 17.7 años; 58.5% de los pacientes tenían un IMC normal; el FEV_1 promedio fue de 67.9%. La frecuencia de las bronquiectasias fue del 39%, 31.7% fueron colonizados por* Pseudomonas aeruginosa*. La mayoría de los pacientes tenía niveles normales de inmunoglobulina; niveles bajos de IgG estaban presentes en menos del 5% de los pacientes. Los pacientes con IgG alta tenían bronquiectasias en el 85.7%. La IgA alta estuvo principalmente presente en varones de entre 10 y 20 años de edad, que también tenían el peor deterioro respiratorio. También tenían una mayor colonización por más de tres meses. La bronquiectasia se encontró en 85% de los casos y fue colonizada por* Pseudomonas aeruginosa*.* ***Conclusión:*** *El aumento de los niveles de inmunoglobulinas se correlaciona con las bronquiectasias e inversamente con el FEV_1.*

Palabras clave: *Fibrosis quística, inmunoglobulinas, inflamación, desnutrición, bronquiectasias,* Pseudomonas aeruginosa*, FEV_1.*

INTRODUCTION

Cystic fibrosis (CF) is an autosomal recessive disease very frequent in USA. It is present in one of every 3,500 alive newborn babies; it is more common in Caucasian population, and the incidence is variable.[1] In Colombia, it is estimated that one in every 5,000 alive, newborn babies would have CF and that one in every 7,000 couples would be in risk of having children with this disease.[2]

It is a disorder caused by a genetic defect in chromosome 7 which encodes the gene that produces the transmembrane regulation protein, called cystic fibrosis transmembrane regulator (CFTR).[2] It mainly affects the respiratory tract, the gastrointestinal system, and the sweat glands of the skin. Its most important clinical signs are recurrent respiratory infection (*Staphylococcus aureus* or *Pseudomona aeruginosa*), intestinal malabsorption syndrome, abnormal electrolyte content in sweat, meconium ileus, abnormal growth, cirrhosis (or other liver malfunctions), pancreatic insufficiency or male infertility (azoozpermia).[3] Literature reports impairment in both innate and acquired immunities, cellular and humoral. A defect in the gen that encodes the transmembrane protein CFTR leads to an abnormal transfer of ions through the epithelial cell surfaces generating the presence of a hypertonic fluid that deactivates defensins which, in turn, enables infections. There is a local inflammatory response with the presence of pro-inflammatory markers which includes the increase of neutrophils and macrophages count, high levels of elastase, inflammatory cytokine (such as IL8), tumor necrosis factor (TNF), and leukotriene B4. The alteration in the immunoglobulin (Ig) levels has been described as a result of inflammation and recurrent chronic infection in the airways[3] with reports of 7.5% of patients with hypogammaglobulinemia and 31 to 69% with hypergammaglobulinemia.[4-6]

The lack of knowledge of the immune system performance in this group of patients, and the scarce reported evidence, motivated the design of the present study. The main objectives were to determine the G, A, M, and E immunoglobulin serum values, as well as to define the frequency of patients with hypogammaglobulinemia, normal levels of IgG, and hypergammaglobulinemia in patients diagnosed with CF in Hospital Universitario Infantil de San José. The patients were in «baseline disease» status and had no acute infection during 2014. Then, a correlation between immunoglobulin values and hypo and hypergammaglobulinemia would be established.

MATERIAL AND METHODS

A case series type descriptive study was designed. CF diagnosed patients of the cystic fibrosis group from Hospital Infantil Universitario de San José de Bogotá DC were included. These patients were at «baseline status» of the disease and did not have acute infection.

Patients with a background of intervention with gammaglobulin, cancer immunosuppression therapy, trans-

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plant or those with acute lung infection at the moment of taking the sample were excluded from the immunoglobulin analysis.

