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BclI Polymorphisms of NR3C1 Gene and sST2 Levels Among Asthmatic Patients Under Steroid Treatment

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Abstract

Background: Asthma is an allergic disorder affecting the lower respiratory tract and causing lung problems such as wheezing, coughing, and a sensation of chest constriction. Environmental, immunological, and genetic factors play a crucial role in the development of hyper-responsivity and bronchial obstruction.

Objectives: This study aimed to estimate the serum concentrations of soluble Growth Stimulating Expression Gene 2 Protein (sST2) and to assess and analyze the Single Nucleotide Polymorphism (SNP) of the NR3C1 gene (BclI rs41423247) in asthmatic patients under treatment and healthy controls.

Patients and Methods: This study included 80 asthmatic patients and 40 controls. sST2 was quantified using an enzyme-linked immunosorbent assay (ELISA). DNA was extracted from blood samples, followed by PCR amplification using a thermocycler with a newly designed, gene-specific primer pair targeting the NR3C1 gene. The Sanger sequencing technique detected the BclI rs41423247 SNP.

Results: The results show a highly significant difference in sST2 levels between asthma patients and controls (55.43±15.81 vs. 38.04±5.215, respectively), with the highest levels observed in severe asthma patients (60.72±21.38). According to the treatment type used, the highest sST2 levels were seen in the G2 group, while the lowest levels were observed in the G1 group. The GC genotype of the BclI rs41423247 SNP is more common in patients (31.25%) than in controls (10%) (P value = 0.0103, $\chi 2 = 6.571$, and OR= 4.091).

Conclusion: The current study concluded that individuals with the BclI rs41423247 polymorphism in the NR3C1 gene can develop asthma compared to individuals without this defect. Furthermore, the GC genotype of the BclI rs41423247 can affect the effectiveness of the steroid used, directly or indirectly, by its role in glucocorticoid receptor expression. This leads to a persistent inflammatory process associated with increased serum sST2 levels.

Keywords: Asthma, BclI, Glucocorticoid receptor, Single nucleotide polymorphism, Soluble growth stimulating expression gene 2 protein.

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Introduction

Asthma is recognised as a chronic inflammatory condition that targets the lower airways and affects over 350 million people worldwide, while causing 0.4 million deaths each year (1). Asthma presents with lung symptoms, including chest constriction, wheezing, coughing, and shortness of breath, which arise from inflammation, bronchoconstriction, hyperresponsiveness, and remodeling (2). The precise a etiology of asthma is complex, in which hereditary predisposition and environmental factors interact with each other, leading to various symptoms. In addition to variations in different genetic loci, epigenetic regulation is also believed to increase the incidence of allergic diseases and asthma (3). Asthma is caused by an immunological mechanism derived from T helper 2 (Th2) cells that is characterized by severe inflammatory dysregulation (4,5). The disease includes interactions between the lung epithelium, adaptive immunity, and the innate immune system, leading to persistent inflammation (6). The immunological response in the pathogenesis of asthma involves impaired metabolism and altered cellular functions (7). Airway hypersensitivity is facilitated by T helper 2 (Th2) dependent-cell IgE, IgE-producing plasma cells, and recruitment of mast cells and eosinophils. Alongside allergen-specific Th2-mediated acquired immunity, natural immunity cells, including epithelial cells, macrophages, granulocytes, mast cells, type 2 innate lymphoid cells (ILC2), eosinophils, natural killer (NK) cells, and dendritic cells (DCs) are also enrolled in atopy and non-atopy pathology involvement in the extracellular acidifying progression of asthma (8). Growth-stimulation expressing gene 2 protein (ST2) is a part of the interleukin-1 receptor/Toll-like receptor family with transmembrane (ST2 L) and soluble form (s ST2) and Interleukin-33 (IL-33) as its single and essential ligand. IL-33 is a member of the IL-1 family and is produced by many cell types, including epithelial, endothelial, dendritic, macrophage, and mast cells (9). The traditional activity of the IL-33/ST2L pathway is regulating the Th2 immune reaction in several stages of the disease by the receptor complex of ST2L and IL-1 receptor-related protein (10). Also, sST2 inhibits IL-33 signaling by acting as a decoy receptor for IL-33 (11). Elevated blood and bronchoalveolar lavage concentrations of sST2 have been observed in individuals with allergic diseases, including asthma (12). Glucocorticoids (GCs) are the primary class of pharmaceuticals employed to manage inflammatory disorders. The diminished response to glucocorticoids in asthma and other disorders results from reduced glucocorticoid receptor (GR) expression, caused by single-nucleotide polymorphisms in the NR3C1 gene (nuclear receptor subfamily 3, group C, 1), which encodes the GR (13). The human NR3C1, a gene made by nine exons, is localized on chromosome 5(q31.3), and alternate splicing of this gene produces transcript variations that encode either identical or distinct isoforms (14, 15). BclI rs41423247 is established due to variations in one base. Localization of a C/G single-nucleotide polymorphism (SNP) inside the h-GR/NR3C1 gene promoter has occurred in the intron 647 bp distant from the intron/exon attaching site. Insensitivity to steroids is seen in the BclI polymorphism (C/G) in the h-GR/NR3C1 gene promoter. It might be vital in severe Bronchial asthma and glucocorticoid sensitivity (16). The current study aimed to estimate serum soluble Growth-Regulatory Protein 2 (sST2) concentrations and to assess the BclI rs41423247 Single-Nucleotide Polymorphism (SNP) in the hGR/NR3C1 gene in Iraqi asthmatic patients receiving steroids and healthy controls.

