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Detection of New Diabetes Cases During Post-COVID-19-Pandemic Period in a Panchayath of South Kerala

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Abstract

Introduction: COVID-19 and diabetes mellitus have a bidirectional relationship as patients with diabetes are more susceptible to COVID and patients end up with new-onset diabetes after COVID-19 (NODAC). This study aims to estimate the proportion and risk factors of newly detected diabetes, during post-COVID19 pandemic period. ***Methods:*** We did analysis of data generated as part of an intensified screening campaign for non-communicable diseases in a Panchayat area in South Kerala. We included data of 2402 participants, who did not have a diagnosis of diabetes before the COVID-19 pandemic. Binary logistic regression was used to find the factors associated with detection of diabetes in post COVID-19 period. ***Results:*** Among 2402 eligible participants screened, 143 (5.95%) new cases of diabetes were detected. Binary logistic regression identified elderly age (P=.001, OR=1.86 [95%CI;1.28-2.71]), smoking habit (P=.001, OR=3.98[1.74-9.09]) and history of COVID-19 infection (P<.001, OR=3.80[2.52-5.73]) as determinants for detection of diabetes. ***Conclusion:*** Detection of new cases of diabetes during post pandemic period has increased. COVID-19 infection emerged as a significant risk factor for development of diabetes in addition to the traditional factors like age, smoking and family history. Community level screening activities has to be intensified, for strengthening secondary prevention of diabetes mellitus.

Keywords: ***Post- COVID, new onset diabetes, long COVID, primary care, Kerala.***

Introduction

The 21st century has seen a huge increase in the Non communicable diseases (NCD) which has increased the burden over the current healthcare systems in a very disproportionate way. Conventional healthcare systems have been built to address acute and emergent diseases which are relatively easier to manage when compared to NCDs which have a long duration and uses up most of the healthcare resources. In 2021 the International Diabetes Federation estimated that 537 million adults were living with diabetes mellitus with a grim projection of reaching a global projection of 783 million cases by 2045 [1]. Diabetes mellitus is a multifactorial disease determined by interaction of genetic factors and environmental exposures with the new evidences pointing towards an epigenetic origin of the disease, especially that of type 2 diabetes mellitus [2]. The recent COVID-19 pandemic identified diabetes as a major risk factor for severe disease and a reason for both rise in all cause deaths and COVID-19 related deaths. Historically viral infections like coxsackie viruses B1-B6, measles, mumps, rubella, varicella, and influenza have been associated as triggers for new onset diabetes with a recent meta-analysis showing that patients with severe COVID-19 were nearly twice as likely to contract diabetes after COVID-19 compared to non-COVID-19 patients, especially in the first three months after the disease [2,3].

There is robust evidence that there is a long term sequelae to infections with SARS-CoV-2, called long COVID which has been implicated to trigger costly chronic diseases including cardiac, neurological and endocrine disorders like diabetes mellitus [4]. Long COVID is defined as the persistence of COVID-19 infection for more than four weeks after the acute phase of the infection. This particular entity is defined as the persistence of signs and symptoms for more than 12 weeks shares common characteristics with chronic inflammatory conditions like type 2 diabetes mellitus [5]. COVID-19 and diabetes mellitus seems to have a bidirectional relationship [6] with patients with diabetes being more susceptible to COVID and the patients with COVID ending up with new onset diabetes mellitus termed as new-onset diabetes after COVID-19(NODAC) [7]. This has garnered much interest in the current literature with upcoming evidences pointing more towards an association than a causal link. The new onset diabetes mellitus following COVID-19 has been showing a steep rise in cases with the recent literature pointing towards an increased diagnosis of diabetes mellitus which seems to be higher with men, higher in onset within three months of the diagnosis and more prevalent in the population with severe COVID-19. The current study makes an effort to understand the phenomenon of new onset diabetes mellitus in post COVID patients by screening for diabetes in the community and trying to find its association with patients with a history of COVID-19 infection.

