ORIGINAL ARTICLE

SIRT1(rs7069102) Gene Polymorphism in Chronic Obstructive Pulmonary Disease in Egyptian Patients

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Key words:
COPD, SIRT-1, IL-26, IL-10

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ABSTRACT

Background: *Chronic obstructive pulmonary disease (COPD) is a prevalent condition characterized by shortness of breath, coughing, and sputum production. In Egypt, the prevalence is around 7.5%, with key risk factors including smoking and pollution.* ***Objective****: This study examined the association between the SIRT1 SNP (rs7069102) and CRP levels, and the roles of IL-26 and IL-10 in Egyptian COPD patients.* ***Methodology:*** *A case-control study involved 100 COPD patients and 100 healthy controls. Participants underwent assessments for BMI and spirometry, along with blood sampling for SIRT1 genotyping and measurement of IL-10 and IL-26.* ***Results:*** *The results highlighted reduced pulmonary function, elevated IL-26 levels, and lower IL-10 levels in COPD patients. Notably, serum IL-26 and IL-10 both demonstrated 100% sensitivity and specificity for diagnosing COPD at defined cutoffs.* ***Conclusion:*** *The SIRT1 (rs7069102) SNP may be a novel link to COPD, with patients showing a higher frequency of certain genotypes and altered cytokine levels.*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a widespread and varied disorder marked by persistent breathing-related symptoms, including dyspnea, cough, and sputum production[1]. It is becoming an increasingly significant cause of mortality worldwide. The occurrence of COPD is frequently connected to using tobacco products[2].

COPD can arise from interactions between genetic and environmental Factors that can harm the lungs or affect their natural growth and phases of aging [3]. A report by the World Health Organization (WHO), around sixty-five million individuals have moderate to severe COPD, which affects 10-20% of the global population aged 40 and older, leading to more than 3 million deaths annually. Projections indicate that by 2030, COPD will become the third leading cause of death worldwide. Notably, 11 Asian countries account for 6.2 percent of the worldwide COPD burden, as reported by the Asian Pacific Society of Respiratory Diseases [4]. In Egypt, the prevalence of COPD is particularly high, affecting around 7.5% of the population [5].

Genetic polymorphisms refer to variations in alleles or point mutations within DNA, including single-nucleotide polymorphisms (SNPs). While most studies on genetic polymorphisms have focused on cancer, there is still a limited understanding of inherited variables that may contribute to the occurrence of COPD [6].

Sirtuins (SIRT) are a class of histone deacetylases (HDACs), specifically class III, that act on histone proteins found in chromatin. Humans have seven members in this family (SIRT1-7). Sirtuins play a crucial role in regulating cell metabolism, the cell cycle, and differentiation. Latest research focused on the involvement of SIRT family members in the regulation of chronic obstructive pulmonary disease (COPD)[7]. Chronic Obstructive Pulmonary Disease (COPD) develops due to several factors, including an imbalance between proteins called proteases and antiproteases, oxidative stress, and inflammation[8].A key factor in this process is the reduction of HDAC2, a protein that helps control inflammation by limiting the expression of certain inflammatory genes [9]. Studies also show that COPD patients have lower levels of Sirtuin 1 (SIRT1) in their lung cells and blood compared to healthy individuals. This indicates that SIRT1 may play an important role in managing inflammation related to COPD[10].

During acute exacerbations of chronic obstructive pulmonary disease (COPD), several bio-substances and cytokines are known to increase, one of which is C-reactive protein (CRP). CRP is an inflammatory marker

that is associated with an increased risk of mortality in COPD patients. Studies have shown that elevated levels of CRP significantly correlate with higher mortality rates, while COPD patients with normal CRP levels do not exhibit a significantly increased risk of death[11].

IL-26 has potential antibacterial effects and is extensively expressed in the human airways by several cell types. Furthermore, IL-26 expression changes have been linked to impaired lung function and neutrophil buildup in individuals with severe COPD[12,13].