The samples were analyzed at Instituto de Referencia Andino (IRA) with the purpose of quantifying G, A, M, and E immunoglobulin, using an *in vitro* test in human serum and plasma. They were analyzed in the Roche/Hitachi (cobas c 311analyzer) and in the Modular-Evo for immunoglobulin E systems which automatically calculate the analyte concentration in each sample. The reference values for G, A, M, and E immunoglobulin were evaluated according to the standardization of CRM 470 proteins from the equipment insert, taken from «age-and sex-specific pediatric reference intervals» *(Tables I and II)*.[7]

The classification of immunoglobulin values –based on age range, established by the laboratory– are shown on the tables with the baseline values according to the laboratory inserts (IRA) «age and sex-specific pediatric reference intervals».[7]

The nutritional status of the patients was assessed considering the body mass index (BMI) classification. The BMI in patients over 18 was directly calculated with the formula weight/size;[2] in patients under 18 years, the percentiles were taken as stated by the BMI tables for age from the Centers for Disease Control and Prevention (CDC). The forced expiratory volume in 1 second was determined (FEV_1) according to the spirometry report of the last 3 months. The presence of bronchiectasis was found in the chest X-ray of the last six months. The sputum cultures in the previous year were studied to establish the colonization by *Pseudomona aeruginosa*. The quantitative variables were analyzed with central tendency and dispersion measures. The qualitative ones were assessed with absolute and relative frequencies. The statistical analysis was performed in STATA 12. This study had the approval of the Institutional Bioethics Committee. All patients signed informed consent. For patients over 7, their parents signed informed consent.

Table I. A, G, and M immunoglobulins ranges.[7]

Range age (years)	IgA (mg/dl)	IgG (mg/dl)	IgM (mg/dl)
4-6	27-195	504-1464	24.210
7-9	34-305	572-1474	31-208
10-11	53-204	698-1560	31-179
12-13	58-358	759-1549	35-239
14-15	47-249	716-1711	15-188
16-19	61-348	549-1584	23-259
Over 19	70-400	700-1600	40-230

Lockitch G, Halstead AC, Quigley G, MacCallum C. Age- and sex-specific pediatric reference intervals: study design and methods illustrated by measurement of serum proteins with the Behring LN Nephelometer. *Clin Chem.* 1988; 34 (8): 1618-1621.

Table II. E immunoglobulin ranges.[7]

Range age (years)	Normales values (UI/mL)
4-6	Below 60
7-9	Below 90
10-15	Below 200
Adults	Below 100

Lockitch G, Halstead AC, Quigley G, MacCallum C. Age- and sex-specific pediatric reference intervals: study design and methods illustrated by measurement of serum proteins with the Behring LN Nephelometer. *Clin Chem.* 1988; 34 (8): 1618-1621.

RESULTS

The total of patients in the CF group was 53. When the immunoglobulin samples were taken, 5 patients voluntarily dropped out of the trial, and in 2 patients, samples were no taken. The total was 41 patients taken and analyzed samples *(Figure 1)*; 51.2% of the participants were male. The median age was 17.7 (SD 5.9) years old, 53.7% was in the group from 10 to 19 years old; 58.5% of the patients had normal BMI. The median FEV_1 was 67.9 (interquantile range - IQR 46.7). Consistent with the severity of the disease based on FEV_1, 43.9% presented mild functional impairment. Four patients could not be tested for pulmonary function because of their age. The bronchiectasis frequency was 39%, 31.7% was colonized by *Pseudomona aeruginosa (Table III)*.

Most of the patients had quantitative normal immunoglobulin levels as expected for their age, according to the normalcy tables of the laboratory; the low levels were present in less than 5% of the patients. IgA low levels were not found *(Table IV)*. Out of the patients with IgA high levels, 71.4% were male. Most of them were between 10 to 20 years old with a greater functional respiratory impairment (minor FEV_1); 85.7% of them had bronchiectasis and 71.4% had bacterial colonization over three months *(Table V)*. Patients with high IgG were mostly male with ages between 10 and 20; 85.7% of them had bronchiectasis. There were no differences in the nutritional status *(Table VI)*. From those who presented IgE normal levels, 40.9% were male. Most of the patients with high IgE had normal weight (58.8%); 64.7% of the patients with IgE high levels were not colonized *(Table VII)*. In patients with IgM high levels, the proportion of women was higher than men (57.1 versus 42.9%) and the 42.8% was malnourished *(Table VIII)*.

