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CORONA VIRUS DISEASE 19 AND ITS ASSOCIATION WITH INTERFERON Γ GENE +874 A/T POLYMORPHISM

SURESH I [1], RITHIKA RAMADUGU[2], SANDEEP KUMAR TIPPARTHI[3], RAJKUMAR H.R.V [4], RAVISHANKAR REDDY A. [5], GURU PRASAD MANDERWAD[*]

[1] Professor, Department of General Medicine, Kamineni Academy of Medical Sciences and Research Centre, LB Nagar, Hyderabad

[2] Intern, Kamineni Academy of Medical Sciences and Research Centre, LB Nagar, Hyderabad.

[3] Assistant Professor, Department of Microbiology, Kamineni Academy of Medical Sciences and Research Centre, LB Nagar, Hyderabad.

[4] HOD and Professor, Department of Microbiology, Kamineni Academy of Medical Sciences and Research Centre, LB Nagar, Hyderabad.

[5] Professor, Department of Microbiology, Kamineni Academy of Medical Sciences and Research Centre, LB Nagar, Hyderabad.

*Professor, Department of Microbiology, Kamineni Academy of Medical Sciences and Research Centre, LB Nagar, Hyderabad.

***Corresponding Author:**Dr. Guru Prasad Manderwad

Professor,Department of Microbiology,Kamineni Academy of Medical Sciences and Research Centre,LB Nagar, Hyderabad.Ph.No :9542536135

Fax:Email: gurukmc@gmail.com

ABSTRACT

Corona Virus Disease 19 **(**COVID-19) has been associated with high mortality and morbidity. Cytokines play a central role in determining the immunity against any infection including COVID-19. The inherent presence of polymorphism determine the production of cytokines, which in turn determines the susceptibility or resistance to COVID-19 infection. Among cytokines, Interferon gamma (IFN γ) plays a central role in activating inherent immunity and presence of polymorphism would derail its activity. The aim of the present study to evaluate the Corona Virus Disease 19 and its association with Interferon γ Gene +874 A/T Polymorphism. The blood samples were collected from 100 COVID-19 cases and 100 controls after taking informed consent. The DNA was extracted, and amplification refractory mutation system (ARMS PCR) was performed to analyze the presence of genotype along with allele frequency. Statistical analysis was performed with application of chi square tests, Shapiro-Wilk tests and Mann-Whitney tests. The study found significant association between the AT heterozygous genotype with COVID-19 (p=0.0006). We also found association of AT heterozygous polymorphism and thyroid disorder more in mortality cases (p=0.040). We could

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not find any correlation between the association of comorbidities and polymorphism in relation with infection.The study found that Corona Virus Disease 19 has been found to be associated with heterozygous interferon γ Gene +874A/T polymorphism. It has also been found to be associated with hypothyroidism. Precautions have to be taken to prevent infection in the susceptible population and diligent monitoring to be undertaken to improve the outcome of the infection in the individuals proven to be more susceptible.

Key Words: Corona virus, infection, mortality, thyroid disorder

INTRODUCTION

COVID-19 pandemic in the present century has been associated with high morbidity and mortality. It has affected wide range of world population irrespective of creed and tribe and has been termed as one of the gravest diseases associated with high mortality especially in individuals with comorbidities such as diabetes, hypertension and cardiovascular diseases. [Parasher et al 2021]It is also known to have affected the individuals with pulmonary diseases including patients with inherent asthma. [Adir et al 2021] The high death rate due to the coronavirus, which has been known to have originated from the Wuhan region of China may be attributed to the virulence factors and appearance of different antigenic variants, to which immune system fail to answer at the appropriate time.[Seyed Hosseini et al 2019]

Immunity plays an important role in the deciding the fate of the corona virus infection. The cell mediated response, at the appropriate time prevents the spread of the infection. The interplay of cytokines decides the fate of the immune activity. This pro and anti-inflammatory cytokine balance, provides a necessary thrust against the deleterious action of the virus, and contains the spread of the infection as well as clearance of the corona virus from the body at a timely manner. [Tovey et al 2010] Literature review revealed that the occurrence of single nucleotide polymorphism (SNP), in the cytokine genes has been associated with the wide range of infections and inflammations. Cytokine polymorphisms has been known to associated with infections such as sepsis [Chousterman et al 2017], infection with toxoplasma gondii[Wujcicka et al 2018], viral infections in transplant patients [Sakharkar et al 2020], tuberculosis [Tipparthi et al 2022] and Hansen's disease [Pragasam et al 2020].

