Article

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Relationship between *IL-6* and *IL-10* Gene Polymorphisms and Susceptibility to Pneumonia and Serum Levels of *IL-6*, *IL-10*, and *C-Reactive Protein* in Children

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Background: Cytokines are molecules that play a crucial role in the development of childhood pneumonia. This study aims to investigate the relationship between gene polymorphisms of interleukin (*IL*)-*6* and *IL-10* and the susceptibility to childhood pneumonia.

Methods: A total of 200 child patients with pneumonia and 200 healthy children were assigned to the disease group and control group, respectively. Peripheral blood was collected from both groups, and the polymorphisms were analyzed by sequencing. Additionally, the serum levels of IL-6, IL-10, and C-reactive protein were analyzed.

Results: The frequencies of certain alleles and genotypes of *IL-6* and *IL-10* gene polymorphisms were found to be higher in the disease group compared to the control group ($p < 0.05$). Specifically, the allele C of *IL-6* gene polymorphism rs762371056, allele A of *IL-6* gene polymorphism rs762759043, and allele A of *IL-10* gene polymorphism rs570186303 were more frequent in the disease group. Additionally, the disease group exhibited higher frequencies of genotype CC of rs762371056, genotype AA of polymorphism rs762759043, and genotype AA of rs570186303 ($p < 0.05$). The two groups also differed in the distributions of the dominant model of rs762759043 and the recessive model of rs570186303 ($p < 0.05$). Besides, there were differences in the distributions of haplotype CA of rs762371056 and rs762759043 and haplotypes AA, AG and GG of rs570186303 and rs575853731 between the two groups ($p < 0.05$). Child patients with genotype TC had higher levels of serum IL-6, while the levels of serum IL-10 were lower in child patients carrying genotype AA. Child patients with genotype AA had a distinctly higher level of serum C-reactive protein ($p < 0.05$).

Conclusions: *IL-6* and *IL-10* gene polymorphisms have been found to be correlated with susceptibility to childhood pneumonia.

Keywords: gene polymorphism; childhood pneumonia; IL-6; IL-10

Introduction

Childhood pneumonia is a respiratory disease caused by bacteria or viruses, and it is the leading cause of death in children under the age of 5 years old, gravely endangering their health and life [1,2]. The number of cases of this disease is negatively correlated with social and economic growth, and 99% of cases occur in developing countries. Environmental pollution and premature birth are among the factors that can cause childhood pneumonia [3,4]. The integrity of the immune system is also an important factor in preventing childhood pneumonia. Interleukin (IL) family molecules, such as IL-2 and IL-4, are associated with the development and progression of childhood pneumonia and play a major role in regulating disease progression by the body's immune system [5]. Exploring the influences of other IL family members on childhood pneumonia helps understand its cause and progression. In recent years, there have been growing studies on gene polymorphism, which is one of the factors for varying susceptibility to diseases among different populations [6,7]. Multiple gene polymorphisms are correlated with disease progression [8,9], and genetic polymorphisms in inflammatory cytokines are risk factors for pneumonia [10]. The *IL-6* gene is located on chromosome 7 and consists of 5 exons and 4 introns with a long sequence length of 5 kb [11]. IL-6-597A/G (rs1800797) and IL-6-174G/C (rs1800795) polymorphisms are closely associated with type 2 diabetes susceptibility [12], while IL-6-572C/G (rs1800796) polymorphism is a potential cause of membranous glomerulonephritis [13]. *IL-10* is located on human chromosome lq31-32 and consists of 5 exons and 4 introns [14]. *IL-10* gene polymorphism is associated with non-small cell carcinoma [15]. Some studies reported that *IL-6* and *IL-10* genes may be as-

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Table 1. PCR primer sequences.

