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OBSERVATION OF DIABETES AMONG COVID-19 PATIENTS HAVING LOW CT VALUE IN RT-PCR

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ABSTRACT

Background and Study aim: To observe diabetes among COVID-19 patients having low Ct-value in RT-PCR.

Methods: An observational study was done using RT-PCR on oropharyngeal and nasopharyngeal samples in April 2021.

Results: A total of 15,831 samples were received in April 2021 out of which 11,210 (71%) were COVID-19 positive and 4,621 (29%) were negative. 55±10 years was the mean age of patients. The age of two-third of patients was 26-50 years, one-third were below 25years. More than three-quarter (68%) of patients were males and rest (32%) were females. Among 11,210 positive patients 998 (9%) were diabetics and 102 (0.9%) patients among diabetics were non diabetic before COVID-19 infection. In diabetic patients mild 130 (13%), moderate 299 (30%) and severe 569 (57%) COVID-19 disease was seen.

Conclusion: The study population either had a previous history of diabetes or developed high blood sugar levels following COVID-19 infection. In our study we report that COVID-19 patients having low Ct value in RT-PCR had high prevalence (57%) of DM.

Keywords: COVID-19, RT-PCR, Ct value, Diabetes.

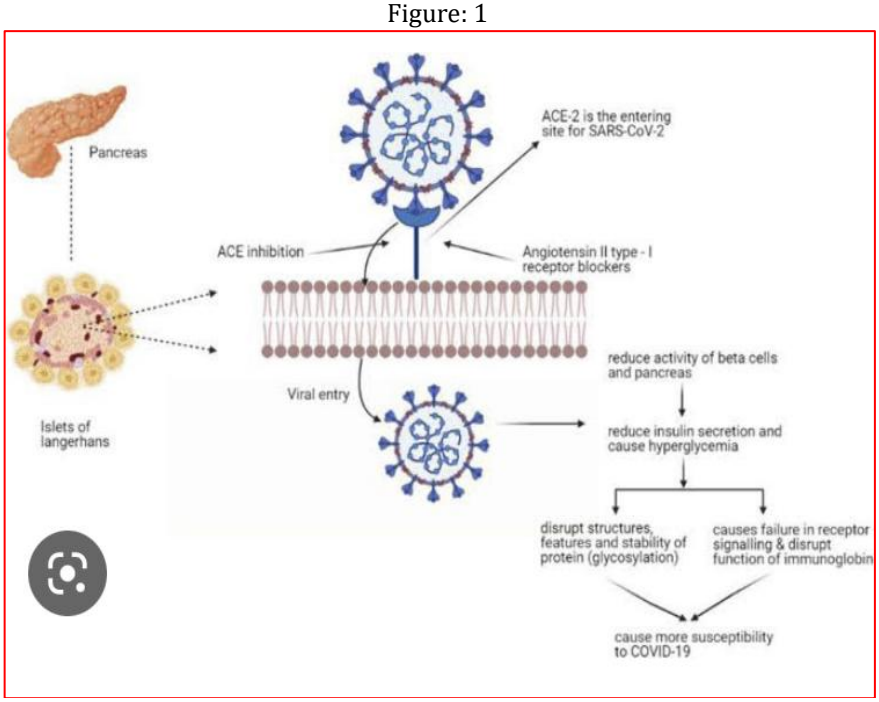
INTRODUCTION

Corona in Latin means crown. The surface of virus having distinct spike and rounded tip provides the appearance of heaving crown, therefore the name "Coronavirus". Coronaviruses are single-stranded (ssRNA) viruses responsible for mild to severe acute infections of respiratory tract. The first case of coronavirus as severe acute respiratory syndrome (SARSE-COV) was reported in 1960. In December, 2019 COVID-19 was first reported in Wuhan, China and soon emerged as a global pandemic [(1)]. In India the first case was reported on 30th January 2020. In July 2021 the World Health Organization (WHO) reported more than 182,319,261 people were infected by COVID-19. There was a significant variation in the rate of infection between developed and low-income countries. The region with highest death rates due to COVID-19 was United States of America (USA), followed by India and other countries. Since COVID-19 has emerged, the burden of diabetes has increased. Diabetic patients were having severe COVID-19 infection [(2)].