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Among the several cytokines, IFN γ plays a pivotal role in initiating the action against the intracellular pathogen, as well as alerting other cells and plays a complex role in activating other cytokines.[Kak et al 2018] It is a soluble cytokine, a member of type II class of interferons. It is a glycoprotein weighing between 17-25 kDa. It promotes macrophage activation, helps mediate antibacterial and antiviral immunity, enhances antigen presentation and activates innate immunity.[Schoenborn et al 2007] SNP in IFN γ mainly +874A/T has been associated with coarse of several infections including autoimmune diseases [Billiau et al 1996], bacterial diseases like tuberculosis [Areeshi et al 2019], viral diseases like SARS [Chong et al 2006] and Hepatitis B [Li et al 2020] , other pathogenic infections like Schistosoma [Gatlin et al 2009].

Association of IFN γ +874T/A and COVID-19 infection is still a debatable. A study from Dhabaan et al evaluated and found the presence of A allele and the AT genotype found more in COVID patients than in healthy controls in the Iraqi population.[Anwar et al 2021] Cytokines play an important role in the pathogenesis of COVID-19. We hypothesize that cytokine gene with polymorphism such as INF gammahas been associated with high or low production of INF gamma cytokine effect the pathogenic effects and outcome of COVID-19 infection. There is a need to evaluate the effect of cytokine polymorphism and outcome of the disease due to the cytokine storm which has been associated with poor prognosis of COVID-19.

The relationship between the types of genotype and allele frequency in Indian population with COVID is not known, we aim to evaluate the Corona Virus Disease 19 and its association with Interferon γ Gene +874 A/T Polymorphism in Southern part of India. Additionally we studied the association of comorbidities, clinical parameters and laboratory parameters with the above mentioned polymorphism. The association of IFN γ +874T/A polymorphism and the clinical and laboratory parameters associated with COVID-19 hasn't been extensively studied yet.

MATERIALS AND METHODS

The present study is a prospective study, and the study conducted from November 2020 to December 2021 at Kamineni academy of medical sciences and research centre, Hyderabad. The cases admitted in the hospitals have been evaluated.

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Study group: A total of 100 blood samples were collected from the COVID-19 cases from the COVID ward in the age group of 29 years to 81 years (case sample size-100), and 100 samples from healthy subjects (controls) in the age group of 24 to 75 years (>18years) (control sample size-100) after taking written informed consent.

The Inclusion criteria for the study group were subjects that presented with clinical signs and symptoms and tested COVID-19 positive through established serological and molecular biology tests. Exclusion criteria was patients with chronic infections, cancers, post-transplant cases and subjects using immuno-suppressants.

Inclusion criteria for Healthy controls was subjects tested negative for COVID-19 through molecular and serological tests. Exclusion criteria for the controls was presence of comorbidities along with other chronic infections, cancers, post-transplant cases and subjects using immuno-suppressants. The controls were not age and sex matched.

The study was approved by the Institutional Ethics Committee of Kamineni Academy of Medical Sciences and Research Centre (ECR/58/INST/AP/2013/RR-19) and was conducted at The Department of Microbiology, Kamineni Academy of Medical Sciences and Research Centre, Hyderabad over a period of two years from 2021-2022. A written consent was taken from all study participants. The demographic data, clinical picture, vitals, CORADS score, COVID profile including C-reactive protein, D-dimer, serum lactose dehydrogenase (LDH) , serum ferritin, serum procalcitonin, serum albumin and leucocyte counts were collected. The comorbidities, clinical parameters, laboratory parameters and CORADS score were used to predict the outcome measures.

