INTERFERON-INDUCED TRANSMEMBRANE PROTEIN 3 (IFITM3) GENE rs12252 POLYMORPHISM AND COVID-19 SEVERITY IN A COHORT OF EGYPTIAN PATIENTS

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INTRODUCTION

The pandemic of Coronavirus disease 2019 (COVID-19) resulted in about 6 million deaths around the world till December 2022 according to the reports of the World Health Organization (WHO). Extensive studies have explored the innate defense mechanisms and cellular proteins involved in immunity against the infection of coronaviruses. Interferon-induced transmembrane proteins (IFITMs) have been identified as key interferon-stimulating genes (ISGs) that interfere with viral endosomal membrane fusion and the infectivity of nascent virions. The rs12252 single nucleotide polymorphism (SNP) within the first exon of the *IFITM3* gene has been associated with increased severity in some viruses such as influenza virus and Human immunodeficiency virus (HIV).

AIM OF THE WORK

The study aimed to investigate the association between interferon-induced transmembrane protein 3 gene (*IFITM3*) rs12252 polymorphism with disease severity in coronavirus disease.

PATIENTS AND METHODS

This case-control study was conducted on 87 laboratory-confirmed COVID-19 patients from Alexandria University Hospitals and 75 healthy controls. The patient group was further subdivided into 3 groups; mild, moderate, and severe including 23, 36 and 28 patients respectively. Laboratory confirmation of the cases was defined as a positive COVID-19 result of real-time reverse-transcription polymerase chain reaction assay of nasopharyngeal swab specimens. Blood samples were collected on K2EDTA tubes for genotyping of *IFITM3* gene SNP (rs12252).Detection of *IFITM3* rs12252 SNP was performed via real-time PCR using TaqMan SNP genotyping assay.

RESULTS

IFITM3 rs12252 polymorphism had no significant association with COVID-19 susceptibility under the homozygote model (GG vs AA: OR=0.829, 95% C.I=0.051–13.538, p=0.895), (AG vs AA: OR=0.829, 95% C.I=0.382–1.799, p=0.635), dominant genetic model (AG+GG vs AA: OR=0.829, 95% C.I=0.389–1.766, p=0.626), and recessive model (GG vs AA+AG: OR=0.860, 95% C.I=0.053 –13.998, p=0.916). (Table 1)

Table 1: Association of IFITM3 rs12252 polymorphism with COVID-19 susceptibility

	Patients (n = 87)		Control (n = 75)		p value	OR (LL – UL 95%C.I)
	No.	%	No.	%		
IFITM3 rs12252 genotype						
AA	70	80.5	58	77.3		1.000
AG	16	18.4	16	21.3	0.635	0.829 (0.382 – 1.799)
GG	1	1.1	1	1.3	0.895	0.829 (0.051 – 13.538)
Allele						
A	156	89.7	132	88.0		1.000
G	18	10.3	18	12.0	0.637	0.846 (0.423 – 1.692)
Dominant model						
AA	70	80.5	58	77.3		1.000
AG + GG	17	19.5	17	22.7	0.626	0.829 (0.389 – 1.766)
Recessive model						
AA + AG	86	98.9	74	98.7		1.000
GG	1	1.1	1	1.3	0.916	0.860 (0.053 – 13.998)

IFITM3 rs12252 polymorphism had no significant association with COVID-19 severity under the homozygote model (GG vs AA: p=1.00), (AG vs AA: OR=2.684, 95% C.I=0.882-8.166, p=0.082) and recessive model (GG vs AA+ AG: p=1.00). However, a significant association was observed under the dominant model (AG+GG vs AA: OR=3.020, 95% C.I=1.017-8.967, p=0.047). Additionally, allele G was significantly associated with COVID-19 severity (G vs A: OR=2.989, 95% C.I=1.109-8.055, p=0.030). (Table 2)

Table 2: Association of IFITM3 rs12252 polymorphism with COVID-19 severity.

	Mild/Moderate (n = 59)		Severe (n = 28)		p value	OR (LL – UL 95%C.I)
	No.	%	No.	%		
IFITM3 rs12252 genotype						
AA	51	86.4	19	67.9		1.000
AG	8	13.6	8	28.6	0.082	2.684 (0.882 – 8.166)
GG	0	0.0	1	3.6	1.000	–
Allele						
A	110	93.2	46	82.1		1.000
G	8	6.8	10	17.9	0.030*	2.989 (1.109 – 8.055)
Dominant model						
AA	51	86.4	19	67.9		1.000
AG + GG	8	13.6	9	32.1	0.047*	3.020 (1.017 – 8.967)
Recessive model						
AA + AG	59	100.0	27	96.4		1.000
GG	0	0.0	1	3.6	1.000	–

CONCLUSION

This study revealed an association between *IFITM3* rs12252 SNP and COVID-19 severity considering that the G allele was significantly associated with disease severity; however, we found no association between *IFITM3* rs12252 SNP and COVID-19 susceptibility in a cohort of Egyptian patients.