Patients and Methods

Study design: The case-control study involved 80 asthmatic patients (37 male and 43 female)

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who were under steroid treatment. The treatment Protocol includes programming long-term medications (ICS) and quick relief medications (SABA), with doses appropriate to the patient's condition and severity of the disease. The patients attended the Baquba Teaching Hospital Consulting Clinic and Consultation Clinic for chest and respiratory diseases in Diyala governorate, Iraq, within the period between November 2024 and February 2025, and forty healthy individuals were chosen as the control group. Their age range was (15 to ≥65) years. Specialized respiratory disease physicians diagnosed patients through clinical aspects, as the diagnosis criteria included recurrent respiratory symptoms, like wheezing, coughing, and chest constriction, along with an X-ray picture to assess the definitive diagnosis. Venous blood specimens were obtained with syringes by vein puncturing. Five milliliters of blood were drawn from all individuals in sterile tubes. The blood specimen was separated into two portions: two milliliters into a sterile tube with EDTA for nucleic acid isolation and three milliliters into a gel or plain tube for serum separation by centrifuging at 4000 rounds per minute for 5-10 minutes.

Estimation of sST2: The serum concentrations of sST2 in each sample were evaluated by the enzyme-linked immunosorbent assay (ELISA) technology based on the procedure protocol of Sunlong Biotech (Zhejiang, China. Catalogue Number: SL2360Hu).

DNA extraction and polymerase chain reaction assay: DNA was extracted from 200 µL of the blood sample using the protocols provided by the TransGen DNA extraction kit (China). Following the extraction, the DNA was used in a PCR assay to amplify the NR3C1 gene at a specific region using a newly designed set of primers, as described in Table 1. The reaction mixture volume was 50 µL, comprising 25 µL of master mix, 13 µL of extracted DNA template, 1 µL each of forward and reverse primers, and 10 µL of nuclease-free water. DNA sample amplification was performed using a Thermal cycler device based on the PCR steps, including an initial denaturation step of 5 minutes at 94°C for only one cycle. The denaturation, annealing, and extension steps take 30 seconds for 30 cycles at 94°C, 59°C, and 72°C, respectively. The final step is called the final extension at 72°C for one cycle. Gel electrophoresis was used for visualization of the PCR product.

DNA sequencing: The PCR products were sent to South Korea/Macrogen Company for sequencing analysis using the Sanger technique. The results sequence aligned with the reference sequence obtained from NCBI in the Blast program. Chromas Pro (Technelysium Pty Ltd) and Jalview are used to analyze and sequence alignments for SNPs detection (17).

Statistical Analysis

The Statistical Package for Social Sciences version 26 was used to perform the analysis. Chi-square was used to compare percentages and find odd ratios. The t-test and ANOVA compared sST2 means between the patient and control groups. Cut-off values, specificity, and sensitivity were estimated according to ROC analysis.

Results

Demographical characteristics of the study groups: The demographic characteristics of the study groups was shown in Table 2, revealed a high significant difference in age (P value = 0.01), family history (P value = 0.001), body mass index (BMI) (P value = 0.002), and groups of treatment (P value = 0.0001) when compared between patient and control groups. The sex, residency, and smoking habits showed no significant difference between the study groups.