DISCUSSION

Cystic fibrosis is a recessive autosomal disease, whose frequency is the same in men and women.[8] We found

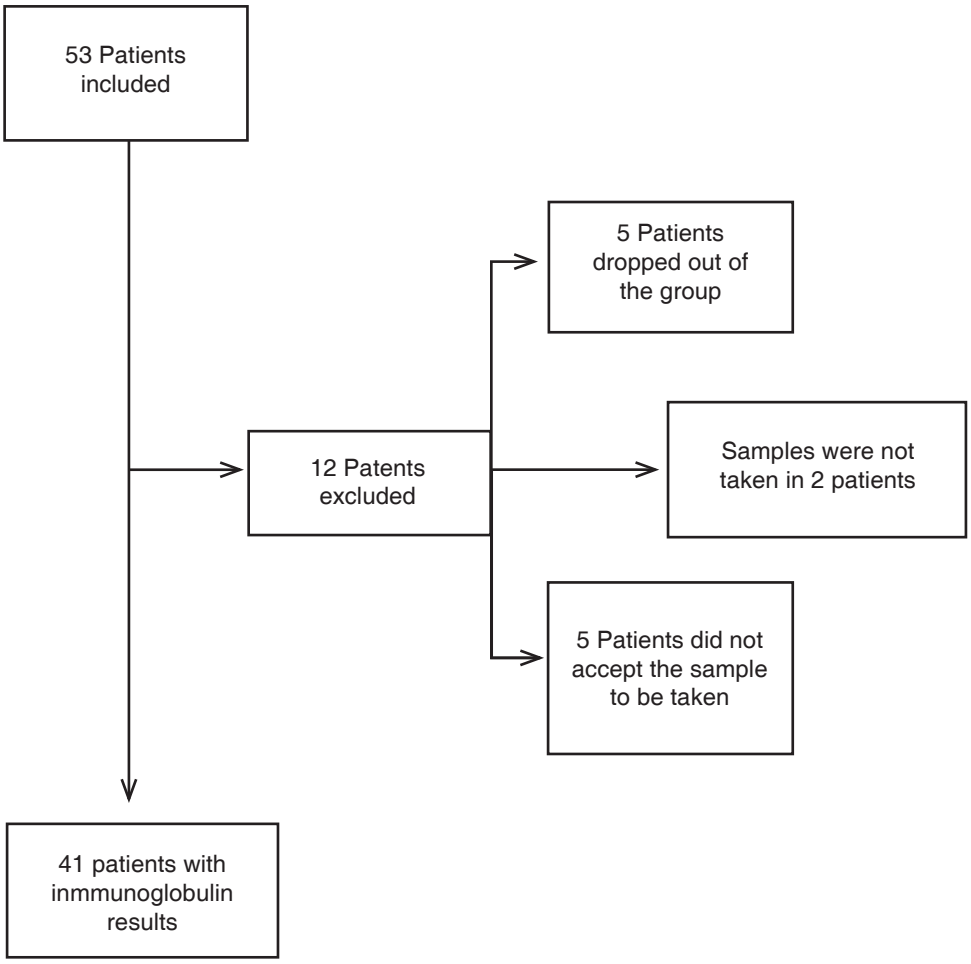

Figure 1. *Patient selection.*

that the disease was similar in men and women in the studied population, the frequency was 1.05:1, which is consistent with the figures reported in the literature.[6]

In 1938, when Andersen discovered CF, life expectancy was two years. During the eighties, CF increased significantly to 25 and 28 years for women and men respectively; by 2010 it increased to 38.3 years.[9]