A dominant receptor of COVID-19 angiotensin-converting enzyme-2(ACE-2) is expressed in different organs of human including pancreas [(2)]. An intricate relationship between pandemic of coronavirus disease and diabetes was seen. SARS-COV receptor, ACE-2 receptor and related entry factors like Transmembrane Serine Protease-2 (TMPRSS2), Transferrin receptor (TRFC) and Neuroplin-1(NRP1) are expressed in beta cells of pancreas. The spike glycoprotein (s) on the surface of coronavirus locks these receptors and enters inside the host cells. Once entered into the cells it releases its gene which uses ribosomes to make new copies of virus. β-cells which are responsible for insulin production were invariably destroyed by SARS-CoV-2[(3)]. It causes apoptosis of beta cells and attenuates pancreatic insulin secretion, hence leading to high blood sugar [(4)].

Hyperglycaemia disrupts structure and stability of protein and also causes failure in receptor signalling, hence disrupting the function of immunoglobulins which in turn causes more susceptibility to COVID-19. (figure 1). COVID-19 poses a problematic situation for those who were pre-diabetic or having new onset of diabetes post infection and the burden of diabetes was increasing significantly [(1)]. While pre-existing diabetes was associated with severe COVID-19, it is unclear whether COVID-19 is a cause or consequence of diabetes [(3)].

Figure: 1



MATERIAL AND METHODS

Study area and period:

This study was conducted in the Department of Microbiology in tertiary health care centre. Data for this study was retrieved of records.

Study design:

An observational study was done. All patients in the study either had previous history of diabetes or developed high blood sugar following COVID-19 infection. All the available records of COVID-19 patients during April 2021 were included in the study.

Sample size and sampling techniques:

There were 15,831 samples tested during the month of April 2021. According to WHO guideline two samples, one from nasopharynx and other from oropharynx were collected in viral transport media (VTM) and were processed in COVID-19 molecular (RT-PCR) laboratory.

RT-PCR determines whether patient is positive or not by converting RNA collected from patient's sample into DNA and amplifying it. The "cycle threshold" (Ct-value) in RT-PCR is the number of cycles it took to detect the viral load.

In the study using COVIsure kit, Ct values <25, 25-30 and > 30 were categorised as high, moderate and low viral load respectively. Ct value >37 was diagnosed as COVID-19 negative [5]. Predictor of COVID-19: Quant Studio 5[6] (figure 2)

Kit: ICMR approved COVI Sure- Genitix Biotech Asia Pvt. Ltd.

Cycle threshold: 45 cycles

Time line: 1:21 min

Cut off: 37

Target gene: 1. FAM (ORF1ab)- confirmatory (red)

2. ROX (N gene)- screening (blue)

3. VIC (RNAse P)- internal control (green)

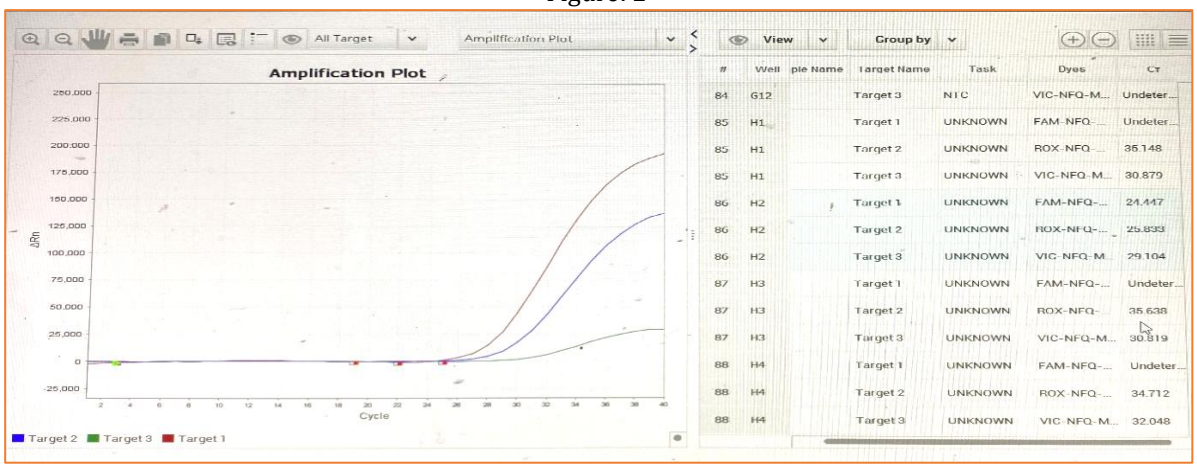
Result interpretation:

ORF GENE	N GENE	Rnase P GENE	RESULT
P	P	P	P
N	N	P	N
N	N	N	I
P	N	P	P
N	P	P	D

P- Positive, N- Negative, I- Invalid, D- Doubtful

Graph showing positive result. (figure 2) [6]

Figure: 2



RESULTS

Total sample received in April 2021 were 15,831 out of which 11,210(71%) were positive and 4,621 (29%) were negative. The male preponderance of 7,623 (68%) and 3,587 (32%) females were seen in positive cases respectively. RT-PCR determines whether patient is positive or not by converting RNA collected from patient's sample into DNA and amplifying it. The "cycle threshold" (Ct value) in RT-PCR is the number of cycles it took to detect the viral load. The study population consists 998 (9%) of diabetics with 679 (68%) males and 319 (32%) females. The outcome variable of this study was prevalence of diabetes mellitus, taken as an event of the study. Our study found high proportion of positive samples with low CT values.

SOCIODEMOGRAPHIC CHARACTERISTICS: (Table 1)

The mean age of patients was 55±10 years. Two- third of patients were in age group of 26-50 years.

Table 1

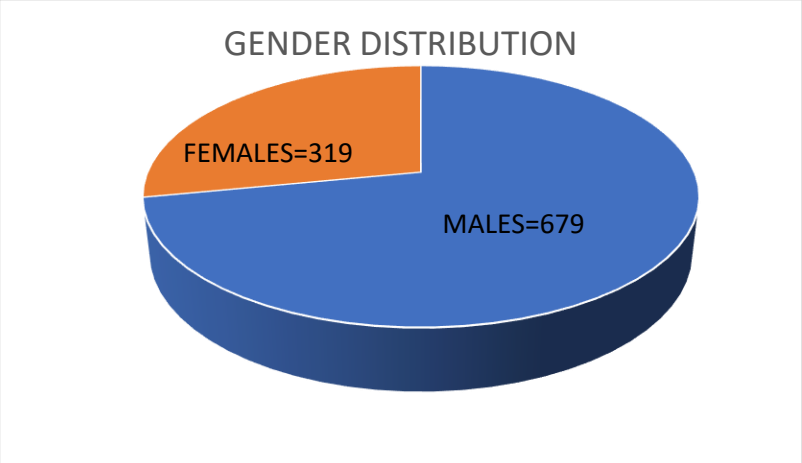
AGE IN YEARS	DIABETICS
55±10	998
<25	279(28%)
26-40	349(35%)
>40	370(37%)

GENDER DISTRIBUTION: (Table 2)

Total diabetic males in the study were 679 (68%) and total female with diabetes were 319 (32%).

Table 2

DIABETIC MALE	DIABETIC FEMALE
679 (68%)	319 (32%)



Diagnosis of diabetes was made as per RSSDI clinical recommendation guidelines 2022 [7] (Table 3).