Genes		Primer sequence
rs762371056	F	CAGACAACGCCCTTGAAGACA
	R	GCCCTGTTGAATGCCTCCA
rs762759043	F	TCAACAGGGCTGTCAAGAGTT
	R	CAGATAGAACGTCAGTTTCCTCC
rs570186303	F	GGGATACCCACCGTTTAACCA
	R	AGGTTTACTCTCCGAAAGCTCTT
rs575853731	F	TTTCGGAGAGTAAACCTGTCCA
	R	AGGCAGGCAACAGTTAAGTTTC

PCR, Polymerase Chain Reaction.

sociated with the susceptibility and severity of community-acquired pneumonia [16,17]. However, the relationship between gene polymorphisms and susceptibility to childhood pneumonia, the important molecules in the immune system, has not yet been delved into in China and abroad.

Therefore, this study aimed to investigate the influence of *IL-6* and *IL-10* gene polymorphisms on childhood pneumonia. The goal was to identify screening indicators and improve the prevention and treatment of childhood pneumonia. The present study analyzed the *IL-6* gene polymorphisms rs762371056 and rs762759043, as well as *IL-10* gene polymorphisms rs570186303 and rs575853731 in the peripheral blood karyocytes in 200 child patients with pneumonia and 200 normal children. This study also analyzed the *IL-6* and *IL-10* gene haplotypes, and serum IL-6, IL-10, and C-reactive protein levels in the subjects. The correlations of *IL-6* and *IL-10* gene polymorphisms with the susceptibility to childhood pneumonia were deeply investigated.

Materials and Methods

Patients

In this study, 200 child patients were enrolled as a disease group and 200 healthy children were enrolled as a control group. The general data and clinical information of the children in both groups, including name, hospitalization ID No., age, sex, history of diseases, family history, and history of drug allergies, were collected. The diagnostic criteria for pneumonia were as follows: (1) the presence of general symptoms, such as fever, apastia, dysphoria, and wheezes; (2) the presence of respiratory symptoms, such as cough and tachypnea; (3) bacterial or viral infections indicated by routine blood examinations; and (4) pneumonia shown in a chest X-ray examination. The inclusion criteria were: (1) children under 12 years old, (2) children with normal thyroid function, (3) no lymphocytosis and positive acid-fast bacilli. The exclusion criteria were: (1) children with diabetes, (2) children with metabolic diseases, (3) children with respiratory tract infections, (4) children with benign or malignant tumors, and (5) children with autoimmune diseases. The present study was approved by Hunan Children's Hospital of Changsha (Changsha, China) and performed following The Declaration of Helsinki. Before the start of the study, written informed consent was obtained from all patient guardians (Approval Number: HNC12990C).

Blood Sample

A total of 3–4 mL of peripheral blood was drawn from each child and centrifuged at 3500 rpm for 8 min in a centrifuge (Allegra X-15R, Beckman Coulter, Brea, CA, USA) within 2 h. The upper-layer serum was then preserved in liquid nitrogen for the determination of C-reactive protein, IL-6, and IL-10 levels. The genomic deoxyribonucleic acids (DNAs) of the mid-layer karyocytes were extracted for detecting gene polymorphism [18].

Genomic DNA Extraction

Genomic DNAs were extracted from peripheral blood samples using the blood genome extraction kit (DP348, TIANGEN, Beijing, China). A centrifuge tube was first added with protease K (1245680100, Solarbio, Beijing, China) solution based on the volume of the sample, peripheral blood sample, and buffer, and mixed evenly. The mixture was then incubated at 65 °C for 8 min, added with absolute alcohol, mixed evenly, and transferred into an adsorption column. Subsequently, the adsorption column was added with buffer, centrifuged, and added with elution buffer. The resulting solution was the genomic DNAs of the subjects. Finally, DNA purity was measured using a spectrophotometer (NanoDrop One, Thermo Fisher, Waltham, MA, USA).