In our population, the median age was 17.7 years; 31.7% were older than 20 years; which suggests an increase in the average of life. This may be explained by the advancements in the disease knowledge, creation of transdisciplinary groups which enable an early diagnosis, as well as appropriate treatments for lung and gastrointestinal exacerbations. Such treatments are preventive and have improved the quality of life of the patients.[10]

According to the latest data from Fundación Internacional de Fibrosis Quística (International Cystic Fibrosis Foundation), 20% of the children affected by CF presented low weight/size (below the acceptable percentile 5 for age). The nutritional status is recognized as an important survival indicator because there is a strong correlation between nutritional disorder and the lung function impairment.[11,12] In this trial, we found that 39% of the patients were malnourished and had a BMI lower than 18. Such clinical condition may derive from exocrine pancreatic failure, and may impair the lipase activity, decreases colipase, phospholipase A, tripsine, amilase, and the ductal secretion of water and bicarbonate. Such impairment and reduction cause a poor digestion and malabsorption of fats and proteins due to the lack of such nutrients. All that ends in malnutrition. Additionally, the increase in energy expenditure due to recurrent lung infections (as well as inappropriate caloric intake) would condition the development of malnutrition in our sample of patients.

The trial findings showed that malnutrition is related to A and G hypogammaglobulinemia. In 2005, Garside et al.[6] stated that in spite of the lack of a clear explanation, malnutrition used to be associated to low immunoglobulin levels; the lowest levels were present in cases of severe malnutrition. The lung impairment reported by a FEV_1 was 74% for the Garside's group.[6] The population was formed mostly by children with a median of age

of 9.2 years; for our group, the FEV_1 median was lower (67.9%), and the impairment was higher because of the lung function impairment.

In patients with CF, there is a colonization of the airways caused by several microorganisms, particularly *Pseudomona aeruginosa*. It has been reported that 50% of the patients who are younger than 18 years are colonized by *Pseudomona aeruginosa*, which exceeds 80% in older patients.[13] In our study, the *P. aeruginosa* colonization reached 31.7%; however, in the studied sample –formed by the higher proportion of adults–, the bacterial colonization was low. That result may be explained by the work and transdisciplinary intervention carried out at the hospital with the use of new systemic and local antimicrobial agents, less use of antimicrobial agents administered empirically, and more patient's compliance to the preventive measures.

Table III. Population characteristics.

Characteristics	n (%)
Gender	
Male	21 (51.2)
Female	20 (48.8)
Age, median (SD)	17.7 (5.9)
Categorical age	
Below 10 years	6 (14.6)
Between 10 and 19	22 (53.7)
Between 20 and 30	13 (31.7)
Body mass index, median (SD)	18.9 (3.3)
Body mass index classification	
Malnutrition	14 (34.2)
Normal	24 (58.5)
Overweight	3 (7.3)
Obesity	0
Bronchiectasis	16 (39.0)
Pseudomona colonization	13 (31.7)
< 3 months	0
> 3 months	13 (31.7)
FEV_1, median (SD)	67.9 (46.7)
Severity (FEV_1)	
Mild	18 (43.9)
Moderate	15 (29.3)
Severe	8 (19.5)
The test was not performed	3 (7.3)

n = Number of patients; SD = Standard deviation; FEV_1 = Forced expiratory volume in 1 second.

In 1980, Matthews et al.[14] found in a trial (which included 332 patients younger than 20 years) that the overall prevalence with hypogammaglobulinemia was 10.8%; the prevalence for hypergammablobulinemia (IgG) was 22% in children younger than 10 years. Perhaps, this hypogammaglobulinemia reflects a minimal impairment in the lung function and less inflammatory response. Our study results showed a low proportion of hypogammaglobulinemia, only 2.4%, finding which may be related to age and the sample size. Our patients were older: 31.7% was over 20 years, those patients were affected by multiple recurrent lung infections, had chronic lung inflammation, and high humoral response caused by more impairment of the lung function in the FEV_1, as well as the presence of bronchiectasis.

