Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2024.234154.2873 Volume 30, Issue 6, Sept. 2024
Manuscript ID ZUMJ-2406-3429
DOI 10.21608/ZUMJ.2024.295112.3429
ORIGINAL ARTICLE

Role of Interleukin7 Gene Polymorphism in Childhood Bronchial Asthma, and its Relation to Asthma Severity

Amru Magdy Abdel Fattah[1*], Bashir Abdallah Hassan[1], Mohammed Sanad Nagiub[1], Rehab A. Rabie[2]
[1] Department of Pediatrics, Faculty of Medicine, Zagazig University, Egypt.
[2]Department of Medical Microbiology and Immunology,Faculty of Medicine, Zagazig University, Egypt.

Correspondingauthor:
AmruMagdy Abdel Fattah

Email:
amru.magdy474@gmail.com

Submit Date 03-06-2024
Revise Date 30-06-2024
Accept Date 04-07-2024

ABSTRACT

Background: Variable and recurrent symptoms, reversible airflow restriction, and bronchospasm characterize asthma, a chronic long-term respiratory disease. One of the key cytokine genes in the formation of the innate and adaptive inflammatory response in the genesis of asthma is interleukin 7. There have only been a few investigations on the connection between children's asthma and interleukin-7 gene polymorphism. In order to evaluate the significance of interleukin 7 gene polymorphism in childhood bronchial asthma and its relationship to asthma severity in Egyptian children, we set out to explore SNP rs766736182**. Methods:** In this case-control research, 27 healthy control children and 108 patients with asthma were matched based on age. Whole blood samples were used to isolate genomic DNA. The polymorphism of the restriction fragment length polymerase chain reaction was used to identify the IL-7 polymorphism rs766736182.

Results: Polymorphism of IL-7 (A missense) the risk of childhood asthma was linked to SNP rs766736182 (odds ratio (OR) = 4.69, 95% confidence interval (CI) = 1.6250-13.5791, P-value <0.001).

Conclusions: This study demonstrated that the interleukin-7 SNP rs766736182 is a risk factor for childhood asthma. We found that children with asthma had higher serum levels of hs-CRP, suggesting that this marker may be useful for asthma severity and follow up.

Keywords: Interleukin-7 polymorphism; children asthma, Cytokines; JAK inhibitors,Hbβ;147.

INTRODUCTION

Asthma affects 300 million people worldwide at the moment, and by 2025, that number could rise to 100 million, making it a significant global health concern. A complex network of interrelated elements at many disease levels and stages, such as the genetic, cellular, tissue, and organ levels, are involved in the etiology of bronchial asthma. Environmental factors and patient-specific non-asthma related factors, such as co-morbidities and lifestyle choices, aggravate these relationships even more [1]. Interleukin genes produce the cytokines necessary for inflammatory processes. A higher incidence of pediatric asthma has been linked to single nucleotide polymorphisms (SNPs) in a few interleukin genes, including interleukin-1, interleukin-2, and interleukin-6. Early in T-cell development, interleukin-7 (25 kDa), which encodes a cytokine essential for B- and T-cell development, acts as a cofactor for the V(D) rearrangement of the T-cell receptor beta (TCRB) and as a pre-pro-B cell growth-stimulating factor. However, it is yet unclear if SNPs in interleukin-7 are linked to asthma [2, 3].

The statistical study revealed that the interleukin-7 gene polymorphism SNP rs766736182 is strongly linked to the risk of asthma, suggesting a potential function for this polymorphism in the pathophysiology of asthma and in predicting treatment response [4]. The aim of this study was to examine role of Interleukin¬7 Gene Polymorphism in Childhood Bronchial Asthma . An inhaled, small molecule selective Janus Kinase 1 (JAK1) inhibitor in development for the treatment of moderate-to-severe asthma.

whose disease is poorly controlled despite high-dose ICSs plus other controllers.The JAK/STAT pathway is an important cascade of signal transduction for cytokines.Hbβ(147aa) mRNA expression increased with airway epithelial maturation [14,4,7].

METHODS

This was a case-control study done in Zagazig University Hospitals.The ethical committee of Zagazig University in Egypt approved this study and in compliance with the Declaration of Helsinki, parents' and patients' signed informed consent was obtained when applicable.108 kids with asthma and 27 kids in the healthy control group children with asthma. Based on (GINA 2018), they were divided into four groups: moderate persistent patients (27), mildintermittent patients (27), mild persistent patients (27), and severe persistent patients (27).