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Table 1. Specific set of primers used in this study.

Primers	Sequence direction 5` to 3`	Reference	Product size	Company
NR3C1F	5`- TGACCTTTTTGGGTCAGACAA -3`	Newly designed	435 bp	Macrogen
NR3C1R	5`- AGTCAAAAGTTGTGCTGCCTTAT -3`			

Table 2. Demographical characteristics of the study groups.

No.	Parameters		Patient No. (%)	Control No. (%)	P value
1	Age	Mean ± SD	45.75 ± 17.61	34.95 ± 14.47	0.01** HS
2	Sex	Male	37 (46)	20 (50)	0.698 NS
		Female	43 (54)	20 (50)	
3	Family history	Positive	43 (54)	0 (0)	0.001** HS
		Negative	37 (46)	40 (100)	
4	Residency	Urbanization	60 (75)	20 (50)	0.07 NS
		Rural	20 (25)	20 (50)	
5	Smoking habit	Smoker	6 (7.5)	0 (0)	0.076 NS
		Non smoker	74 (92.5)	40 (100)	
6	Body mass index	Normal	28 (35)	31 (77.5)	0.002** HS
		Overweight	19 (23.75)	9 (22.5)	
		Obese	33 (41.25)	0 (0)	
		Mean ± SD	29.3 ± 6.3	24.65 ±1.1	
7	Treatment	G1	40 (50)	0 (0)	0.0001 **HS
		G2	31 (38.75)	0 (0)	
		G3	9 (11.25)	0 (0)	

** HS: Highly significance at P ≤0.01; NS: No Significance at P ≤0.05; No: number; %: percentage; SD: Standard deviation; G1: Salmeterol, fluticasone; G2: Salbutamol, dexamethasone; G3: Formoterol, budesonide.

Mean levels of sST2 in study groups: The results presented in Table 3 indicated that the serum concentrations of sST2 were increased in asthmatic patients compared to healthy controls (55.43±15.81 vs 38.04±5.215, respectively), at (P value = 0.0001).

Table 3. Mean levels of sST2 in study groups.

Biomarker	Patient (80) Mean±SD	Control (40) Mean±SD	T-test	P value
sST2 (pg/ml)	55.43±15.81	38.04±5.215	4.82	0.0001** HS
SD: Standard deviation, ** (HS): Highly significant at P ≤0.01				

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Mean levels of sST2 in treatment groups: The asthmatic patients were divided into three groups according to the type of treatments used. The first group used Salmeterol and fluticasone (G1), the second group used Salbutamol and dexamethasone (G2), and the third group used Formoterol and budesonide (G3). Table 4 presents the mean levels of sST2 concentrations among these groups. The concentration of sST2 showed a significant difference (P value =0.02) among the groups of treatments used in this study (at P ≤0.05), with their highest levels in the G2 group and lowest levels in the G1 group.

Table 4. Mean levels of sST2 according to treatment type.

Biomarker	Treatment type (M± SD)			*P*
	G1 (Salmeterol, fluticasone) n=40	G2 (Salbutamol, dexamethasone) n=31	G3 (Formoterol, budesonide) n=9	
sST2 (pg/ml)	50.64±6.77	61.6±22.32	57.11 ±12.31	0.02* S
M: Mean, SD: Standard deviation, *S: Significant at P ≤0.05.				

Mean levels of sST2 according to asthma severity: Patients are classified by asthma severity as mild (5), moderate (40), or severe (35). Table 5 presents the concentrations of sST2 mean levels according to the severity of asthma. The results indicated that the highest sST2 levels were found in the severe asthma patients (60.72 ±21.38) and the lowest levels in the mild asthma patients (46.6 ±5.78) (P value = 0.004).

Table 5. Mean levels of sST2 in asthma patients according to severity.

Biomarker	Asthma severity groups Mean±SD			*P*
	Mild (5)	Moderate (40)	Severe (35)	
sST2 (pg/ml)	46.6 ±5.78	52.14 ± 8.18	60.72 ±21.38	0.004** HS
SD: Standard deviation, ** HS: High significance at P ≤0.01.				