Polymerase Chain Reaction (PCR) Amplification and Analysis of IL-6 and IL-10 Gene Polymorphisms

The polymorphic regions of four genes (rs762371056 and rs762759043 of *IL-6* gene, and rs570186303 and rs575853731 of *IL-10* gene) were amplified using a PCR instrument (NA301, Vazyme, Nanjing, China). The PCR was performed in a system (25 μL in total) composed of 1 μL each of forward and reverse primers, 0.5 μL of DNA templates, 12.5 μL of Taq polymerase, and 10 μL of dH_2O under the following conditions: 95 °C for 5 min, (95 °C for 30 s, 55 °C for 40 s, and 72 °C for 35 s) × 35 cycles, and 72 °C for 5 min. Table 1 shows the primers for the polymorphic regions of rs762371056 and rs762759043 for the *IL-6* gene and rs570186303 and rs575853731 for the *IL-10* gene. The PCR products were sent to Sichuan Biotechnology Co., Ltd. (Chengdu, China) for sequencing, and the polymorphisms of *IL-6* and *IL-10* genes were analyzed in disease and control groups.

Determination of Serum IL-6 and IL-10 Levels

Serum IL-6 and IL-10 levels in the peripheral blood were measured using enzyme-linked immunosorbent assay (ELISA) kits (555220 and 555157, BD Biosciences, San

Table 2. General information.

Variable	Control group (n = 200)	Disease group (n = 200)	t/χ^2	p
Age (year)	4.53 ± 0.79	4.62 ± 0.82	1.12	0.264
Sex (n, %)			0.52	0.472
Male	126 (63.0)	119 (59.5)		
Female	74 (37.0)	81 (40.5)		
Heart rate	94.86 ± 5.74	165.93 ± 7.85	103.40	<0.001
Respiratory rate	31.12 ± 3.68	64.25 ± 4.26	83.23	<0.001
Blood oxygen saturation	97.92 ± 2.37	84.46 ± 4.88	35.09	<0.001
White blood cell count	6.38 ± 1.42	13.54 ± 2.79	32.34	<0.001
C-reactive protein (mg/L)	0.18 ± 0.02	2.49 ± 0.41	79.58	<0.001

Table 3. Allele distributions of *IL-6* gene polymorphisms rs762371056 and rs762759043, and *IL-10* gene polymorphisms rs570186303 and rs575853731.

Gene	Polymorphism	Allele	Control group	Disease group	Odd ratio (OR)	95% confidence interval (CI)	χ^2	p
IL-6	rs762371056	T	218 (0.545)	179 (0.448)	1.47	1.11–1.95	7.61	0.005
		C	182 (0.455)	221 (0.552)				
	rs762759043	C	209 (0.522)	169 (0.422)	1.49	1.13–1.97	8.02	0.004
		A	191 (0.477)	231 (0.578)				
IL-10	rs570186303	A	202 (0.505)	254 (0.635)	1.72	1.28–2.26	13.79	0.000
		G	198 (0.495)	146 (0.365)				
	rs575853731	G	198 (0.495)	232 (0.580)	0.71	0.53–0.93	5.33	0.055
		A	202 (0.505)	168 (0.420)				

IL, interleukin.

Jose, CA, USA). The wells for the standard curves were set in triplicate wells for each patient. After the assay, a microplate reader (1681130, iMark, Bio-Rad, Hercules, CA, USA) was used to read the absorbance of each well. The concentrations of serum IL-6 and IL-10 in each subject were then calculated based on the standard curves.

Detection of C-Reactive Protein

After performing daily routine quality control, the levels of C-reactive protein were measured in the subjects of the disease group using an automatic biochemical analyzer (BS-280, Mairui, Shenzhen, China) at the Laboratory Hunan Children's Hospital.

Statistical Analysis

The statistical analysis was performed using SPSS 23.0 software (IBM Co., Ltd., Armonk, NY, USA). Measurement data are presented as mean ± standard deviation ($\bar{x} \pm SD$), while enumeration data are presented as (n, %). The *t*-test was used to compare measurement data, and the Hardy-Weinberg equilibrium test was performed. Haplotype analysis was completed at the SHEsis website (http://analysis.bio-x.cn/SHEsisMain.htm). A p-value < 0.05 was considered statistically significant. The strength of association was described by the odds ratio (OR) at 95% confidence interval (CI) using the Logistic Regression Model. Moreover, multiple linear regression analysis was applied to compare the biochemical parameters among individuals with IL-6 and IL-10 genotypes.