All of the groups studied were subjected to the following:

Gathering the history: the patient's complete medical history, asthma medication regimens, and family history were all gathered.

Clinical examination: this includes anthropometric measurements such as height, weight, and body mass index (BMI) (weight/height m2). It also includes general examinations and **vital signs.** People who had a BMI between 85th and 95th were categorized as overweight, Obese patients (BMI >30) were defined as those whose BMI was higher than the 95th percentile. ANDHealthy weight: BMI is equal to or greater than the 5th percentile and less than the 85th percentile for age, gender, and height.

Additionally measured were the waist circumference and blood pressure **[**5, 6**].**

Routine testing for high-sensitivity C-reactive protein, liver function, renal function, lung function, and total blood count. Pulmonary function analyses were performed on patients with asthma who had been diagnosed with the condition for at least five years by using the forced spirometry program D-97024 Hochberg, Germany uses a tidal breathing analysis to quickly and accurately assess the subjects' respiratory resistance; PEF, FVC%, FCV1%, and PEF% are all calculated. Bronchial asthma influences some chronic diseases such as coronary heart disease, diabetes mellitus, and hypertension, and chronic kidney disease **[**18**].**

Genomic DNA extraction

Following the manufacturer's instructions, a gSYNC DNA extraction kit (Geneaid Blood Kit, Taiwan) was used to extract genomic DNA from venous blood samples of asthma patients and healthy controls ,at -20°C DNA was stored.

Interleukin 7 gene polymorphism :

The restriction fragment length polymorphism method was employed in the polymerase chain reaction to genotype the missense SNP, rs766736182, of the IL-7 gene. (PCR-RFLP) (using Primer3and BLAST). The primers are:

Forward, primer5'TTGGAATAAAATTTTGATGGGC ACT -3' and the Reverse primer 5' AGCAGATAGATTCTTGGAGGATGC -3'.

The 20µl reaction mixture used for the PCR reaction included 10µl of PCR Master Mix (iTaqTM, iNtRON, Korea), 1µl each of the forward and reverse primers, 6µl of DNA extract, and 2µl of nuclease-free water. Next, first denaturation at 95°C for 10 minutes. The following settings were used for 35 amplification cycles: 95°C for 30s, 58°C for 30s, and 72°C for 30s. The five-minute extension at 72°C comes last. The VeritiTM 96-Well Thermal Cycler (Applied Biosystems, California, USA) was used to conduct the PCR. The PCR products underwent an overnight digestion at 37°C with 2.5 U of the restriction enzyme Eco57I (AcuI). The digested products underwent analysis using ethidium bromide-stained 3% agarose gel electrophoresis. at 80V.

Statistical analysis

The Hardy-Weinberg equilibrium of IL-7 genotype and allele frequencies in controls was examined. The chi-square test was used to examine the frequency of the different IL-7 genotypes and alleles between asthma patients and healthy controls. In respect to the analyzed IL-7 (SNP) gene polymorphisms, the odds ratio (OR) and 95% confidence interval (95% CI) were computed for disease susceptibility. A one-way ANOVA test was used to assess the data for quantitative

independent variables; P value < 0.05 was considered statistically significant. An analysis of all the data was conducted using IBM SPSS Statistics (version 26).

RESULTS

Our study included 108 patients with asthma, their age ranged from 5 to 14 years with a mean age ± SD of 6.48±1.25 years, 77 males and 58 females and 27 healthy control subjects whose clinical characteristics are listed in Table 1

We observed that there was a statistical significance increase in frequency of +ve family history among mild and Severe group compare to other groups. On the other hand, the studied 5 groups showed no statistical significance differences between in age, sex, weight, height or BMI (Table 1).

The levels of hs-CRP in asthmatic patients were significantly higher than those in the control cases (<0.001). The serum hs-CRP levels in the sever persistent asthmatics were significantly higher than those in the others asthmatic ones (p=0.04). The FEV1 in asthmatic patients were significantly lower than those in the control cases (<0.001). The FEV1 in the sever and moderate persistent asthmatics were significantly lower than those in the mild asthmatic ones (p=0.04). IGE level differed significantly as they were higher in asthmatic groups (<0.01). (Table 2).