Receiver operative curve of sST2: Receiver Operative Curve analysis determined the cut-off point for sST2. Table 6 and Figure 1 show the area under the curve (AUC), sensitivity, and specificity, along with a 95% confidence interval for sST2. The result of the ROC analysis of sST2 has 85.0% specificity and 98.6% sensitivity, with an AUC of 0.955. The 41.64 cut-off point distinguished between the healthy and diseased individuals, with a 93.2% positive predictive value (PPV%) and 93.75% negative predictive value (NPV%).

Table 6. Receiver Operative Curve testing of the validity of sST2 in study groups.

Biomarker	Cut-off	AUC	P value	Asymptotic 95% C.I.		Specificity	Sensitivity	PPV%	NPV%
				L.B.	U.B.				
sST2 (pg/ml)	>41.64	0.955	<0.001** HS	0.905	1000	85.0	98.6	93.2	93.75
AUC: Area under curve; C.I.: Confidence interval; **HS: Highly significant at P ≤0.01, PPV: Positive predictive value, NPV: Negative predictive value									

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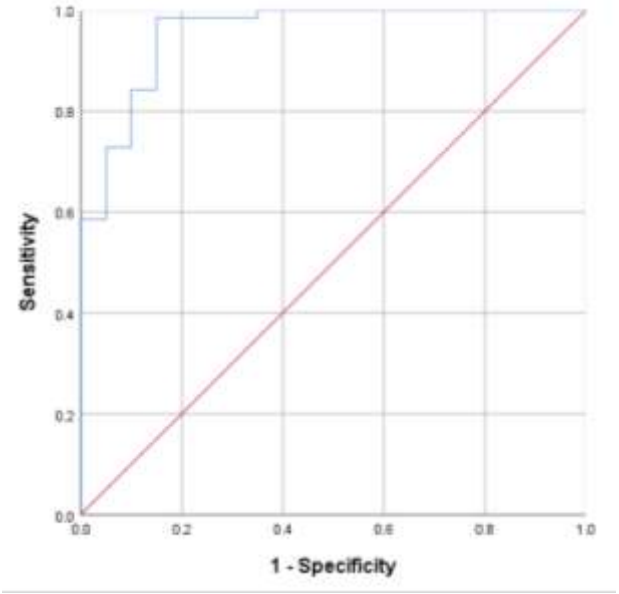

Figure 1. ROC analysis for sST2.

Variations and genotypes of the BclI rs41423247 polymorphisms: The Figure 2 presented the (435 bp) PCR product of NR3C1 gene amplification that were stained with red safe dye. The result presented in Table 6 revealed the genotypes frequencies of BclI rs41423247 SNP in the NR3C1 gene described as follows: GG (55), GC (25), and CC (0) for the patients, and GG (36), GC (4), and CC (0) in healthy controls. The genotypes significantly differ between the patients and the control groups (P value = 0.0103, $\chi 2 = 6.571$). The 4.091 results of the odds ratio indicated that patients with the heterozygous genotype (GC) have a risk of getting asthma and glucocorticoid resistance four times more than patients with the (CC) and (GG) genotype. Table 7 also showed that the frequency of the G allele was 0.69 in patients and 0.9 in healthy controls, while the C allele was 0.31 in patients and 0.1 in healthy controls. All the genotypes are in Hardy-Weinberg equilibrium.