Results

Clinicopathological Features of Patients

The study found that there were no statistically significant differences in general data, such as age and sex distribution, between the disease group and the control group ($p > 0.05$) (Table 2). However, there were significant differences in several health indicators between the two groups, including heart rate, respiratory rate, oxygen saturation, white blood cell count, and C-reactive protein ($p < 0.05$) (Table 2). Specifically, heart rate, respiratory rate, white blood cell count, and C-reactive protein were higher in the disease group, while oxygen saturation was lower, compared to the control group ($p < 0.05$) (Table 2).

Allele Distributions of IL-6 Gene Polymorphisms rs762371056 and rs762759043, and IL-10 Gene Polymorphisms rs570186303 and rs575853731

The allele distributions of three gene polymorphisms were analyzed in the disease group and the control group. The *IL-6* gene polymorphisms rs762371056 ($p = 0.005$) and rs762759043 ($p = 0.004$), and the *IL-10* gene polymorphism

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Table 4. Genotype distributions of *IL-6* gene polymorphisms rs762371056 and rs762759043, and *IL-10* gene polymorphisms rs570186303 and rs575853731.

Gene	Polymorphism	Genotype	Control group	Disease group	χ^2	*p*
IL-6	rs762371056	TT	59 (0.295)	45 (0.225)	8.36	0.015
		TC	100 (0.500)	89 (0.445)		
		CC	41 (0.205)	66 (0.330)		
	rs762759043	CC	54 (0.270)	44 (0.220)	10.71	0.004
		CA	101 (0.505)	81 (0.405)		
		AA	45 (0.225)	75 (0.375)		
IL-10	rs570186303	AA	53 (0.265)	84 (0.420)	13.01	0.001
		AG	96 (0.480)	86 (0.430)		
		GG	51 (0.255)	30 (0.150)		
	rs575853731	GG	54 (0.270)	71 (0.355)	5.12	0.068
		GA	90 (0.450)	90 (0.450)		
		AA	56 (0.280)	39 (0.195)		

Table 5. Analysis of *IL-6* gene polymorphisms rs762371056 and rs762759043, and *IL-10* gene polymorphisms rs570186303 and rs575853731.

	Gene	Polymorphism	Genotype	Control group	Disease group	χ^2	*p*
Dominant model	*IL-6*	rs762371056	TT+TC	159 (0.795)	134 (0.670)	4.66	0.097
			CC	41 (0.205)	66 (0.330)		
		rs762759043	CC+CA	155 (0.775)	125 (0.625)	7.42	0.024
			AA	45 (0.225)	75 (0.375)		
	IL-10	rs570186303	AA+AG	149 (0.745)	170 (0.850)	5.35	0.069
			GG	51 (0.255)	30 (0.150)		
		rs575853731	GG+GA	144 (0.720)	161 (0.805)	4.43	0.109
			AA	56 (0.280)	39 (0.195)		
Recessive model	*IL-6*	rs762371056	TT	59 (0.295)	45 (0.225)	2.76	0.252
			TC+CC	141 (0.705)	155 (0.775)		
		rs762759043	CC	54 (0.270)	44 (0.220)	2.4	0.301
			CA+AA	146 (0.730)	156 (0.780)		
	IL-10	rs570186303	AA	53 (0.265)	84 (0.420)	7.04	0.030
			AG+GG	147 (0.735)	116 (0.580)		
		rs575853731	GG	54 (0.270)	71 (0.355)	4.98	0.083
			GA+AA	146 (0.730)	129 (0.645)		

rs570186303 ($p = 0.000$) showed significant differences between the two groups (Table 3). In the disease group, allele C of *IL-6* gene polymorphism rs762371056, allele A of *IL-6* gene polymorphism rs762759043, and allele A of *IL-10* gene polymorphism rs570186303 had higher frequencies than those in the control group (Table 3).