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Aim: To estimate the proportion and risk factors of newly detected diabetes, during post-COVID-19 pandemic period among residents of a Panchayath in South Kerala.

Methods

The current study did analysis of data generated as part of an intensified screening campaign for non-communicable diseases in a Panchayath area in South Kerala. A team of health workers including field workers, laboratory technician and ASHA (Accredited Social Health Activist) workers led by the Medical Officer of the Primary Health Centre, conducted screening camps in all 14 wards of the Panchayat with the support of the Local Government. Total Population of the Panchayat was 21154, of which 10845 residents were above 30 years of age. Screening was done for type 2 Diabetes Mellitus, hypertension, overweight and cancer among all residents above 30 years. Trained health workers did anthropometric measurements and estimation of 2 hour post prandial blood sugar (PPBS). Those persons with PPBS value above 140 mg/dl or symptomatic were considered screen positive. This cohort of patients were further assessed by the Medical Officer following the standard diagnostic criteria for diabetes, and further management initiated. The survey was done from January 2023 to February 2023. For the purpose of this study, we have taken data of persons who were screened for diabetes in these camps. Data of patients who were diagnosed with diabetes before the COVID-19 pandemic were excluded. Using a structured data extraction form, basic demographic and clinical details were collected. Permissions from department and informed consent for using unlinked data for research purpose was obtained. Study protocol was approved by the Institutional Ethics Committee.

Statistical analysis: Quantitative variables were summarized as mean (standard deviation) and categorical variables as percentages. We estimated the proportion of new cases of diabetes detected during the pandemic period. Univariable analysis was done using Chi square test. We did multivariable analysis using binary logistic regression. P<0.05 was considered significant.

Results

Out of the total 10845 persons who were above 30 years in the Panchayat, 1392 (12.84%) were known diabetic patients on treatment. Of the 9453 persons who were eligible for screening for diabetes, 2406 (25.45%) underwent screening. Data of four participants were incomplete. Hence, the sample size for analysis was 2402. Mean (SD) age of the participants was 52.64 (14.27). Range for age was between 30-98 years. Females were more in the study group, whose frequency was 1775 (73.9%). There were 627 (26.1%) males in the group.

Among those screened 323 (13.45%) persons had a history of confirmed COVID-19 infection, whereas 390 (16.24%) reported history of viral fever similar to COVID 19, though not confirmed by laboratory test. Thus 713 (29.68%) persons among 2402 screened were considered as having history of probable or confirmed COVID-19 infection.

From this screening done in the post COVID-19 period among 2402 eligible persons, 270 (11.2%) persons had Post Prandial Blood sugar value above 140 mg/dl. Medical officer of the team assessed all screen positive patients. On applying defined diagnostic criteria, 143 (5.95%) new cases of diabetes were detected. Out of these newly detected cases, 89 (62.24%) were among those with history of probable or confirmed COVID-19 infection. This accounted for 3.71% of the total 2402 persons screened. Socio-demographic and clinical characteristics of the participants is given in table 1 and 2.

On univariable analysis to find out the factors associated with detection of new cases of diabetes; elderly age, male gender, smoking habit, family history of diabetes and history of confirmed or probable COVID-19 infection were found to be statistically significant. Table 3 shows factors associated with new onset diabetes among participants. Binary logistic regression identified elderly age (P=.001, OR=1.86 [95%CI;1.28-2.71]), smoking habit (P=.001, OR=3.98[1.74-9.09]) and history of COVID-19 infection (P<.001, OR=3.80[2.52-5.73]) as determinants for detection of diabetes during post COVID-19 period. Table 4 shows results of multivariable analysis.