Table 3

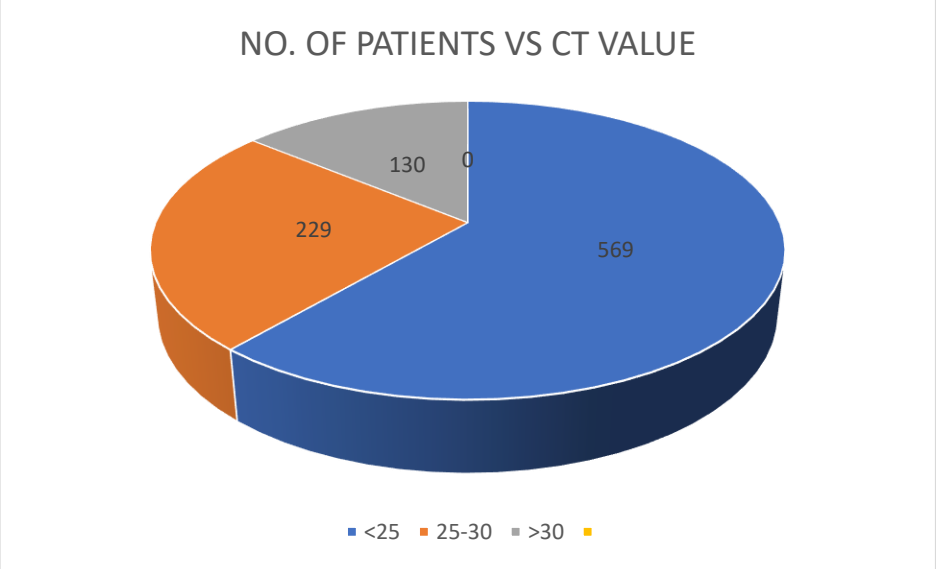
PARAMETER	PREDIABETES/ INTERMEDIATE HYPERGLYCEMIA	DIABETIC
FPG	110-125(IFG)	≥126
2-hPG	140-199(IGT)	≥200
HbA1C	5.7-6.4%	≥6.5%
RPG	-	≥200 + symptoms of diabetes

*IFG- Impaired fasting glucose, *IGT- Impaired glucose tolerance, * RPG- Random plasma glucose

CLINICAL MENIFESTATIONS:
All the RT-PCR positive patients were having clinical features of COVID-19. In the study of 998 diabetics, 102 patients had no previous history of diabetes before COVID-19 infection.

IN RT-PCR [8] (Figure 4)
569(57%) diabetics had Ct value <25.
229(30%) diabetics had Ct value 25-30.
130(13%) diabetics had Ct value >30.
Ct value >37 was considered COVID-19 negative and were not included in the study.

Figure: 4



Covid-19 patients were divided into two groups: A and B (Table 4). Patients in group A had no diabetes and their HbA1C was <5.7mg/dl; patients in group B were diabetic and there HbA1C was ≥6.5. There were 10,210 (91%) in group A and 998 (9%) in group B. 896 (90%) patients in group B were having previous history of diabetes and 102 (10%) patients had no previous history and were newly diagnosed with diabetes.

Table 4

PARAMETERS	GROUP A	GROUP B	
HbA1C	5.4-5.6	6.5-7.1	
No. Of Patients	10212	998	
		Had previous history	Newly diagnosed
		896(90%)	102(10%)

DISCUSSION

Out of total 11,210 covid positive cases 10% were newly diagnosed diabetics in this study. The study also identified that age > 40 years and male preponderance were having low Ct value. Furthermore, the findings in the study were

supported by the study done in India with mean age of 20% of newly diagnosed diabetic patients who were above 50 years of age [8].

This study has its limitations, as the data was retrieved from the records which might have missed essential information that could influence the occurrence of DM. This study could not identify stress hyperglycaemia occurred due to gradual manifestation of DM which might be undiagnosed during the study period. As HbA1C is not a routine investigation therefore, it could not be clearified whether the DM was definitely due to covid-19.

CONCLUSION

High blood sugar was found to reduce immunity and more susceptibility to coronavirus infection. Consequently, new onset hyperglycaemia and insulin resistance have been reported in patients with coronavirus. All patients in the study were either having a previous history of a diabetes or were newly diagnosed of high blood sugar following coronavirus infection. Hence, diabetes is one of the most important predisposing factors of COVID-19. However, it is unclear whether metabolic alterations are transient or permanent. In our study a higher prevalence [9] of diabetes in COVID-19 patients with low Ct value was found.

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