Genotype Distributions of IL-6 Gene Polymorphisms rs762371056 and rs762759043, and IL-10 Gene Polymorphisms rs570186303 and rs575853731

The genotype distributions of *IL-6* gene polymorphisms rs762371056 ($p = 0.015$) and rs762759043 ($p = 0.004$) and *IL-10* gene polymorphism rs570186303 ($p = 0.001$) were found to be different between the disease group and the control group (Table 4). The disease group exhibited higher frequencies of genotype CC of *IL-6* gene polymorphism rs762371056, genotype AA of *IL-6* gene polymorphism rs762759043, and genotype AA of *IL-10* gene polymorphism rs570186303 than the control group (Table 4).

Analysis of IL-6 Gene Polymorphisms rs762371056 and rs762759043 and IL-10 Gene Polymorphisms rs570186303 and rs575853731 in the Disease Group and Control Group

The two groups showed differences in the distributions of the dominant model of *IL-6* gene polymorphism rs762759043 ($p = 0.024$) and the recessive model of *IL-10* gene polymorphism rs570186303 ($p = 0.030$) (Table 5).

Table 6. Analysis of haplotypes of *IL-6* gene polymorphisms rs762371056 and rs762759043, and *IL-10* gene polymorphisms rs570186303 and rs575853731.

Gene	Polymorphism	Haplotype	Control group	Disease group	Odd ratio (OR)	95% confidence interval (CI)	χ^2	*p*
IL-6	rs762371056	CA	91.47 (0.229)	147.09 (0.368)	1.962	1.440–2.673	18.478	0.000
		CC	90.53 (0.226)	73.91 (0.185)	0.775	0.549–1.093	2.115	0.146
	rs762759043	TA	99.53 (0.249)	83.91 (0.210)	0.801	0.576–1.115	1.726	0.189
		TC	118.47 (0.296)	95.09 (0.238)	0.741	0.541–1.015	3.491	0.062
IL-10	rs570186303	AA	116.54 (0.291)	90.43 (0.226)	0.71	0.517–0.977	4.445	0.035
		AG	85.46 (0.214)	163.57 (0.409)	2.546	1.865–3.476	35.577	0.000
	rs575853731	GA	85.46 (0.214)	77.57 (0.194)	0.886	0.628–1.250	0.479	0.489
		GG	112.54 (0.281)	68.43 (0.171)	0.527	0.375–0.740	13.897	0.000

Table 7. Relationships of *IL-6* gene polymorphisms rs762371056 and rs762759043, and *IL-10* gene polymorphisms rs570186303 and rs575853731 with serum IL-6 and IL-10 levels.

Gene	Polymorphism	Genotype	IL-6 (pg/mL)	*p*	IL-10 (pg/mL)	*p*
IL-6	rs762371056	TT	101.23 ± 4.34	0.000	12.52 ± 1.25	0.214
		TC	156.42 ± 11.24		13.93 ± 2.15	
		CC	98.24 ± 4.24		12.65 ± 2.74	
	rs762759043	CC	112.33 ± 4.51	0.241	13.45 ± 2.43	0.311
		CA	108.45 ± 5.25		12.25 ± 3.21	
		AA	114.85 ± 5.87		12.87 ± 3.21	
IL-10	rs570186303	AA	108.42 ± 5.32	0.284	9.34 ± 0.84	0.034
		AG	112.15 ± 4.46		13.24 ± 1.24	
		GG	103.25 ± 5.37		12.87 ± 2.31	
	rs575853731	GG	106.44 ± 5.12	0.432	11.35 ± 6.31	0.129
		GA	109.98 ± 4.79		12.79 ± 3.01	
		AA	107.27 ± 4.75		12.75 ± 3.21	

Analysis of Haplotypes of IL-6 Gene Polymorphisms rs762371056 and rs762759043, and IL-10 Gene Polymorphisms rs570186303 and rs575853731 in the Disease Group and Control Group

There were differences in the distributions of haplotype CA of *IL-6* gene polymorphisms rs762371056 and rs762759043 ($p = 0.000$) and haplotypes AA ($p = 0.035$), AG ($p = 0.000$) and GG ($p = 0.000$) of *IL-10* gene polymorphisms rs570186303 and rs575853731 between the disease group and the control group (Table 6).