IL-10 is a crucial protein that plays a key role in reducing inflammation in the body. Produced by immune cells and epithelial cells, it has the potential to help manage inflammation related to COPD [14]. Research indicates that individuals with COPD, particularly those who smoke, often have lower levels of IL-10. This reduction is linked to increased severity of the disease. By raising IL-10 levels, we could potentially mitigate inflammation and tissue damage, making it an encouraging target for future treatment strategies [15].

Limited studies have explained the relationship between interleukin-26 (IL-26) and interleukin-10 (IL-10) in COPD. Our study aimed to investigate the association of the SIRT1 (rs7069102) SNP in Egyptian patients with COPD and C-reactive protein levels in COPD patients in comparison to normal control, also to asses serum level of IL-10 and IL-26 in COPD patients in comparison to controls.

METHODOLOGY

Patients:

This observational case-control study included 100 patients with Chronic Obstructive Pulmonary Disease (COPD) who attended the Chest, and Tuberculosis Department at Sohag University Hospital. In addition, 100 healthy control subjects of similar age were randomly chosen from individuals who visited the hospital for routine check-ups, ensuring they had no known chest diseases or significant comorbidities, including liver, kidney, or cancer-related conditions. The study took place from September 2023 to September 2024. Ethical Committee of the Faculty of Medicine at Sohag University accepted the research with IRB registration number Soh-Med-23-09-10PD, and it was recorded on ClinicalTrials.gov (ID: NCT06055634). All participants provided written informed consent after a comprehensive explanation of the study procedures, benefits, and possible adverse effects.

Inclusion criteria: Patients with COPD attended to Sohag University Hospital's Chest and Tuberculosis Department.

Exclusion criteria: Individuals with a history of known chronic cardiorespiratory illnesses, cancers, or collagen vascular problems were excluded.

Methods:

All individuals were exposed to the followings: (1) A detailed history taking included age, gender, smoking history, presence of a persistent cough, persistent sputum production, chest wheezing, and difficulty of breath; grading of breathlessness using a modified Medical Research Council (MMRC). The dyspnea scale (2) General examination, including measurements of body weight, height, and BMI. Body mass index (BMI) was calculated by dividing weight per Kg by height by meter squared (kg/m2). (3) Local chest examination. (4) A spirometer was performed on those with one or more positive symptoms in the respiratory questionnaire. The best of three measurements was obtained while the patients were in the seated position. Values obtained while the participant exerted his or her maximum efforts were used to avoid any expected error in diagnosis. COPD patients were those who were diagnosed under both definitions and were examined using a chest radiograph,

Laboratory investigations of the studied groups included:

Complete blood count was done using automated hematology analyzer, cell- Dyn ruby (Abbott Diagnostic, USA, serial number: 5506BG), ESR was done by Westergren method. ALT, AST, serum creatinine were done using (Cobas C 311 chemistry analyzer (Roche Diagnostic GmbH, Mannheim, Germany, serial number: 16D3-16). Screening for HIV HBV and HCV was done using (Coba s e 601 (Roche Diagnostics Japan, serial number 2486-20).

Detection of SIRT1 (rs7069102) polymorphism:

Five ml sample of blood were collected under complete a septic condition from peripheral veins, from every patient who was included in the study. Three mLs of the blood sample were placed in an EDTA tube for genotyping, while the remaining 2 mLs was placed in a plain tube for the ELISA test. Both tubes were immediately transferred to the central research laboratory. In the central research laboratory, the venous blood samples were processed as follows: the EDTA tubes were centrifuged in a microcentrifuge at a speed of 5300 rpm for 15 minutes to obtain a buffy coat of polymorphonuclear leukocytes for genotyping. Meanwhile, the plain tubes to collect serum were centrifuged at 3000 rpm for 5 minutes for the ELISA test.

For the ELISA measurements of serum IL-26 and IL-10, serum samples were taken and frozen at -20 C^{o}.