DNA extraction and PCR: Peripheral blood samples were collected in Ethylene diamine tetra-acetic acid (EDTA) vacutainers from COVID-19 patients and healthy individuals without any comorbidities and infections. DNA extraction was performed using DNA extraction kit (Nucleospin, Microbial DNA, Germany) according to the manufacturer's instructions, and stored at -20 °C. [8]

Polymerase chain reaction (PCR): The ARMS-PCR (Amplification refractory mutation system-Polymerase chain reaction) was performed in a thermal cycle (*Takara gradient thermal cycler dice.* Japan) with primers, specific to IFN γ +874 A/T

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polymorphism. [8] The primer sequence with appropriate annealing temperature and amplicon size was mentioned in figure 1.

Gene	Primer Sequence	Annealing temperature	Amplicon Size	Reference
IFN-Ÿ +874 A/T	Allele A- 5'-TTC TTA CAA CAC AAA ATC AAA TCA- 3'	62	261 bp	Mansouri et al 2018
	Allele T- 5'-TTC TTA CAA CAC AAA ATC AAA TCT- 3'			
	Common Primer- 5'- TCA ACA AAG CTG ATA CTC CA-3'			

Figure 1 showing primer sequence, Annealing temperature, Amplicon size

Statistical analysis: All data was presented as the mean standard deviation (SD) for quantitative variables/ percentages for categorical variables. The genotypic and allelic frequencies were compared using a chi-square test or Fisher's exact test between case and control groups. P value of < 0.05 were considered significant for both Pearson and Fisher's exact tests. The odds ratio (OR) and 95% confidence interval (CI) for allele and genotype forms were calculated by univariate and multinomial logistic regression was applied respectively. Hardy-Weinberg Equilibrium (HWE) has been determined by applying the equation ($p^2+2pq+q^2$). The Shapiro-Wilk test revealed non-normal distributions for several clinical parameters and the Mann-Whitney U test results was used for non-normal variables

RESULTS: Genotyping of IFNG (+874 T/A)

Lanes: AA Homozygous- lanes –3,4; 12,13

AT Heterozygous- lanes- 1,2; 8,9

TT Homozygous- lanes- 5,6; 10,11

100 Bp Ladder: 7 lanes

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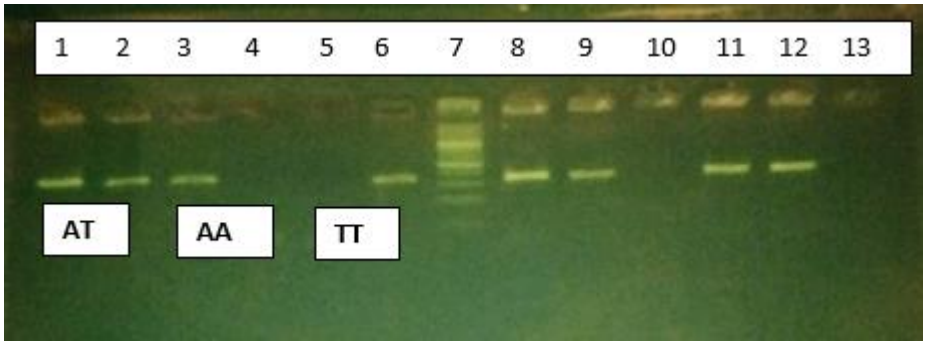

Figure 2: ASO PCR for the detection of IFN-γ (+874 A/T)

The Figure shows gel electrophoresis of Allele specific oligonucleotide- Polymerase chain reaction (ASO PCR) images showing the polymorphisms and ladder. The wells showing different polymorphisms have been mentioned above.

Statistically significant allele frequency A has been found in association with COVID-19 cases compared with healthy controls (p 0.00001, OR-2.44) . AT was most frequent genotype found in both cases and controls, but statistically significant association has been noted in COVID-19 cases, implying the persons with genotype AT are prone to develop COVID-19 related symptoms compared to controls (p=0.00006, OR-4.57) (Figure 3, Figure 4)

		Cases	Controls	P Value	Odds ratio
ALLELES	A	107	64	**0.00001**	2.44
	T	93	136		
GENOTYPES	AT	85	49	**0.00006**	4.57
	TT	4	22	0.251129	0.48
	AA	11	29		

Figure 3 showing frequencies of alleles (A,T); genotypes (AT,TT,AA) and odds ratios

The data was analysed using chi square test and presented as P-value and odds ratio. P value for allele A: 0.00001 , P value for genotypes AT: 0.00006 and AA:0.251129.