Relationship of IL-6 Gene Polymorphisms rs762371056 and rs762759043, and IL-10 Gene Polymorphisms rs570186303 and rs575853731 with Serum IL-6 and IL-10 Levels

The genotypes of *IL-6* gene polymorphism rs762371056 were associated with the levels of serum IL-6 in child patients in the disease group ($p = 0.000$). Child patients with genotype TC had higher levels of serum IL-6. Additionally, the genotypes of *IL-10* gene polymorphism rs570186303 were correlated with the levels of serum IL-10 in child patients in the disease group ($p = 0.034$). The levels of serum IL-10 were lower in child patients carrying genotype AA (Table 7).

Relationship of IL-6 Gene Polymorphisms rs762371056 and rs762759043, and IL-10 Gene Polymorphisms rs570186303 and rs575853731 with C-Reactive Protein

Several studies have suggested that serum C-reactive protein is closely related to the progression of pneumonia [19,20]. Therefore, we investigated the relationship between *IL-6* and *IL-10* gene polymorphisms and serum C-reactive protein levels to determine whether genetic polymorphisms can predict disease progression. The results found that the genotypes of *IL-6* gene polymorphism rs762759043 were associated with the levels of serum C-reactive protein in child patients ($p < 0.05$), and child patients with genotype AA had a distinctly higher level of serum C-reactive protein (Fig. 1A–D).

Discussion

Childhood pneumonia is a serious health issue that causes over 2 million deaths in children worldwide every year, with about 15% of these deaths occurring in China [21,22]. Childhood pneumonia is characterized by antibiotic resistance, increasingly novel pathogens, and an incomplete immune system, which makes it a significant threat to children's health and leads to a high mortality

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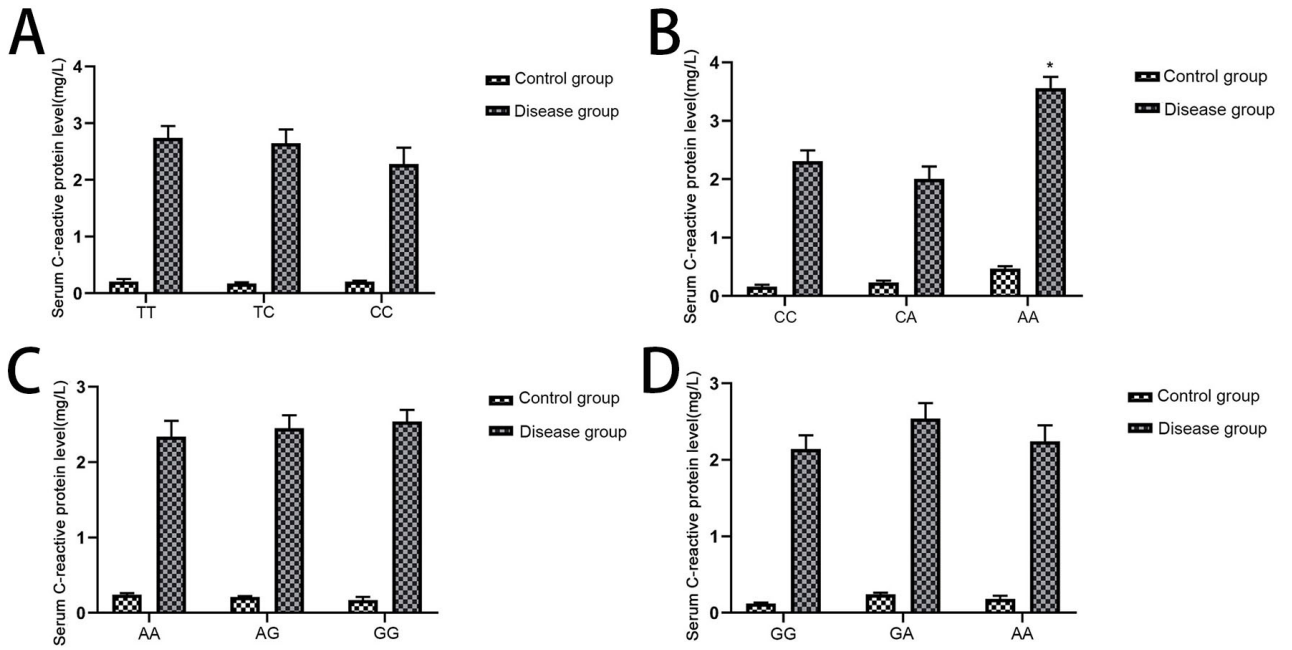