Higher serum hs-CRP and LOWER FEV1 values in children with asthma, Receiver operating characteristic curve of FEV1(the cut off <80%) for the diagnosis of asthma (AUC = 0.892, sensitivity = 30.22%, specificity = 95%. Otherwise (ROC curve of (hs CRP) (the cut off (>1 mg/L)) for the diagnosis of asthma (AUC = 0.91, sensitivity = 77.8%, specificity = 77.8% (Table 3.)

The rs766736182 AG polymorphism and asthma severity varied considerably throughout the groups. The distribution of the gene polymorphism among the asthmatic group was 50%, 43% and 5% for the AA, AG and GG genotypes, respectively. The frequency among the control group was 85%, 14% and 0% the AA, AG and GG genotypes, respectively.

The distribution of Interleukin-7 gene polymorphisms in the control group was in line with what the Hardy–Weinberg model predicted. There isn't any notable deviation (X2 test P value =0.67)..Compatibility with the HWE is a way to address that the control group is representative, homogenous and have no significant stratification bias. Since the case or the patient group is a non-random selection of individuals, it does not necessarily follow this equation (19). (Table 4).

The G allele rate of rs766736182 was greater in asthmatic patients than in normal subjects (P-value <0.001, OR = 4.69, 95% Confidence interval CI = 1.6250-13.5791)Table (5).

Compared to controls, we found that asthmatic children had a significantly higher number of carriers of AG genotypes of rs766736182 (OR = 4.4; CI: 1.434-13.686, P<0.05). Conversely, children with asthma had a lower frequency of the AA genotype than did controls (OR = 0.18; CI: 0.58-0.557, P<0.05)Table 6.

Mild asthma is linked to the AA genotype of rs766736182 (OR= 2.28; 95% CI: 1.06-4.94, P<0.05). However, in cases of moderate/severe asthma, the AG genotype was less common (OR=0.043; 95% CI: 0.19-0.93, P<0.05**)** The distribution of the gene polymorphism among mild intermittent/persistent asthmatic group was 60%, 38% and 50% for the AA, AG and GG genotypes, respectively. The frequency among the moderate/severe group was 40%, 61% and 50% the AA, AG and GG genotypes, respectively. Nonetheless, there was no discernible variation in the GG genotype distribution between mild and moderate/severe asthmatics. (OR=1; 95% CI:0.193-5.19, P> 0.05) Table 7.

Table 1- Characters of the five studied groups

Variable	Mild intermittent (Group I) (*n*=27)	Mild persistent (Group II) (*n*=27)	Moderate persistent (Group III) (n=27)	Severe persistent (Group IV) (n=27)	Healthy Control (Group V) (n=27)	P
Age: years	7.67±2.84	6.48±1.25	7.78±3.07	8.22±2.5	7.93±3.54	0.35

	5-13	5-14	5-10	5-14	5-14	
Female: **Male:**	**15** (55.6%) **12** (44.4%)	**9** (33.3%) **18**(66.6 %)	**14** (51.8 %) **13**(48.1 %)	**12** (44.4 %) **15**(55.5 %)	**8** (29.6 %) **19**(70.3 %)	0.23
Weight: (Kg)	28.33±7.928	27.44±8.196	31.52±13.88	31.96±13.58	33.00±13.32	0.333
Height: (cm)	124.81±14.98	123.59±9.598	125.67±24.260	133.74±20.65	128.37±15.51	0.238
BMI: (Kg/m2)	18.06±2.79	17.71±3.51	19.33±3.47	17.18±3.62	19.15±4.04	0.117
_ve **+ve** **Family history**	**6** (22.2%) **21** (77.8%)	**6** (22.2%) **21** (77.8%)	**4** (14.8%) **23** (85.2%)	**2** (7.4%) **25** (92.6%)	**20** (74.1%) **6** (22.2%)	<0.001 **

Body mass index (*BMI*). Data presented as mean &,SD: Stander deviation χ^2: Chi square test , **: Highly significant (P<0.001).F: ANOVA test. NS: Non significant (P>0.05)