Association between the clinical symptoms and polymorphism

Clinical symptoms such as fever, cold and shortness of breath (SOB) were found to be associated with all COVID-19 cases and were not specifically associated with a particular genotypes, but majority of cases were observed in AT heterozygous genotype (Figure 4).

Clinical Symptoms		AA	AT	TT	TOTAL

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Fever	Present	10	73	2	85 (85%)
	Absent	1	12	2	15 (15%)
	Total	11	85	4	
Cough	Present	7	68	4	79 (79%)
	Absent	4	17	0	21 (21%)
	Total	11	85	4	
SOB	Present	7	69	4	80 (80%)
	Absent	4	16	0	20 (80%)
	Total	11	85	4	

Figure 4 : Clinical symptoms and its association with INF gamma genotypes

CO-RADS score in relation with polymorphism

The study analyzed the correlation between the CO-RADS score with polymorphism, but couldn't draw any significant association with polymorphism (P value: 0.522), but it has significance in predicting the outcome of COVID-19 treatment. (Figure 5)

CO-RADS SCORE	2	3	4	5	P value
POLYMORPHISM					0.522
AA	0	0	1	10	
AT	1	4	25	54	
TT	0	0	0	4	

Figure 5: CO-RADS score and its association with IFN γ Genotypes

Chi square test was used to determine the p value: 0.522

Association of comorbidities in cases with polymorphism

Comorbidities play an important role in the infections, present study evaluated with occurrence of hypertension -57 (57)%, diabetes mellitus-50 (50%), thyroid disorders- 13 (13%), coronary artery disease (CAD) – 15 (15%) and cerebrovascular accident (CVA) – 4 (4%) in COVID-19 cases and its association with polymorphism. (Figure 6) No significant association has been noted with respective to different genotypes ((hypertension) p=0.279, Diabetes mellitus p=0.114, CAD p=0.733, CVA p=0.692, thyroid disorders p=0.69)

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		AA	AT	TT	P- Value
HYPERTENSION (HTN)	PRESENT	4	50	3	0.279
	ABSENT	7	35	1	
	TOTAL	11	85	4	
DIABETES MELLITUS (DM)	PRESENT	5	40	4	0.114
	ABSENT	6	45	0	
	TOTAL	11	85	4	
CORONARY ARTERY DISEASE (CAD)	PRESENT	1	13	1	0.733
	ABSENT	10	72	3	
	TOTAL	11	85	4	
CEREBROVASCULAR ACCIDENT (CVA)	PRESENT	0	4	0	0.692
	ABSENT	11	81	4	
	TOTAL	11	85	4	
HYPOTHYROIDISM	PRESENT	2	11	0	0.651
	ABSENT	9	74	4	
	TOTAL	1	85	4	

Figure 6: Comorbidities and the association with IFN γ Genotype

The above table shows the occurrence of comorbidities (Hypertension, diabetes mellitus, coronary artery disease, cerebrovascular accidents and thyroid disorders) among the cases and p value calculated using chi square test with p values as follows. Hypertension :0.279, diabetes mellitus:0.114, coronary artery disease:0.733, cerebrovascular accident: 0.692, thyroid disorders: 0.651.

Association of laboratory analysis to establish COVID-19 and its relation with polymorphism

The D-dimer levels exhibited a notably wide range, with values extending from 184 to 22900 ng/mL, and a mean of 1748.73 ng/mL, which is substantially above the standard reference range, indicating a hyper coagulable state often associated with severe COVID-19.

The Shapiro-Wilk test revealed non-normal distributions for several clinical parameters including CRP, D-dimer, LDH, ferritin, and procalcitonin and total leucocyte count, as evidenced by significant p-values ($p < .001$), suggesting that the clinical course of COVID-19

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in the studied population was associated with a broad range of values for the clinical parameters. Significant association with genotypes in relation with the laboratory diagnosis has been not found, instead it signifies the importance of analysis of different laboratory parameters in reference to COVID-19 for establishment of infection to initiate appropriate therapy. (Figure 7)