Steps for detection of The SIRT1 (rs7069102) SNP:

DNA extraction was performed from the buffy coat using ABT Blood DNA Mini Extraction Kits (Catalog No. ABT003), and the extracted DNA was stored in 1.5mls Eppendorf tubes at -20 degrees Celsius for use Genotyping of A one-step real-time PCR (Polymerase chain reaction) approach with an allelic discrimination assay was used to detect the single-nucleotide polymorphism (SNP) rs7069102 C > G in the SIRT1

gene (Applied Biosystems TaqMan Master Mix). Thermo Fisher Scientific (catalog no. 4351379) provided the qPCR Master Mix (300×) context sequence. The sequence is as follows. AGAAGAAAGAAAGGCATAATCTCTG(C/G)AGAA AAGCCATTATTTCTGCAGATA.

Genetic study of the SIRT1 (rs7069102) variations

To perform the SNP genotyping experiment, we added 1.25 µLs of primer mix, 3.75 µLs of DNAase-free water, and 10 µLs of master mix. For each sample, we added 5 µLs of genomic DNA extract and 5 µLs of DNAase-free water for the negative control reaction.

The Polymerase chain reaction, settings were as follows: a 5-minutes initial denaturation step was followed by 40 cycles of primer annealing at 60°C for 60 seconds, denaturation at 95°C for 15 seconds, extension at 72°C for 1 minute, and a final extension at 72°C for 5 minutes. Information has been assessed using the Applied Biosystems Step One™ Instrument Thermo Fisher, USA.

Measurement of Human serum interleukin-26

It was analyzed using the Sandwich kit Enzyme Linked Immunosorbant assay (ELISA) from Thermo Fisher Scientific, catalog no EH270RB, with measurements taken on a Stat Fax 2000 apparatus.

Measurement of Human serum interleukin-10

It was analyzed using the Sandwich (ELISA) from WUXI DONGLIN SCI&TECH DEVELOPMENT CO., LTD, catalog no. DL-IL 10-HU, with measurements taken on a Stat Fax 2000 apparatus.

Statistical analysis:

The Data was checked, coded, and analyzed using IBM-SPSS 26.0 (IBM-SPSS Inc., Chicago, Illinois, USA)[16]. Descriptive stats: The mean, standard deviation, median, range, frequency, and percentages were computed. Test of significance: The difference in frequency distribution between groups was compared using the chi-square test. The Shapiro-Wilk test was used to determine the normality of continuous variables. The Mann-Whitney U test was used for continuous variables with two categories. To evaluate the independent predictors of COPD disease, a multivariable logistic regression analysis was performed (Odds Ratio -OR-, 95% confidence interval -CI-, and p-value-). ROC Curve for COPD diagnosis using IL-26 and IL-10. A p-value < 0.05 indicated significance.

RESULTS

Our sample consists of 200 individuals in a 1:1 design (100 chronic obstructive lung disease (COPD) cases, and 100 healthy controls. COPD cases (mean age 56.39 ± 10.4 years, range 40-75 years; 61 males (61%)). One hundred there were also groups of normal controls that were both gender and age-matched to the patient groups.

The Hardy-Weinberg equilibrium equation (HW) was used in the research of SNP. Using Genepop software version 4.7, the chi-square (test of goodness of fit) with one degree of freedom was used to determine Hardy-Weinberg equilibrium (x2 = 1.7, p-value = 0.426, >0.05).