Table 2: Lab parameters and spirometry of studied groups

Variable	Mild intermittent (Group I) (*n*=27)	Mild persistent (Group II) (*n*=27)	Moderate persistent (Group III) (n=27)	Sever persistent (Group IV) (n=27)	Healthy Control (Group V) (n=27)	P
WBC: ($x10^3/mm^3$)	7.94±1.38	8.66±1.78	8.14±1.95	8.68±1.86	7.97±1.38	0.6
HB: (gm/dl)	11.83±0.76	12.04±0.75	12.22±0.90	12.06±0.76	11.83±0.76	0.34
PLT: ($x10^3/mm^3$)	281.61±30.52	283.17±42.29	302.72±50.19	283.34±42.33	281.61±30.52	0.212
hsCRP: (mg/dl)	0.64±0.51	0.65±0.52	0.67±0.63	2.5 ±1**	0.4±0.3	<0.001 **
ALT: (U/L)	15.63±3.63	15.30±4.39	16.87±5.82	14.40 ±5.82	14.40 ±4.82	.315
AST: (U/L)	20.433 ±5.7	23.396±5.7	20.256±5.6	21.641±5.4	22.756±5.8	.203
Urea: (mg/dl)	10.71±2.31	10.24±1.45	11.52±2.58	10.23±1.46	10.71±2.31	.194
Creatinine: (mg/dl)	0.40±0.14	0.352±0.01	0.41±0.11	0.35±0.071	0.40±0.14	.580
FEV1: (%)	90.61±2	83.37 ±2	66.70±4	57.82±9	93.8±1.33	<0.001 **
IGE (IU/L)	153.58±14.62	153.58±14.62	158.20±15.05	162.20±9.23	46.10±7.52	<0.001

Data are presented as mean± standard deviation
FEV1: forced expiratory volume in one second, high-sensitivity C-reactive protein, liver function, renal function, lung function, and total blood count. Pulmonary function
F: ANOVA test,
NS: Non significant (P>0.05) **: Highly significant (P<0.001)

Table 3: Sensitivity and specificity of spirometry and C-reactive protein (hsCRP) for an asthma diagnosis

Index and threshold	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	AUC
FEV1 <80%	30.22	95	47	89	0.892
Hs CRP (>1 mg/L)	77.85	77.8	92.2	44.4	0.91

FEV1: forced expiratory volume in one second, high-sensitivity C-reactive protein
ROC curve (receiver operating characteristic curve)

Table 4: Interleukin-7 gene polymorphism distribution among the studied groups

Gene polymorphism	Mild intermittent (Group I) (n=27)	Mild persistent (Group II) (n=27)	Moderate persistent (Group III) (n=27)	Severe persistent (Group IV) (n=27)	Healthy control (Group V) (n=27)	P	HWE
AA (wild)	**18** 66.7%	**15** 55.6%	**14** 51.9%	**8** 29.6%	**23** 85.2%		
AG	**7** 25.9%	**11** 40.7%	**12** 44.4%	**17** 63.0%	**4** 14.8%	0.01*	0.677635
GG (variant)	**2** 7.4%	**1** 3.7%	**1** 3.7%	**2** 7.4%	**0** 0.0%		
Total	**27** 100%	**27** 100%	**27** 100%	**27** 100%	**27** 100%		

*Hardy-Weinberg equilibrium (*HWE*), Chi square test*

Table 5: Comparison between cases and control groups as regards to Interleukin-7 gene allele distribution

Gene Allele	Control (n=54)	Case (n=216)	Total 100%	P	OR	95% CI
A (wild) N=207	**50 24.2%**	**157 75.8%**	100%	<0.001 **	4.69	1.6250-13.5791
G (variant) N=63	**4** 6.3%	**59** 93.7%	100%			

χ^2: Chi square test, **: Highly significant (P<0.001)

Table 6: Distribution of Interleukin-7 gene polymorphism rs766736182 in asthmatic and healthy children

Gene polymorphism	Asthmatic group (n=108)	Control group (n=27)	P	OR	95% CI
AA (wild) N=78	**55** 70.5%	**23** 29.5%	<0.001**	0.18	0.58-0.557
AG N=51	**47** 92.2%	**4** 7.8%	<0.001**	4.4*	1.434-13.686
GG (variant) N=6	**6** 100.0%	**0** 0.0%	0.21	0.8	0.724-0.864
Total=135	**108** 100%	**27** 100%			

χ^2: Chi square test, **: Highly significant (P<0.001)

Table 7: Relation between Interleukin-7 gene polymorphism and asthma severity**.**