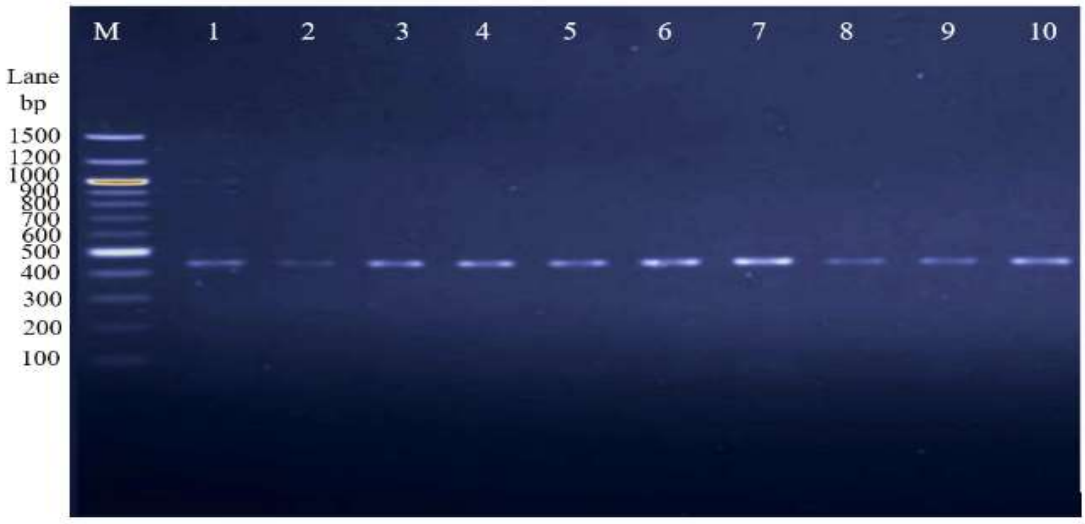

Figure 2. Amplification of the NR3C1 gene (435 bp) in asthmatic patients and healthy controls using 1.5% agarose gel electrophoresis with red safe dye, 100-1500 bp DNA ladder marks 1-10.

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Table 7. Genotype and allele frequency of BclI rs41423247.

Genotype	Patients		Controls		OR	95% C.I.	Test	P value
	Observed No. (%)	Expected No. (%)	Observed No. (%)	Expected No. (%)				
GG	55 (68.75)	56.95 (71.19)	36 (90)	36.1 (90.25)	4.091	1.314 to 12.741	χ^2 = 6.571	0.0103* S
GC	25 (31.25)	21.1 (26.375)	4 (10)	3.8 (9.5)				
CC	0 (0)	1.95 (2.435)	0 (0)	0.1 (0.25)				
Total	80		40					
Allele Frequency					-			
Allele	Frequency							
G	0.69		0.9					
C	0.31		0.1					

OR: Odd ratio, C.I.: Confidence interval, χ2: Chi-square, *(S): Significance at P ≤0.05

Mean levels of sST2 in patients according to the BclI rs41423247: The results in Table 8 indicate the mean serum sST2 concentrations in asthmatic patients and their association with genotypes. There were no significant differences in serum sST2 concentrations between asthma patients with GG and GC genotypes (53.78±14.43 vs. 59.01±18.34; P ≤).

Table 8. Mean levels of sST2 according to genotypes in asthma patients.

Parameter	Genotypes	No. Of patients (%)	Mean±SD	T-test	*P*
sST2 (pg/ml)	GG	55(68.75)	53.78±14.43	1.290	0.201 NS
	GC	25(31.25)	59.01±18.34		

No: Number, %: Percentage, SD: standard deviation, NS: No significance at P ≤0.05

Discussion

Asthma is a condition characterized by chronic bronchial obstruction, often reversible spontaneously or after treatments, bronchial hyper responsiveness, and accelerated deterioration of lung function, which may progress to irreversible airway obstruction in specific instances (18). Asthma may occur at any age, as adult-diagnosed asthma has been reported to be more often related to environmental and lifestyle factors compared to child-diagnosed asthma, which again is frequently associated with atopy and genetic factors, making the family history a common risk factor for persistent asthma (19, 20). The increasing in the body mass index (BMI) is associated with increased airflow limitation and directly influences through increased airway hyper responsiveness in populations with asthma, then effects on human airway smooth muscle was exaggerated in the obese adult population, as people with severe asthma become less active and deconditioned, weight increases, leads to increased usage of oral corticosteroids (OCS) further aggravates the weight gain cycle (21-23) Studying the role of sST2 in the inflammatory process of chronic asthma has important diagnostic and management implications. The increase in sST2 concentrations in asthmatic patients is consistent with findings from Quoc et al. (24) and Feng et al. (25). In this study, serum sST2 levels were higher in patients with severe asthma than in those with moderate or mild asthma. The IL-33/ST2 axis is central to allergic inflammatory response and asthma. In patients with bronchial asthma, IL-33 is released from immune cells during atopic inflammatory processes. The sST2 suppresses the complex of