There was an insignificant difference among cases and controls in terms of age, BMI, and Sex (P 0.699, 0.556, 0.773), respectively. There was a significant decrease in pulmonary function test (FEV1, FEV1% %%, FEV1/FVC Ratio) in cases in comparison to controls (p=0.0001). **(Table 1).**

Table 1: Demographic data of the studied Groups

	COPD (n = 100)	**Control (n = 100)**	***P*-value**
Age (years)			
• Mean ± SD	56.4 ± 10.4	57.06 ± 11.4	0.699NS
• Median (Range)	55 (40 - 75)	59.5(40- 75)	
BMI (Kg/m^2)			
• Mean ± SD	26.57 ± 5.46	25.7 ± 4	0.556NS
• Median (Range)	26 (20- 41)	26 (20 - 35)	
Sex			
• Female	39 (39%)	41 (41%)	= 0.773
• Male	61 (61%)	59 (59%)	
FEV1			
• Mean ± SD	1.12 ± 0.7	3.5 ± 0.42	**=0.0001***
• Median (Range)	0.83 (0.51- 2.6)	3.5 (2.8- 4.2)	
FEV1 %(Pred)			
• Mean ± SD	36 ± 16.3	83.5 ± 5.6	**=0.0001***
• Median (Range)	30 (19- 70)	83 (75- 95)	
FEV1/FVC Ratio			
• Mean ± SD	49.95 ± 15.12	81.8 ± 4.4	**=0.0001***
• Median (Range)	**53 (27- 70)**	**82 (75- 90)**	

The median difference between groups was compared using the Mann-Whitney test*, while the frequency difference was compared using the Chi-square test **. A p-value < 0.05 indicates statistical significance.

One hundred of the cases had a Chronic cough. Sixty-one of the cases are smokers. Thirty-nine of the cases are biomass fuel exposure. One hundred of the cases had exertional dyspnea. Disease duration of more than ten years was represented by sixty patients. As regards mMRC dyspnea score, we found that 5% of patients scored 1, 30% of them were Score 2, 59% of them were Score 3, and 6% of them were Score 4. COPD stage (GOLD stage), we found that 28% of patients were stage 2, 33% of them were stage 3, and 39% of them were stage 4. **(Table 2)**

The average IL-26 level in COPD patients was 211.7 ± 95.9, compared to 19.96 ± 7.9 in controls. In COPD patients, IL-26 levels were substantially greater than in healthy controls. **(p<0.0001).** In COPD patients, the mean IL-10 level was 187.6 ± 18.1, while in controls it was 329.16 ± 48.48. Compared to healthy controls, COPD patients had considerably decreased IL-10 levels. (p<0.0001). There were also significant changes in the mean parameters, namely WBCs, platelet count, and CRP (p-value = 0.0001). There were no significant changes in the mean Hg (p = 0.840).. **(Table 3).**

Regarding SIRT1 gene polymorphisms, 37% of COPD patients expressed the GG genotype of rs7069102 SNP, 60% of them expressed the GC genotype, and 3% expressed the CC genotype. Meanwhile, 40% of the control group expressed the GG genotype, 45% of them expressed the GC genotype, and 15% expressed the CC genotype. There were significant differences in CC genotype expression found between patients with COPD and controls (p=0.006). 67% of COPD patients expressed allele G of rs7069102 SNP, and 33% of them expressed the allele C while 55.5% of controls expressed allele G of rs7069102 SNP, and 45.5% of them expressed the allele C with a significant difference between allele frequency in studies groups (p=0.0001) as allele C more in control group than diseased group. **(Table 4)**.

Table 2: The clinical features of the observed COPD patients.

Parameter	Category	n = 100
Chronic cough	**Yes**	
	No	
	Yes	100 (100%)
	No	0
Smoking	**Yes**	61(61%)
	No	39(39%)
Biomass fuel exposure	**Yes**	39(39%)
	No	61(61%)
Exertional dyspnea	**Yes**	100 (100%)
	No	0
Disease duration years	**<10 Years**	40(40%)
	>10years	60(60%)
mMRC dyspnea score	**1**	5(5%)
	2	30(30%)
	3	59(59%)
	4	6(6%)
COPD Stage	**2**	28(28%)
	3	33(33%)
	4	39(39%)

COPD (chronic obstructive pulmonary disease). **mMRC score mean (**modified British Medical Research Council).