Hypergammaglobulinemia was found in 34.2% of the patients, which is similar to the trial by Richard Moss et al.[5], who demonstrated that IgG serum levels were high in patients with CF, compared to controls. Such findings are like Proesmans' (2011)[15], who in a cohort study described that IgG high levels were present in 16% of the patients at the beginning of the follow-up and went up to 25% four years later. Those results confirm that these levels increase as long as the patients get old; likewise, they are the result of chronic and progressive lung infections (product of the IgG fragmentation against *Pseudomona*, which makes it a poor opsonizer). Thus, these G immunoglobulin levels may be useful for assessing the lung function damage.[16,17]

In our series of cases, the IgA levels were high in 17.1% of the patients, which is different from the results obtained by Garside et al.[6] (5.2%). The IgA analysis may be useful when *P. aeruginosa* is present in secretions of the upper airway, because it would be a predictive factor of lung infection.[18]

In the study and follow-up of patients with CF, IgA and IgG levels should be regarded as a routine strategy to indirectly assess the lung functions damage. High lev-

Table IV. Immunoglobulin percentage distribution according to category.

Immunoglobulin	Quartile 25%	Median (IQR)	Quartile 75%	Low (%)	Normal n (%)	High n (%)
				41 (100)	41 (100)	41 (100)
IgA	138.8	210 (IQR 163.1)	301.9	0	34 (82.9)	7 (17.1)
IgM	95	121.6 (IQR 79.1)	174.1	2 (4.9)	32 (78.0)	7 (17.1)
IgG	1019.3	1395.7 (746.7)	176.6	1 (2.4)	26 (63.4)	14 (34.2)
IgE	17.1	60.245 (IQR 203.5)	220.7	2 (4.9)	22 (53.7)	17 (41.4)

IQR = Interquartile range; n = Number of patients.

Table V. Population characteristics according to A immunoglobulin levels.

	A immunoglobulin levels	
Characteristics, n (%)	Normal n = 34	High n = 7
Gender		
Male	16 (47.1)	5 (71.4)
Female	18 (52.9)	2 (28.6)
Categorical age		
Younger than 10 years	5 (14.7)	1 (14.2)
Between 10 and 19	18 (52.9)	4 (57.1)
Between 20 and 30	11 (32.4)	2 (28.6)
BMI		
Malnutrition	12 (35.9)	2 (28.6)
Normal	19 (55.8)	5 (71.4)
Overweight	3 (8.8)	0
Obesity	0	0
FEV_1, median (SD)	73.39 (25.04)	32.02 (13.21)
FEV_1 classification		
Mild	18 (52.9)	0
Moderate	10 (29.5)	2 (28.6)
Severe	3 (8.8)	5 (71.4)
The test was not performed	3 (8.8)	0
Bronchiectasis	10 (29.4)	6 (85.7)
Pseudomona colonization		
No colonization	26 (76.5)	2 (28.6)
Colonization < 3 months	0	0
Colonization > 3 months	8 (23.5)	5 (71.4)

BMI = Body mass index; n = Number of patients, FEV_1 = Forced expiratory volume in one second.

Table VI. Population characteristics according to G immunoglobulin levels.