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IL-33 to ST2L and regulates IL-33 negatively, which has links with different immune conditions (26). IL-33 functions by forming a heterodimeric combination with the ST2 receptor and the IL-1 receptor accessory protein (IL-1RAcP), which serves as a signaling receptor component (27). IL-33 has been proposed as a trigger of allergic inflammation by enhancing the activation, maturation, and chemotaxis of multiple leukocyte subsets, including Th2 cells, ILC2s, CD34+ cells, mast cells, eosinophils, natural killer cells, and basophils. Treatment with anti-IL-33 or sST2 in an OVA-challenge murine model reduced airway hyper responsiveness, IL-5 levels in BALF, and eosinophil counts (28). Clinical investigations focusing on the IL-33 receptor ST2 have yielded favorable results. Treatment with astegolimab, which inhibits explicitly the IL-33 receptor, reduces respiratory neutrophilic inflammation in individuals with severe asthma, even those with type 2 low ST2 (29). IL-33 mRNA expression is markedly higher in epithelial cells from airway biopsies of patients with asthma than in healthy controls, with severe asthmatics expressing markedly higher levels than mild or moderate asthmatics. Similarly, high levels of IL-33 and sST2 have been found in the plasma and sputum of children and adults with acute asthma compared to healthy controls (30). Episodes of asthma are frequently adequately managed in several people by β2-adrenergic agonists and inhaled anti-inflammatory corticosteroids for bronchodilation (31-33). However, 5-10% of patients present with a form of treatment insensitivity disorder that is usually characterized by recurrent exacerbations (34). Significantly, the mentioned participants are often treated with repeated courses of high-dose systemic Glucocorticosteroids, which are linked to severe side effects (35). The serum level of sST2 appears to be lower in patients using Salmeterol and Fluticasone than others, this indicates that this type of steroid is more effective and has a critical role in controlling asthma exacerbations, and this result is consistent with the study of Park et al (36). The inflammation in asthmatic patients may persist despite treatment use because of a process called glucocorticoid resistance. Patients with glucocorticoid resistance can be grouped into two broad categories, Type 1 steroid resistance which it is either immune-mediated or acquired as the result of environmental triggers or lifestyle. Clinically, such patients will develop steroid side effects, including adrenal gland suppression, osteoporosis, and cushingoid features from pharmacologic doses of systemic steroids, and Type 2 steroid resistance which is rare but involves a generalized primary cortisol resistance that affects all tissues and is likely associated with a mutation in the GR gene or genes that modulate GR function. This form is not associated with the development of steroid side effects or suppression of morning cortisol levels. It is analogous to genetically inherited familial cortisol resistance (37). The study's results aligned with those of Pan et al. and Panek et al. (38, 39), as the GC genotype is more frequent among patients with severe-to-moderate asthma than among those with mild asthma or healthy controls. The single-nucleotide polymorphisms (SNPs) in the NR3C1 gene may reduce the synthesis of glucocorticoid receptor/glucocorticoids complexes, minimize transcription, and affect the transrepression of the genes of the synthesised proteins encoding in the form of cell reactions to glucocorticoids. It may lower glucocorticoid receptor expression, reducing the response to GCs and impairing GCR function. Glucocorticoid insensitivity is a significant problem in many inflammatory disorders, making clinical control hard (40). In effect, it was documented that children with moderate-to-severe asthma exacerbation, who were homozygous carriers of the G allele of rs41423247, showed a higher improvement in FEV1 at 4 hours when treated with high-dose ICS. However, it has also been reported that

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corticosteroid resistance can be associated with BclI polymorphism (41). In-vitro and in vivo models have shown that the G allele of the rs41423247 locus at the NR3C1 gene was associated with hypersensitivity to glucocorticoids (42). Allele G of BclI rs41423247 is particularly associated with sensitivity to GCs, as it increases the cellular response to GCs and occurs less frequently than allele C (43). Finally, the current study found that the GC genotypes of BclI rs41423247 have a critical role in the development of asthma and GC insensitivity, especially in severe asthma patients with elevated serum sST2 levels.

Conclusion

It was concluded that individuals with the BclI rs41423247 polymorphisms in the NR3C1 gene can develop asthma compared to individuals without this defect. Furthermore, the GC genotype of the BclI rs41423247 polymorphisms of the NR3C1 gene can affect the effectiveness of the steroid used, directly or indirectly, by its role in GR expression and influencing the receptor activity. This leads to a persistent inflammatory process associated with increased serum sST2, especially in severe asthma patients. Our study also concluded that patients receiving salmeterol and fluticasone have the lowest sST2 levels compared with patients receiving other treatments, suggesting that these agents are more effective and play a critical role in controlling asthma exacerbations. We recommended investigating the roles of other SNPs in genes potentially related to uncontrolled asthma and glucocorticoid resistance, and in larger populations. We also suggested studying the active sites and mechanisms of treatments used to treat and manage asthma.