There was significant relation between IL-26 and IL-10 and SIRT1 gene (p=0.007, 0.012 respectively) as GC genotype had significantly higher in IL-26 and IL-10. **(Table 5)**.

Multivariable logistic regression models of the independent association between SIRT1 gene polymorphism and COPD disease. After adjusting for all factors, our study failed to prove that any factor is a predictor of COPD. **(Table 6).**

Table 3: Difference in Laboratory Findings between Groups

Parameter		COPD (n = 100)	Control (n = 100)	*P-value*
Hgb (g/dl)	**Mean ± Std.**	13.98 ± 2.1	13.98 ± 2.3	= 0.840*
	Median (Range)	14 (9-18)	13.9 (12-16)	
WBCs *10^3	**Mean ± Std.**	9.7 ± 3.1	7.8 ± 2.3	**= 0.0001***
	Median (Range)	10 (5-23)	8 (4-11)	
Platelet *10^3	**Mean ± Std.**	209.9 ± 73.4	290.1 ± 99.5	**= 0.0001***
	Median (Range)	200 (65-345)	250 (160-450)	
C-reactive protein	**Positive**	100%		**= 0.0001***
	Negative	0		
IL-26 pg/ml	**Mean ± Std.**	211.7 ± 95.9	19.96 ± 7.9	**= 0.0001***
	Median (Range)	205 (60-450)	20.5 (8-63)	
Il-10 pg/ml	**Mean ± Std.**	187.6 ± 18.1	329.16 ± 48.48	**= 0.0001***
	Median (Range)	189 (146-218)	319.9 (223.7-432)	

Hemoglobin (Hgb), white blood cells (WBCs), interleukin-10 (IL-10), and interleukin-26 (IL-26). P-value < 0.05 indicates statistical significance.

Table 4: Variations in the SIRT1 (rs7069102) gene genotypes

	COPD	Control	*P*
SIRT1 genotypes			
GG	42 (42%)	31 (31%)	**= 0.03***
GC	50 (50%)	49 (49%)	
CC	8 (8%)	20(20%)	
SIRT1 Alleles			
G	134 (67%)	111(55.5%)	
C	66 (33%)	89(44.5%)	**=0.0001**

***The Chi-square test was used for comparing frequency between groups. P-value < 0.05 indicates statistical significance.

Table 5: Relation between SIRT1 genotype and IL-26 among cases, Relation between SIRT1 genotype and IL-10 among cases.

Parameters		IL-26 pg/ml		
		Mean± SD	**Median (range)**	***P-value***
SIRT1	**GG**	206.5± 91.8	210 (60-450)	0.007
	GC	221.2 ± 103.2	203 (60-432)	
	CC	176 ± 65.1	162.5 (96-276)	
Parameters		**IL-10 pg/ml**		
		Mean ±SD	**Median (range)**	**P-value**
SIRT1	**GG**	184.8± 19.6	188.5 (146-218)	**0.012**
	GC	190.3 ± 15.7	190 (150.3-213.5)	
	CC	185 ± 23.4	178.5 (150.3-213.5)	

Table 6: Independent Association between SIRT1 Gene Polymorphism and COPD: Multivariable Logistic Regression

	Odds (95% Confidence Interval)	p-value
WBCs*10^3	0.176(0)	= 0.999
Platelets Count*10^3	1.06(0)	= 0.999
IL-26	0.782 (0)	= 0.999
IL-10	1.44 (0)	= 0.999
Sirt1		
GG	1 (Reference)	
GC	3.068(0)	= 0.999
CC	0.001 (0)	= 0.999

The ROC Curve for serum IL-10 can be used for the diagnosis of COPD. Our study found that serum IL-26 may be used in the diagnosis of COPD, where there was a sensitivity of 100% and specificity of 100%. The cut-off point for IL-26 for the diagnosis of COPD was equal to 48 pg/ml. Also, we found serum IL-10 may be used in the diagnosis of COPD, where there was a sensitivity of 100% and a specificity of 100%. The cut-off point for IL-10 for the diagnosis of COPD was equal to or above 281 pg/ml. **(Table 7) (Fig A).**

Table 7 Validity testing for IL-10 and IL-26 as a COPD prognostic.