	G immunoglobulin levels		
Characteristics, n (%)	Low n = 1	Normal n = 26	High n = 14
Gender			
Male	1 (100)	10 (38.5)	10 (71.4)
Female	0	16 (61.5)	4 (28.6)
Categorical age			
Younger than 10 years	0	4 (15.4)	2 (14.3)
Between 10 and 19	1 (100)	10 (38.5)	11 (78.6)
Between 20 and 30	0	12 (46.1)	1 (7.1)
BMI			
Malnutrition	0	11 (42.3)	3 (21.4)
Normal	1 100)	13 (50)	10 (71.4)
Overweight	0	2 (7.7)	1 (7.2)
Obesity	0	0	0
FEV_1, median (SD)	42.5 (0)	70.59 (30.7)	58.66 22.9)
FEV_1 classification			
Mild	0	14 (53.9)	4 (28.6)
Moderate	1 (100)	5 (19.2)	6 (42.8)
Severe	0	5 (19.2)	3 (21.5)
The test was not performed	0	2 (7.7)	1 (7.1)
Bronchiectasis	0	10 (29.4)	6 (85.7)
Pseudomona colonization			
No colonization	1 (100)	20 (76.9)	7 (50)
Colonization < 3 months	0	0	0
Colonization > 3 months	0	6 (23.1)	7 (50)

BMI = Body mass index; n = Number of patients, FEV_1 = Forced expiratory volume in one second.

els of these immunoglobulins are inversely related to the FEV_1, which increases in the presence of bronchiectasis.

High levels of IgG and IgA in pediatric patients with CF should be a guide to evaluate the lung function with FEV_1, images, colonization by *P. aeruginosa* in ears and sinuses. Screening of the IgA and IgG levels must be used in combination with other measures like lung function (FEV_1) as an additional follow-up parameter to evaluate the lung impairment of the patients with CF.[18]

Unlike other trials, our study analyses the IgE. The clinical need of quantifying this immunoglobulin arises because most of these patients have allergic disease, allergic rhinitis, allergic sinusitis, nasal polyps, and the confirmation of sensitization by *Aspergillus fumigatus*. IgE was high in 41.4% of the patients.

In relation to the intervention of the patients with CF, the literature lately has proposed the use of anti-inflammatory drugs in order to decrease the inflammation in the airway, to preserve the lung function, and diminish the disease progression.[19,20] In a clinical trial, it was proved that patients who received ibuprofen presented a slower annual rhythm in the FEV_1 change, compared with patients who received placebo.[21]

Regarding the current evidence, our study enables to suggest screening and follow-up of the patients diagnosed with CF with immunoglobulins G, A, M, E, and take early action with polyclonal immunoglobulins like immunomodulatory substances of the chronic inflammatory response in order to diminish and delay the structural and functional lung damage secondary to bronchiectasis.

The pharmacological mechanisms of the polyclonal immunoglobulins activity are depicted in the literature: opsonization increase, complement, phagocytosis against the encapsulated bacteria, antibody-dependent cell cytotoxicity, reinforcement of the function of neutrophils, natural killer cells and regulatory T cells; decrease in the inflammatory pathway triggered by cytokines (IL2, IL 6, MCP-1, IFN, FNT alpha, TNF-beta), modulation of the activation of complement, chemokines, adhesion molecules in endothelium; passive immunity against microbial triggers and anti-idiotype antibodies, reduction of the neutrophils NO, increase of the IL-10 anti-inflammatory activity, neutralization of the bacterial growth, modulation of the cell migration by ICAM-1, VCAM-1, inhibition of the monocyte activation, induction of self-reacting B cell apoptosis, neutralization of self-antibodies

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Table VII. Population characteristics according to E immunoglobulin levels.

	E immunoglobulin levels		
Characteristics, n (%)	Low n = 2	Normal n = 22	High n = 17
Gender			
Male	1 (50)	9 (40.9)	12 (70.6)
Female	1 (50)	13 (59.1)	5 (29.4)
Categorical age			
Younger than 10 years	1 (50)	1 (4.6)	4 (23.5)
Between 10 and 19	1 (50)	15 (68.2)	7 (41.2)
Between 20 and 30	0	6 (27.2)	6 (35.3)
BMI			
Malnutrition	0	7 (31.8)	6 (35.2)
Normal 18-25	0	14 (63.4)	10 (58.8)
Overweight > 25	1 (100)	1 (4.6)	1 (5.8)
Obesity > 30	0	0	0
FEV_1, median (SD)	82.2	65.36 (30.3)	64.08 (25.8)
FEV_1 classification			
Mild	1 (50)	10 (45.5)	7 (41.2)
Moderate	0	5 (22.7)	7 (41.2)
Severe	0	5 (22.7)	3 (17.6)
The test was not performed	1 (50)	2 (9.1)	0
Bronchiectasis	0	9 (40.9)	7 (41.2)
Pseudomona colonization			
No colonization	2 (100)	15 (68.2)	11 (64.7)
Colonization < 3 months	0	0	0
Colonization > 3 months	0	7 (31.8)	6 (35.3)