Gene polymorphism	Mild intermittent / persistent asthma (n=54)	Moderate/ severe asthma (n=54)	P	OR	95% CI
AA (wild)	**33** 60%	**22** 40%	**P<0.001**	**2.28**	**1.06-4.94**
AG	**18** 38.3%	**29** 61.7%	**P<0.001**	**0.43**	**0.198-0.939**
GG(variant)	**3** 50%	**3** 50%	**P> 0.05**	**1**	**0.193-5.19**
Total	**100%**	100%			

χ^2: Chi square test, **: Highly significant (P<0.001)

DISCUSSION

Childhood-onset asthma is a chronic respiratory condition with reversible airflow restriction, bronchospasm, and a range of variable and recurrent symptoms. The missense mutation rs766736182 on the interleukin-7 gene results in a replacement of Glu for Lys at the 175th position in the amino acid sequence of the interleukin-7 protein (ORF2). changes the rate at which airway inflammation advances and impacts the prevalence of asthma [2].

We aimed in this study to determine the role of Interleukin7 Gene Polymorphism rs766736182 in Childhood Bronchial Asthma, and its Relation to Asthma Severity to provide a new potential target for treatment.

A total 135 participants were enrolled in this case/control study and were categorized into 5 groups (27 patients each); mild intermittent, mild persistent asthma, moderate asthma, severe asthma and finally the apparently healthy controls.

Initially, we investigated missense SNP, rs766736182 of the IL-7 gene by using the polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) in all study groups and found that the G allele of rs766736182 was higher in asthma patients than that in controls (P-value <0.001, OR = 4.69, 95% Confidence interval CI = 1.6250-13.5791) and the risk of children asthma. Asthmatic children had a significantly higher proportion of bearers of the AG genotype of rs766736182 than controls (OR = 4.4; CI: 1.434-13.686, P<0.05.

These findings are consistent with those of Cao et al. [2], who found that children with the G allele had a 2.18-fold increased chance of getting asthma. Comprised 489 age-matched healthy controls with a mean age ± SD of 4.62 ± 3.69 years and 437 asthma patients with a mean age ± SD of 4.1 ± 3.16 years.

Interestingly, our results did not show any significant relationship between age, sex, weight, height or BMI. But increase in frequency of +ve family history among mild and Sever group compare to other groups. These results are in line with those of Hedman et al. [8], who found that early childhood asthmatic family history is associated with varying ages at which asthma attacks first appear.

Our findings showed that, in terms of IgE distribution between cases and controls, cases had significantly greater levels than controls; also, IgE was much higher in cases than in control, with no discernible difference between other subgroups. So that when the IgE is higher in cases than the control, we can use it to produce treatment. Our result was supported by Bush et al. [9] who studied a humanised monoclonal antibody which binds to circulating IgE, thus stopping IgE binding to the high affinity receptor. Managing severe allergic asthma Higher serum hs-CRP and FEV1 levels were seen in children with asthma in the current investigation; these findings were consistent with those of Kumar et al.[10] greater blood hs-CRP levels (cutoff 1.1 mg/L) in kids with uncontrolled asthma, suggesting that, in line with our findings,

Loman et al. [11] this biomarker might be used for asthma follow-up. Children's C-ACT scores were substantially lower for those with a FEV1 of 80% or less than for those with a FEV1 > 80% (p =.023).

Our results were consistent with those of Yalçın et al. [12], they discovered that there were no statistically significant differences between the patient and control groups in the laboratory data (hemoglobin, , white blood cell, and platelets). [14].

Notably, we found that, in contrast to moderate/severe asthma, the AA genotype was associated with mild asthma. Conversely, moderate asthma had a lower frequency of the AG genotype (38.3%). When compared with moderate/severe asthma (61.7%). Nonetheless, there was no discernible variation in the GG genotype distribution between moderate and moderate/severe asthmatics. This indicates that the IL 7 polymorphism rs766736182G is a possible determinant of asthma severity in Egypt population. In contrast, Zhang et al. [2] in the Chinese Han population found no significant changes (P<0.38) in the differences in rs766736182 genotype frequencies across patients with various stages of asthma differences in the racial and ethnic.

CONCLUSIONS:

According to this study, the interleukin-7 SNP rs766736182 is a risk factor for childhood asthma. Children with asthma had higher serum hs-CRP concentrations, which may indicate that this biomarker is useful for tracking asthma control.