Variable	Cut off point	AUC	P-value	Sensitivity (%)	Specificity (%)	PPV (%) (Positive predictive value)	NPV (%) (Negative predictive value)
IL-26 pg/ml	48	1	0.0001	100%	100%	100%	100%
IL-10pg/ml	≥281	1	0.0001	100%	100%	100%	100%

AUC= Area Under the curve

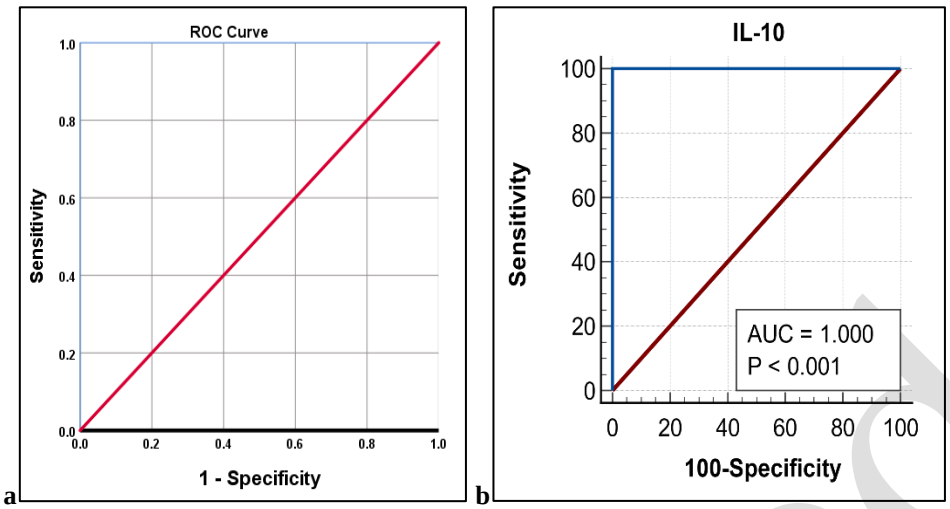

Fig. 1: a) IL-26 ROC curve, b) IL-10 ROC curve

DISCUSSION

COPD is a common and permanent respiratory disorder. It is presently the world's fourth biggest cause of death, and its incidence is anticipated to climb by 2030[17]. COPD affects about 10% of those over the age of 45 [18], and the disease is equally prevalent in men and women in developed countries. Smoking is a major risk factor for the development of COPD [19].

In the course of our study, we noticed a reduction. in pulmonary function test parameters in COPD patients compared to control groups. Specifically, we found reductions in FEV1, FEV1 percentage, and the FEV1/FVC ratio. These findings are in line with most of the prior research that demonstrate a significant decline in FEV1 and FEV1/FVC ratio among COPD patients, which are critical indicators of airflow limitation, as reported by Habib[20], Whittaker et al.[21], and Wang et al.[22].

Regarding the mMRC dyspnea scores, 5% of patients scored 1; 30% scored 2; 59% scored 3, and 6% scored 4. In terms of COPD stages, according to the GOLD classification. We discovered that 28% of the individuals were in stage 2, 33% in stage 3, and 39% in stage 4. These findings are consistent with the results published by other researchers [23,24].

Numerous immunological and structural cells in the human airways release IL-26, a cytokine that is a member of the IL-10 superfamily, in response to microbial stimuli. It has both direct and indirect antibacterial effects and alters human airway host defence mechanisms [25,26]. Remarkably, this specific cytokine has inhibitory and pro-inflammatory actions on immune cells and airway epithelial cells, even while it causes neutrophils to congregate in infection sites. The discovery that IL-26 overexpression is associated with lower lung function, increased systemic inflammation, and impending worsening symptoms in COPD patients suggests a significant role in disease monitoring as well as a biomarker of disease progression and relapse risk [26].