	MEAN	STD. DEVIATION	IQR	SHAPIRO-WILK	P-VALUE OF SHAPIRO-WILK	MINIMUM	MAXIMUM
AGE	60.090	14.505	19.250	0.983	0.244	29.000	95.000
PULSE RATE	96.870	17.615	17.250	0.958	0.003	56.000	170.000
RESPIRATORY RATE	25.150	6.034	9.250	0.958	<0.001	0.003	40.000
C-RP	24.530	17.317	12.000	0.741	<0.001	2.000	134.000
D-DIMER	1748.73	3203.526	1025.75	0.455	<0.001	184.000	22900.00
LDH	419.570	278.031	162.750	0.678	<0.001	32.000	2216.000
FERRITIN	404.238	429.598	419.500	0.746	<0.001	13.700	2490.000
PROCALCITONIN	0.640	1.499	0.200	0.403	<0.001	0.100	8.100
ALBUMIN	3.463	0.378	0.500	0.980	0.139	2.300	4.300
TOTAL LEUCOCYTE COUNT	8745.560	4389.440	4342.50	0.890	<0.001	1286.00	23980.00

Figure 7: Laboratory parameters and the association with INF gamma genotypes

The above table shows the various clinical and laboratory parameters, presented as mean, standard deviation, interquartile range, p value calculated using Shapiro wilk test, Shapiro wilk statistic, the minimum and maximum values among the data. The p values as follows: Age-0.244, pulse rate:0.003, Respiratory rate:<0.001, C-RP:<0.001, D-Dimer:<0.001, LDH: <0.001, Ferritin: <0.001, procalcitonin:<0.001, Albumin:<0.001, Total leucocyte count: :<0.001.

Analysis of mortality association with various factors

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In the present study, mortality was found to be 18 (18%) due to complications of COVID-19. The study also analyzed the association of different factors correlating with mortality.

The analysis of mortality against CO-RADS scores, which are indicative of radiographic assessment of COVID-19, showed a significant correlation (Chi-Squared p = 0.031). (Figure 8). A higher mortality rate was observed in patients with CO-RADS scores of 5, which represent the most severe radiographic findings. Investigating the relationship between genotype polymorphisms and CO-RADS scores did not yield any significant correlations for IFN γ genotypes, with p-value of 0.522 (Figure 5), suggesting that these polymorphisms did not influence the radiographic severity of COVID-19 in this cohort.

CO-RADS SCORE	2	3	4	5
MORTALITY(N)	1	1	1	15
P VALUE	0.031			

Figure 8: CO-RADS Score and the association with COVID 19 mortality

The above table shows the corads value among the mortality with p value of 0.031 calculated using chi-square test.

Analysis of the laboratory results through application of The Mann-Whitney U test for non-normal variables to evaluate the mortality association of D-Dimer (p<0.001), LDH (p=0.002), Ferritin (p=0.032), and Procalcitonin (p=0.007) Total Leucocyte count (p=0.050) and albumin (p=0.001) were found to be statistically significant. (Figure 9)

	TEST	**STATISTIC**	**Df**	**P VLAUE**
C-RP	STUDENT	0.097	98.000	0.923
	WELCH	0.116	31.730	0.909
	MANN-WHITNEY	773.500		0.747
D-DIMER	STUDENT	2.850	98.000	0.005
	WELCH	1.814	18.598	0.086
	MANN-WHITNEY	1143.00	but	<.001
LDH	STUDENT	3.173	98.00	0.002
	WELCH	2.026	18.625	0.057

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	MANN-WHITNEY	1084.00		0.002
FERRITIN	STUDENT	1.913	98.00	0.083
	WELCH	1.771	23.236	0.090
	MANN-WHITNEY	978.00		0.032
PROCALCITONIN	STUDENT	1.753	98.00	<0.001
	WELCH	1.400	23.877	0.003
	MANN-WHITNEY	1011.500		
ALBUMIN	STUDENT	-3.519	98.00	<.001
	WELCH	-3.356	23.877	0.003
	MANN-WHITNEY	359.00		
TOTAL LEUCOCYTE COUNT	STUDENT	2.280	98.00	0.025
	WELCH	1.774	20.480	0.091
	MANN-WHITNEY	957.00		0.050