BMI = Body mass index; n = Number of patients, FEV_1 = Forced expiratory volume in one second.

Table VIII. Population characteristics according to M immunoglobulin levels.

	M immunoglobulin levels		
Characteristics, n (%)	Low n = 2	Normal n = 32	High n = 7
Gender			
Male	0	18 (56.3)	3 (42.9)
Female	2 (100)	14 (43.7)	4 (57.1)
Categorical age			
Younger than 10 years	0	5 (15.6)	1 (14.3)
Between 10 and 19	1 (50)	17 (53.1)	4 (57.1)
Between 20 and 30	1 (50)	10 (31.3)	2 (28.6)
BMI			
Malnutrition <18	0	11 (34.4)	3 (42.8)
Normal 18-25	2 (100)	18 (56.2)	4 (57.2)
Overweight > 25	0	3 (9.4)	0
Obesity > 30	0	0	0
FEV_1, median (SD)	69.4 (12.8)	69.1 (28.8)	47.6 (24.6)
FEV_1 classification			
Mild	1 (50)	15 (46.9)	2 (28.6)
Moderate	1 (50)	9 (28.1)	2 (28.6)
Severe	0	6 (18.8)	2 (28.6)
The test was not performed	0	2 (7.0)	1 (14.2)
Bronchiectasis	0	10 (29.4)	6 (85.7)
Pseudomona colonization			
No colonization	2 (100)	26 (81.2)	0
Colonization < 3 months	0	0	0
Colonization > 3 months	0	6 (18.8)	7 (100)

BMI = Body mass index; n = Number of patients, FEV_1 = Forced expiratory volume in one second.

and immune complexes; increase of the self-antibodies catabolism by FcRn via; activation of C1q, C3b, C4 C3a, C5a, regulation of the expression receptor, and dendritic cell migration.[22]

Therefore, the quality of life of the affected patients would improve, like it was demonstrated by I M Balfour-Lynn et al. in 2004.[23]

CONCLUSION

Most of the patients had normal levels of immunoglobulins; low IgG levels were present in less than 5% of the examined patients. There were no reports of low levels of IgA. BMI was normal in 58.5% of the patients. The median of FEV_1 was 67.9% (interquartile range 46.7). The bronchiectasis frequency was 39% and 31.7% in colonization by *Pseudomona aeruginosa*.

According to the findings, we suggest to further the study of the patients with immunoglobulins G, A, M, and E when it was intended as the main diagnosis of CF, as well as to consider the use of IV or subcutaneous polyclonal immunoglobulins as an immunomodulator in case of chronic and recurrent infection by CF.

ACKNOWLEDGEMENTS

We thank to the patients of the group of cystic fibrosis for participating in the trial. We also thank to Mrs. Martha Gantiva (Coordinator of the Grupo de Fibrosis Quística) for bringing the patients closer and for the approach of the patients.

AUTHORSHIP CONTRIBUTIONS

All the authors participated in the data interpretation and in the manuscript writing.

CONFLICT OF INTEREST

The A, G and M immunoglobulins levels were financed by Laboratorio Amarey Novamedical through Hospital Univesitario Infantil de San José. The trial was carried out as part of the requirements for Adriana Escobar and Diana Carolina Barrero to obtain the grade in the pediatrics specialization at Fundación Univestitaria de Ciencias de la Salud- Hospital Universitario Infantil de San José, Bogotá, Colombia.

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