Fig. 1. Relationship between *IL-6* and *IL-10* gene polymorphism and serum C-reactive protein level. (A) Relationship between *IL-6* gene polymorphism rs762371056 and serum C-reactive protein level. (B) Relationship between *IL-6* gene polymorphism rs762759043 and serum C-reactive protein level. (C) Relationship between *IL-10* gene polymorphism rs570186303 and serum C-reactive protein level. (D) Relationship between *IL-10* gene polymorphism rs575853731 and serum C-reactive protein level. * indicates $p < 0.05$.

rate [23,24]. To prevent childhood pneumonia and reduce its mortality rate, measures such as reducing exposure to pathogens, screening susceptible populations, and enhancing immunity should be taken [25]. Screening susceptible people plays a crucial role in preventing childhood pneumonia. Numerous factors, including gene polymorphism and a history of contact with high-risk pathogens, are correlated with susceptibility to childhood pneumonia. The polymorphism of multiple genes, such as *IL-1RA* and *FokI*, is associated with the development and progression of childhood pneumonia [23,26,27]. Hence, it is important to study the correlation between gene polymorphism and susceptibility to childhood pneumonia for the prevention and screening of this disease.

The immune system is crucial for protecting the body from external pathogen infestation. When harmful bacteria or viruses enter the body, the intact humoral and cellular immune systems will work together to protect normal cells in the human body. The IL family plays a crucial role in regulating the immune system's normal functioning, including the differentiation of immunocytes and the promotion of their proliferation [28]. IL-6 is a pro-inflammatory mediator that mainly functions to induce inflammation and immune reactions, while IL-10, functionally complementary to IL-6, has anti-inflammatory and anti-immune functions and inhibits immunocyte proliferation to weaken immune reactions [29]. Both IL-10 and IL-6 regulate the immune system to induce immune reactions to pathogens in the body, and gene polymorphisms are correlated with disease development and mainly affect disease susceptibility [30,31]. This research tested the *IL-6* gene polymorphisms rs762371056 and rs762759043, and *IL-10* gene polymorphisms rs570186303 and rs575853731 in the peripheral blood karyocytes in 200 child patients with pneumonia and 200 normal children. The study observed differences in the allele distributions of *IL-6* gene polymorphisms rs762371056 and rs762759043 and *IL-10* gene polymorphism rs570186303 between the disease group and the control group. The allele C of *IL-6* gene polymorphism rs762371056, allele A of *IL-6* gene polymorphism rs762759043, and allele A of *IL-10* gene polymorphism rs570186303 in the disease group had higher frequencies than those in the control group. Besides, the genotype distributions of gene loci *IL-6* gene polymorphisms rs762371056 and rs762759043 and *IL-10* gene polymorphism rs570186303 were different between the disease group and the control group. The disease group exhibited higher frequencies of genotype CC of *IL-6* gene polymorphism rs762371056, genotype AA of *IL-6* gene polymorphism rs762759043, and genotype AA of *IL-10* gene polymorphism rs570186303 than the control group. The results suggest that *IL-10* and *IL-6* gene polymorphisms are correlated with childhood pneumonia susceptibility, and gene polymorphism may be an important factor in affecting the development and progression of this disease.