Table 1: Demographic and Clinical characteristics of patients (N=2402)

Characteristic	Categories	Number	Percentage
Age Group	30-45	716	29.8
	45-60	889	37
	60-75	641	26.7
	>75	156	6.5
Gender	Male	627	26.1
	Female	1775	73.9
BMI (Kg/m^2)	<18.5	123	5.1
	18.5-22.9	860	35.8
	23-24.9	528	22
	≥ 25	894	37.2
Smoking habit	Present	42	1.7
	Absent	2360	98.3
Regular exercise	Present	307	12.67
	Absent	2095	87.33
Family history of diabetes	Present	257	10.7
	Absent	2145	89.3
Hypertension	Present	634	26.4
	Absent	1768	73.6
New onset Diabetes	Present	143	5.95
	Absent	2259	94.05
History of confirmed COVID-19	Present	323	13.45

	Absent	2079	86.55
History of probable COVID-19	Present	390	16.24
	Absent	2012	83.76

Table 2: Summary of quantitative clinical and laboratory parameters

Parameter	Mean	Standard deviation
Height (Cms)	151.17	24.59
Weight (Kg)	60.38	25.35
Body Mass Index (Kg/m^2)	24.88	9.74
Systolic BP (mmHg)	129.91	23.20
Diastolic BP (mmHg)	75.63	21.06
PPBS (mg/dl)	97.56	42.17

Table 3: Factors associated with newly diagnosed diabetes among participants.

Factors	Categories	Newly diagnosed diabetes [143(6%)] N (%)	Non-Diabetic [2259 (94%)] N (%)	*P* value
Age group	≥60	66 (8.1)	732 (91.9)	0.001*
	<60	77 (4.7)	1527 (95.3)	
Gender	Male	49 (7.8)	577 (92.2)	0.021*
	Female	94 (5.3)	1682 (94.7)	
BMI	Overweight	94 (6.6)	1317 (93.3)	0.079
	Normal/under-weight	49 (4.9)	942 (95.1)	
Smoking habit	Present	14 (33.3)	28 (66.7)	<0.001*
	Absent	129 (5.5)	2231 (94.5)	
Regular exercise	Present	14 (4.18)	321 (95.82)	0.139
	Absent	129 (6.24)	1938 (93.76)	
Family history of diabetes	Present	29 (11.3)	228 (88.7)	<0.001*
	Absent	114 (5.2)	2031 (94.8)	
Hypertension	Present	33 (5.2)	601(94.8)	0.353
	Absent	110 (6.2)	1658 (93.8)	
History of confirmed COVID-19	Present	52 (16.1)	271 (83.9%)	<0.001*
	Absent	91 (4.4)	1988 (95.6)	
History of probable COVID-19	Present	54 (13.8)	336 (86.2)	<0.001*
	Absent	89 (4.4)	1923 (95.6)	

**Significant P value (chi square test)*

Table 4: Determinants of newly detected diabetes during post-COVID-19 pandemic period

Determinants	Adjusted odds ratio	95% CI for OR	*P* value
Age>60 years	1.86	1.28-2.71	0.001*
Male gender	1.04	0.68-1.60	0.844
Smoking habit	3.98	1.74-9.09	0.001*
Family history of diabetes	1.54	0.94-2.52	0.087
History of Confirmed COVD-19	3.80	2.52-5.73	<0.001*
History of probable COVD-19	3.23	2.18-4.78	<0.001*

**Significant at P< .05 (Binary logistic regression)*

Discussion

Preexisting diabetes mellitus in COVID-19 has been associated with severe morbidity and mortality with diabetics more prone to ICU admissions with the mortality ranging from 22% to 31% of all COVID-19 patients [8]. Pre-existing diabetes mellitus seems to be a pointer towards increase in severity of disease with obesity being the most important independent risk factor implicated with COVID-19 hospitalization and risk of critical illness. Since obesity is often associated with metabolic syndrome which includes diabetes mellitus, hypertension as other measurable components, the association of severe COVID can be traced back to dysglycaemia as a major factor for severe illness. Viral infections especially HHV 8 and SARS-CoV have been associated with altered glucose metabolism and insulin resistance [9] resulting in acute hyperglycaemia as a normal reactive response with an increased risk for developing type 1 and 2 Diabetes Mellitus [10]. The current evidences point towards both COVID-19 patients with pre-existing diabetes and new-onset diabetes ending up with severe complications like ARDS, acute renal failure, shock, or hypoalbuminemia with the newly diagnosed, post-COVID-19 diabetic patients required admission, intermittent mandatory ventilator assistance,[11] and demonstrated higher risk of all-cause mortality than those COVID-19 who are normoglycaemic or present with transient hyperglycaemia.