The average levels of IL-26 in COPD serum were considerably greater than in healthy controls, indicating that this cytokine may play a role in the disease's inflammatory processes. Another investigation indicated that IL-26-induced sputum was higher than that of healthy subjects [13]. In the industrialized world, the use of cigarettes remains the principal cause of chronic obstructive pulmonary disease (COPD) and a key contributing factor to the prevalence of chronic bronchitis [27]. Chronic bronchitis or COPD patients who have smoked for a long time have an overabundance of neutrophils in their airways, a type of inflammation that does not respond well to traditional treatment [28]. Che et al. found higher levels of extracellular IL-26 in the airways after investigating bronchial wash (BW), bronchoalveolar lavage (BAL), and induced sputum samples from long-term smokers with and without COPD and chronic bronchitis [29]. In vitro exposure to water-soluble tobacco smoke components increased IL-26 gene and protein levels in human alveolar macrophages and increased IL-10, a pleiotropic anti-inflammatory cytokine generated by activated monocytes, macrophages, helper T-cells, and B-cells [30]. It significantly reduces the production of IL-6 and TNF-α. The mean levels of IL-10 in patients with Chronic Obstructive Pulmonary Disease (COPD) were found to be considerably lower than in healthy controls, indicating that this cytokine may have a role in the disease's inflammatory processes. This finding adds to the assumption that IL-10 is critical for modifying immune responses in COPD. Our findings are congruent with those published by Jiang et al. [31].

However, there are contradicting investigations, such as those conducted by Kumari et al. [32], that provide

opposing results. IL-10 levels gradually increased from 10.31 ± 0.061 pg/mL in stage I to 39.78 ± 0.048 pg/mL in stage IV. In comparison, the control group had significantly lower IL-10 levels (7.90 ± 0.04 pg/mL).

The link between IL-26 and IL-10 levels in COPD patients' serums is significant, as both cytokines play critical roles in the disease's inflammatory processes. IL-26, an IL-10-related cytokine, has been associated to impaired lung function and enhanced neutrophilic inflammation in COPD patients [33]. In contrast, IL-10, an anti-inflammatory cytokine, decreases with COPD severity, indicating a possible cytokine imbalance that may aggravate inflammation[34].

SIRT1 was the first sirtuin discovered in mammals and is the most extensively studied of them. It resides mostly in the nucleus but can also be detected in the cytoplasm [35]. SIRT1 is a histone deacetylase (HDAC) protein that deacetylates several important regulatory proteins and transcription factors involved in DNA repair, inflammation, antioxidant defence, and cellular aging [36]. SIRT1 affects inflammatory reactions, oxidative stress, autophagy, apoptosis, and aging.

SIRT1 levels have been found to be lower in lung cells and peripheral blood mononuclear cells of patients with chronic obstructive pulmonary disease (COPD) than in healthy individuals[10]. This decline could be linked to increased acetylation and heightened inflammatory responses. As a result, SIRT1 may play an important role in controlling inflammation during the progression of COPD.

New studies have also studied the relationship between the SIRT1 gene polymorphism (rs7069102) and COPD, indicating a substantial association. The SIRT1 gene is particularly significant for its involvement in controlling inflammation and oxidative stress, both of which are key contributors in the etiology of COPD, especially concerns aging and chronic inflammation.[1]

In our study, we discovered that 37% of COPD patients displayed the GG genotype of the rs7069102 SNP, 60% expressed the GC genotype, and 3% expressed the CC genotype. The control group contained 40% GG, 45% GC, and 15% CC genotypes. A substantial difference in CC genotype expression was seen between COPD patients and controls (p = 0.006).