Figure 9: Laboratory parameters and the association with COVID 19 mortality

The above table shows the various clinical and laboratory parameters correlated with mortality, p value calculated using Mann Whitney Test, Student test and Welch tests presented along with the test statistic and degrees of freedom. The p values using Student test as follows: C-RP: 0.923*, D-Dimer:* 0.005*, LDH:* 0.002*, Ferritin:* 0.083*, procalcitonin:<0.001, Albumin:<0.001, Total leucocyte count: :* 0.025*. The p values using welch tests as follows: C-RP:* 0.909*, D-Dimer:* 0.086*, LDH:* 0.057*, Ferritin:* 0.090*, procalcitonin:* 0.003*, Albumin:* 0.003*, Total leucocyte count: :* 0.091*. The p values using mann whitney u tests as follows: C-RP:* 0.747*, D-Dimer:* <.001*, LDH:* 0.002*, Ferritin:* 0.032*, procalcitonin:-, Albumin:-, Total leucocyte count:* 0.050*. Multiple tests have been applied as some of the tests didn't yield any results. Mann whitney test for procalcitonin and albumin were inconclusive*

The mortality rate did not differ significantly among patients with comorbidities such as hypertension (P Value: 0.697), DM (P Value: 0.925), CAD (P Value: 0.610) and CVA (P Value: 0.339) as indicated by Chi-Squared test p-values greater than 0.05. However, a close

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association was observed between mortality and thyroid dysfunction (p = 0.040), suggesting that thyroid conditions may impact the prognosis of COVID-19. (Figure 10)

COMORBIDITY		MORTALITY (N)	MORTALITY(%)	P VALUE
HYPERTENSION	PRESENT	11	61.11%	0.697
	ABSENT	7	38.88%	
DIABETES MELLITUS	PRESENT	9	50%	0.925
	ABSENT	9	50%	
THYROID DISORDERS	PRESENT	5	27.77%	0.040
	ABSENT	13	72.22%	
CAD	PRESENT	2	12.5%	0.610
	ABSENT	16	88.88%	
CVA	PRESENT	0	0%	0.339
	ABSENT	18	100%	

Figure 10: Comorbidities and the association with COVID 19 mortality

The above table shows the mortality as number and percentage among the different comorbidities among the cases in the study. P Values as following, Hypertension: 0.697, Diabetes mellitus: 0.925, Thyroid disorders: 0.040, Coronary artery disease:0.610, Cardiovascular accident:0.339.

Association of mortality with polymorphism has been evaluated and found significant association. High mortality has been noticed in patients having AT polymorphism, a total of 90% cases of mortality has been noticed with AT heterozygous polymorphism. No significant association has been found in relation with allele frequency. (Figure 11, 12)

POLYMORPHISM	MORTALITY	RECOVERY	TOTAL	P Value
AA	1 (5.55%)	10 (12.19%)	11	0.427
AT	17 (94.44%)	68 (82.92%)	85	
TT	0 (0%)	4 (4.87%)	4	

Figure 11: IFN γ genotypes and the association with COVID 19 mortality

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The above table presents the mortality and recovery among the 3 polymorphisms- AA, AT and TT, with p value of 0.427 calculated using chi-square tests. Among those with AA genotype, 10% mortality was seen, AT- 20% and TT-0% mortality was seen.

ALLELE	MORTALITY	RECOVERY	TOTAL	P Value
A	19 (52.77%)	88 (53.65%)	107	0.923
T	17 (42.22%)	76 (46.34%)	93	

Figure 12: IFN γ alleles and its association with COVID 19 mortality

The above table presents the mortality and recovery among the 2 existing alleles- A and T, with p value of 0.923 calculated using chi-square tests. A allele had a 17.757% mortality and 82.24% recovery and T allele had a 18.27% mortality and 81.72% recovery.

DISCUSSION

COVID-19 has been considered as one of the most contagious infectious diseases and has been termed as global health calamity claiming millions of lives within short period of time. The grave clinical symptoms has been seen associated with the cytokine storm, activation of several cytokines such as IL-6. Presence of pro-inflammatory cytokines along with interference of COVID-19 open reading frame 3b (ORF3b), ORF6, ORF7, ORF8, and the nucleocapsid (N) protein down regulates of IFN γ production. Lack of IFN and hyper inflammation makes the person succumb to the infection. [Mansouri et al 2018].