Further analysis of polymorphisms revealed that there were differences in the distributions of the dominant model of *IL-6* gene polymorphism rs762759043 and the recessive model of *IL-10* gene polymorphism rs570186303 between the disease group and the control group. Additionally, there were differences in the distributions of haplotype CA of *IL-6* gene polymorphisms rs762371056 and rs762759043, and haplotypes AA, AG, and GG of *IL-10* gene polymorphisms rs570186303 and rs575853731 between the two groups. A high degree of linkage disequilibrium was observed between *IL-6* gene polymorphisms rs762371056 and rs762759043. These results suggest that the development of childhood pneumonia may not be affected by a single gene polymorphism, but by synergy.

Finally, the correlations of gene polymorphisms with the levels of serum molecules in patients were explored to determine whether the progression of pneumonia can be predicted via gene polymorphism. Serum IL-6, IL-10, and C-reactive protein levels are closely related to the progression of pneumonia [32–34]. Therefore, we investigated the relationship between *IL-6* and *IL-10* gene polymorphisms and serum IL-6, IL-10, and C-reactive protein levels. The genotypes of *IL-6* gene polymorphism rs762371056 were associated with serum IL-6 in child patients in the disease group, and child patients with genotype TC had a higher serum IL-6. The genotypes of *IL-10* gene polymorphism rs570186303 were found to be correlated with serum IL-10 in child patients in the disease group. Child patients with genotype AA had lower serum IL-10. Additionally, the genotypes of *IL-6* gene polymorphism rs762759043 were associated with serum C-reactive protein in child patients. Patients carrying genotype AA had a distinctly higher serum C-reactive protein. In summary, *IL-6* and *IL-10* gene polymorphisms may play a pivotal role in assessing the progression of childhood pneumonia.

However, this study has some limitations. First, the research results may have errors. Some studies have found that *IL-10* gene polymorphism is associated with disease severity in patients with community-acquired pneumonia, while TNF-α-308G/A and IL-6-174G/C single nucleotide polymorphisms are not associated with disease. The reason for the difference from the results of this study may be the small sample size selected in this study. However, *IL-6* gene polymorphism may be associated with pediatric pneumonia [35], which is similar to the results of this study. In addition, C-reactive protein (CRP)/IL-6/IL-10 single nucleotide polymorphisms are associated with susceptibility and severity of community-acquired pneumonia [36], further supporting the findings of this study. Secondly, this study did not analyze the correlation between *IL-6* and *IL-10* gene polymorphisms and serum IL-6, IL-10 and C-reactive protein levels in healthy children, which is expected to be further explored in future studies.

Conclusions

In summary, *IL-6* and *IL-10* gene polymorphisms are linked to pneumonia susceptibility and serum levels of IL-6, IL-10, and C-reactive protein in children. *IL-6* and *IL-10* genes can serve as screening indicators for childhood pneumonia to assist in the prevention and treatment of childhood pneumonia.

Abbreviations

IL, interleukin; DNAs, deoxyribonucleic acids; PCR, Polymerase Chain Reaction; ELISA, enzyme-linked immunosorbent assay; SD, standard deviation; OR, odds ratio; CI, confidence intervals.

Availability of Data and Materials

The datasets used or analysed during the current study are available from the corresponding author on reasonable request.

Author Contributions

XZ designed the research study, performed the research and drafted this manuscript. QYZ participated in the experiments. TJ analyzed the data, the definition of intellectual content, literature research and clinical studies. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The present study was approved by Hunan Children's Hospital of Changsha (Changsha, China) and performed following the Declaration of Helsinki. Before the start of the study, written informed consent was obtained from all patient guardians (Approval Number: HNC12990C).

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Conflict of Interest

The authors declare no conflict of interest.

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