Furthermore, 67% of COPD patients had the G allele of the rs7069102 SNP, whereas 33% had the C allele. In comparison, 55.5% of controls had the G allele, while 45.5% had the C allele. The difference in allele frequencies between the two groups was statistically significant (p = 0.0001), showing that allele C was more common in the control group than in the sick group. This shows that the C and G alleles may be linked to COPD risk (Kalemci et al.[37]. Furthermore, 67% of COPD patients had the G allele of the rs7069102 SNP, whereas 33% had the C allele. In comparison, 55.5% of controls had the G allele, while 45.5% had the C allele. The difference in allele frequencies between the two groups was statistically significant (p = 0.0001), showing that allele C was more common in the control group than in the sick group. Furthermore, a study of 100 COPD patients and 100 healthy controls discovered substantial variations in the allele frequencies of rs7069102. This shows that the C and G alleles may be linked to COPD risk (Kalemci et al., 2014) [38].

Strengths of our study: A relatively small number of studies investigated the link between the SIRT1 (rs7069102) single-nucleotide polymorphism (SNP) and interleukin-10 (IL-10) in chronic obstructive pulmonary disease. COPD is an irreversible respiratory disorder that ranks as the fourth greatest cause of mortality worldwide.

CONCLUSION

SIRT1 (rs7069102) single-nucleotide polymorphism may be associated with Chronic Obstructive Pulmonary Disorder (COPD). Patients with COPD had considerably greater frequencies of the GG, GC, and G alleles than the control group. Furthermore, a strong link was discovered between IL-10 levels and COPD; specifically, IL-10 levels were lower in COPD patients than in controls. Another substantial connection was found between IL-26, IL-10, and the SIRT1 genotype, with the GC genotype having significantly higher IL-26 and IL-10 levels than the GG and CC genotypes. Our data reveals that serum IL-26 and IL-10 could be used in the diagnosis of COPD, demonstrating both 100% sensitivity and 100% specificity. The cutoff point for IL-26 in diagnosing COPD was determined to be equal to 48 pg/ml. The cutoff point for IL-10 in diagnosing COPD was determined to be equal to or greater than 281 pg/ml.

Recommendation:

Despite the limited sample size, our study was a case-control study, which is susceptible to selection bias. As a result, new research with a larger sample size are required, as the results may be more significant when more patients are included in the study.

Abbreviations

COPD Chronic obstructive pulmonary disease
CRP C-reactive protein,
HDACs Histone deacetylases
IL-26: Interleukin-26,
IL-10 Interleukin-10,
SIRT Sirtuin,
SIRT 1 Sirtuin 1
SNP` Single-nucleotide polymorphism

Author contribution

Z.M. K and Ebtisam Mohammed researched data. Z.M., ALshimaa Hafez, and Noha Saber Shafik wrote the

manuscript and researched data. E.M., Z.M.K., and A.H. contributed to the discussion and reviewed/edited the manuscript. Noha Saber and Ebtisam Mohammed researched data and contributed to the discussion. Z.M.K, Noha Saber and Ebtisam Mohammed, and. ALshimaa Hafez wrote the first draft of the manuscript. Sara Mostafa helped in collecting clinical data, and writing the manuscript. Asmaa Tarazan helped in performing molecular techniques. All authors reviewed/edited the manuscript.

Disclosure statement

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript.

Writing disclosure

No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained approval from the Ethical Committee of the Faculty of Medicine at Sohag University with IRB registration number Soh-Med-23-09-10PD, and it was recorded on ClinicalTrials.gov (ID: NCT06055634). All participants provided written informed consent after a comprehensive explanation of the study procedures, benefits, and possible adverse effects.

Supplementary material

Due to privacy and ethical considerations, the datasets produced and/or examined in this study are not publicly accessible; however, they can be obtained from the corresponding author upon reasonable request.

Additional information

Funding

The author declares that there is no received funding.

Acknowledgements

I would like to express my deepest thanks to the authors of the included studies in this study.

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