Along with down regulation of IFN γ due to the COVID-19 cell components, genetic polymorphism also play a role in the production of central cytokine which plays an important role imparting cellular immunity to fight against the COVID-19. Our results were similar to the study conducted by Anwar Abed Nasser Dhabaan et al., in Iraqi population found presence of heterozygous AT genotype in COVID-19 cases.[Anwar et al 2021] The presence of heterozygous AT implies the intermediate production of IFN γ and subsequent less defense activity against the pathogenesis of SARS-CoV2. Similar to above mentioned study, we also found the presence of AA genotype in COVID-19 cases, but less in number. Thus presence of heterozygous AT and homozygous AA are prone to develop infection.[Anwar et al 2021] A

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study by Sarges KML reported association of T allele at IFN γ T/A to susceptibility to COVID-19 [Sarges et al 2024] .Further study by Almeri IAF has found that A allele showed poor antibody response, which could lead to susceptibility to COVID-19 and also poor response to vaccination.[Alameri et al 2022] A study from Caspar I Van Der Made et al has found that the down-regulation of IFN γ has been associated with COVID-19, highlights the importance of IFN γ in controlling the COVID-19 infection. [Ramasamy et al 2021]

CO-RADS has been considered as a vital in determining the accuracy of diagnosis and prognosis. [van der Made et al 2020] In our study we found the high score CO-RADS 5 has been found to more in patients having the heterozygous polymorphism, although we couldn't conclude its association. It might implies that intermediate production of cytokine due to AT polymorphism favors severe infection which can be estimated by CO-RADS score.

Along with immunological factors, presence of co-morbidities play an exceptional role for the recovery and survival of patients. Elderly people along with co-morbidities such as diabetes, CVA, CAD and thyroid disorders are having higher death rate. A study conducted by Feng et al has in detail evaluated the potential gene polymorphism associated with comorbidities in COVID-19 cases and found TLR4, NLRP3, MBL2, IL6, IL1B, CX3CR1, CCR5, AGT, ACE AND F2 gene polymorphisms were predictors of susceptibility and severity of COVID-19. The presence of comorbidities such as hypertension, CAD and diabetes mellitus can effect metabolic and immune system disorders changes in the expression and activity of cytokines, resulting in changes in susceptibility to infection.[Elnaggar et al 2023] Our study for the first time evaluated the relation between the thyroid disorders and cytokine gene polymorphism in COVID-19 cases, but found mainly with AT polymorphism, although with no statistical significance.

Laboratory parameters plays an important role to predict the severity and outcome of the infection. Parameters such as D-Dimer, CRP, LDH, Ferritin, procalcitonin, albumin and TLC has seen elevated in COVID-19 cases, similar to study conducted by Mardhani R et al found altered level of LDH, CRP, and ALT helps in the detection of COVID-19 cases. [Feng et al 2022]

COVID-19 infection has been found to be associated with high morbidity and mortality. Feng We also found the patients with thyroid disorder were significantly associated with high

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mortality, similar to a study conducted by [Permana et al 2022] and found prognostic value of thyroid disorder in predicting COVID-19 associated with poor outcome. [Mardani et al 2020]

Further studies can help in the better recover of those with AT polymorphism by ensuring hospitalization and intensive treatment of those susceptible to severe infection and thereby help decrease the morbidity and mortality. The possible association between the cytokine production, or polymorphism and infectious diseases like COVID-19 could help us implement personalized primary prevention programs to help prevent the susceptible populations from exposure to infections, which could help prevent mortality and could also eliminate the need for complete lockdown. Personalized medicine could help for each person to have a customized plan for them to prevent infections and extensive care among the infected susceptible subjects to aid in a complete recovery.

LIMITATIONS

The study has its limitations with the sample size of 100 subjects and concentrating on only one polymorphism.

CONCLUSION

The present study concludes the significant association between IFN γ heterozygous AT genotype with the COVID-19. The analysis of comorbidities and laboratory parameters help in early diagnosis of the infection and outcome of the disease. Its association with polymorphism helps to identify the susceptible person at the earliest. The present study emphasizes the need to analyze the presence of IFN γ polymorphism in COVID-19 cases along with the other parameters in larger population.

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