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Ethical clearance: The ethical committees of the Middle Technical University- College of Health and Medical Techniques approved this study with their approval certificate reference number MEC 62.

Conflict of interest: None.

Use of Artificial Intelligence (AI): The authors state they did not use any generative AI tools for creating or editing the manuscript's language.

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تعدد أشكال BclI لجين NR3C1 ومستويات بروتين التعبير عن الجين ٢ المحفز للنمو القابل للذوبان لمرضى الربو الذين يتلقون العلاج الستيرويدي

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الملخص

الخلفية: الربو هو اضطراب تحسسي يصيب الجهاز التنفسي السفلي، ويسبب مشاكل في الرئة مثل الصفير والسعال والشعور بالضيق في الصدر. وان العوامل البيئية والمناعية والوراثية لها دور حاسم في تطور فرط الاستجابة وانسداد الشعب الهوائية.

الأهداف: هدفت هذه الدراسة إلى تقدير مستويات بروتين التعبير عن الجين ٢ المحفز للنمو القابل للذوبان وتعدد أشكال النيوكليوتيدات المفردة BclI (rs41423247) لجين hGR/NR3C1 للمرضى تحت العلاج.

المرضى والطرق: شملت هذه الدراسة ٨٠ مريضًا بالربو و٤٠ شخصًا سليمًا كمجموعة ضابطة. تم تقييم تراكيز بروتين التعبير عن الجين ٢ المحفز للنمو القابل للذوبان باستخدام اختبار الامتزاز المناعي المرتبط بالأنزيم (الإليزا). تم استخلاص الدنا من عينات الدم وتبعها عملية تضخيم بعملية تفاعل البلمرة المتسلسل باستخدام جهاز مدور حراري وباستخدام مجموعة مصممة حديثًا من البادئات والمصممة خصيصًا لجين NR3C1. واستخدمت تقنية تسلسل سانجر للكشف عن تعدد أشكال النيوكليوتيدات المفردة BclI (rs41423247).

النتائج: تشير النتائج إلى وجود فرق معنوي كبير في بروتين التعبير عن الجين ٢ المحفز للنمو القابل للذوبان لدى مرضى الربو مقارنةً بالمجموعة الضابطة (٥٥,٤٣±١٥,٨١ ضد ٣٨,٠٤±٥,٢١٥، على التوالي) مع اعلى مستوياته في مرضى الربو الحاد (٦٠,٧٢±٢١,٣٨) وبالنسبة لمجاميع العلاج المستخدمة فأن اعلى مستويات لبروتين التعبير عن الجين ٢ المحفز للنمو القابل للذوبان كانت ضمن المجموعة G2 وأقل مستوياته كانت ضمن المجموعة G1. وكان النمط الجيني GC لتعدد اشكال النيوكليوتيدات المفردة BclI (rs41423247) في جين NR3C1 أكثر شيوعًا لدى مرضى الربو (٣١,٢٥٪) مقارنةً بالمجموعة الضابطة (١٠٪) (القيمة الاحتمالية = ٠,٠١٠٣ وكاي سكوير= ٦,٥٧١ ونسبة الارجحية = ٤,٠٩١).

الاستنتاج: نستنتج من هذه الدراسة الحالية إلى أن الأفراد الذين يحملون تعدد أشكال BclI rs41423247 في جين NR3C1 قد يُصابون بالربو مقارنةً بالأفراد الذين لا يعانون من هذا الضرر. علاوة على ذلك، يمكن أن يؤثر النمط الجيني GC لجين BclI rs41423247 على فعالية الستيرويد المستخدم، بشكل مباشر أو غير مباشر، من خلال دوره في التعبير عن مستقبلات الجلوكوكورتيكويد والتأثير على نشاطها. يؤدي هذا إلى عملية التهابية مستمرة مرتبطة بارتفاع مستويات بروتين التعبير عن الجين ٢ المحفز للنمو القابل للذوبان في المصل.

الكلمات المفتاحية: الربو، BclI، مستقبل الجلوكوكورتيكويد، تعدد اشكال النيوكليوتيدات المفردة، بروتين التعبير عن الجين ٢ المحفز للنمو القابل للذوبان.

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