References:

1. **Paramonova N, Trapina I, Gradauskiene B, Plavina S, Tamasauskiene L, Bastyte D et al.** Genetic Diversity in Bronchial Asthma Susceptibility: Exploring the Role of Vitamin D Receptor Gene Polymorphisms in Varied Geographic Contexts. Int J Mol Sci. 2024 5;25(3):1943.
2. **Cao J, Tian L, Li Z, Zhang C, Ji Q, Zhang C et al.** Interleukin-7 gene polymorphism rs766736182 associates with the risk of asthma in children. J Clin Lab Anal. 2019 ;33(2):e22675.
3. **Toghraie FS, Sharifzadeh SM, Ramezani A, Maymand EM, Yazdanpanah-Samani M**, Ghaderi A. Cloning and expression of recombinant human Interleukin-7 in Chinese Hamster Ovary (CHO) Cells. Rep Biochem Mol Biol. 2017 ;6(1):66.
4. **Kamaruzaman NA, Sulaiman SA, Kaur G, Yahaya B.** Inhalation of honey reduces airway inflammation and histopathological changes in a rabbit model of ovalbumin-induced chronic asthma. BMC Complement Altern Med. 2014. 14: p. 1-11.
5. **Ghareeb D, Abdelazem AS, Hussein EM, Al-Karamany AS.** Association of TNF-α-308 G> A (rs1800629) polymorphism with susceptibility of metabolic syndrome. J Diabetes Metab Disord. 2021 ;20:209-15.
6. **Morgan AD**. Unravelling the obesity–asthma connection in childhood and adolescence: does body shape matter?. Thorax. 2024;79(5):393-4.
7. **Marozkina N, Smith L, Zhao Y, Zein J, Chmiel JF, Kim J et al.** Somatic cell hemoglobin modulates nitrogen oxide metabolism in the human airway epithelium. Sci Rep. 2021 ;11(1):15498.
8. **Hedman L, Almqvist L, Bjerg A, Andersson M, Backman H, Perzanowski MS et al.** Early-life risk factors for development of asthma from 8 to 28 years of age: a prospective cohort study. ERJ Open Research. 2022 ;8(4);00074.
9. **Bush A.** Update in paediatric asthma 2024. Paediatr Respir Crit Care Med. 2024 Jan 1;8(1):3-10.
10. **Kumar A, Jat KR, Sankar J, Lakshmy R, Lodha R, Kabra SK.** Role of high-sensitivity C-reactive protein (hs-CRP) in assessment of asthma control in children. J Asthma. 2023 ;60(7):1466-73.
11. **Loman DG, Borgmeyer AE, Henry LD, Mahl CS, Ellis AG**. Childhood Asthma Control Test and spirometry values in school-age children. J Asthma. 2024 ;61(4):322-7.
12. **Yalçın SS, Emiralioğlu N, Yalçın S.** Evaluation of blood and tooth element status in asthma cases: a preliminary case–control study. BMC Pulm Med. 2021 ; 21(1):201.
13. **Justiz-Vaillant AA, Gopaul D, Akpaka PE, Soodeen S, Arozarena FR**. Severe Combined Immunodeficiency Classification, Microbiol Association and Treatment. Microorganisms. 2023 ;11(6):1589.
14. **Riff C, Larsson J, Nilsson M, et al**. Inhaled AZD4604: local Janus Kinase 1 inhibition without systemic activity. [Thematic Poster Session]. Presented at the American Thoracic Society International Conference 2024 (17-22 May).
15. **Global Initiative for Asthma (2017):** Global strategy for asthma management and prevention. https://ginasthma.org/wp-content/uploads/2018/04/wms-GINA-2018-report-tracked_v1.3.pdf
16. **Huang HL, Ho SY, Li CH, Chu FY, Ciou LP, Lee HC, Chen WL, Tzeng NS.** Bronchial asthma is associated with increased risk of chronic kidney disease. BMC Pulm Med. 2014;14:80.
17. **Namipashaki A, Razaghi-Moghadam Z, Ansari-Pour N.** The Essentiality of Reporting Hardy-

Weinberg Equilibrium Calculations in Population-Based Genetic Association Studies. Cell J. 2015 Summer;17(2):187-92.

Citation:

Abdel Fattah, A., Hasan, B., Nagiub, M., Rabie, R. Role of InterleukinGene Polymorphism in Childhood Bronchial Asthma, and its Relation to Asthma Severity. *Zagazig University Medical Journal*, 2024; (2599-2606): -. doi: 10.21608/zumj.2024.295112.3429