There is robust evidence on the mechanism by which COVID-19 causes altered glycaemic status as SARS-CoV-2 infects pancreatic β-cells via the angiotension-converting enzyme 2 receptor and causes programmed cell death [12]. This mechanism has been implicated in the development of both type1 and 2 diabetes mellitus as severe COVID-19 infection can activate the endoplasmic reticulum stress response in β-cells of the pancreas resulting in apoptosis of these cells. Type 1 diabetes mellitus has been postulated as an antibody mediated disease with production of anti-β-cell autoantibodies postulated as a possible mechanism of altered glucose metabolism [13]. Insulin resistance and impaired insulin secretion have been described in individuals without diabetes recovering from SARS-CoV-2 infections with the upregulated cytokines and TNF-α implicated to induce beta cell dysfunction and insulin resistance resulting in new onset diabetes mellitus post COVID [14]. Further stress of the disease and the fear about the complications of the disease especially during the early phase of the pandemic could have triggered a progress from a prediabetes state to diabetic state. In short term the stress response of hyperglycaemia during acute COVID-19 illness would require treatment but the increase in the newly diagnosed diabetes mellitus in long COVID has provided a new twist in the line of management of diabetes. Long COVID and diabetes mellitus also seem to have a bidirectional association as patients with both type 1 and 2 diabetes mellitus are more likely to develop long Covid-19 syndrome and long Covid-19 syndrome being associated with new onset diabetes both type 1 and 2 [15]. Long COVID has been implicated to exacerbate microvascular dysfunction especially in patients with diabetes mellitus resulting in symptoms like fatigue, shortness of breath, neurocognitive deficiencies, neurological manifestations, and cardiovascular sequelae [16].

The association between COVID and new onset DM up to 12 weeks post infection has been documented with increased use of prescribed insulin within 3 months of COVID-19 diagnosis, though this can be implicated to hyperglycaemia due to a systemic inflammatory response [8]. There is a clear association between new onset diabetes mellitus, insulin resistance and β-cell exhaustion post systemic inflammatory syndromes, this association seems to be more coherent with post COVID syndrome as the evidences are accumulating [10]. There is enough evidence to support the increased severity and mortality in severe COVID with pre-existing diabetes a meta-analytic study showed that new onset diabetes mellitus due to COVID-19 had the highest mortality rate compared to COVID-19 cases who had a history of diabetes mellitus as well as non-diabetic COVID-19 cases [17]. Further new onset diabetes in patients with COVID-19 had the highest adverse events like ICU admission, intubation, severe COVID and long COVID compared to patients with a history of diabetes or non-diabetics with COVID-19. Though there is conflicting evidence on the gender involvement of new onset diabetes in COVID, the evidence on new onset diabetes in hospitalized patients is very evident. Many factors including increased testing, prediabetes, undiagnosed diabetes and an increased access to healthcare services have implicated a detection bias [15] in the increase in the new onset diabetes mellitus post COVID but the same cannot be taken as an explanation in a setting where the health screening for NCDs has been robust in the pre COVID time. Further the treatment of COVID with glucocorticoids may result in hyperglycaemia which could unmask the diabetes but evidence both supporting and against this hypothesis are compelling at the present time [18]. The more relevant question is whether the risk of developing DM in COVID-19 patients is underestimated as a consequence of the presence of undiagnosed or asymptomatic SARS-CoV-2 infections which have not been documented as positive COVID cases [19]. The new-onset DM COVID India study reported patients with new-onset DM during the COVID-19 pandemic had higher glycaemic indices, HbA1c, and CRP levels than new onset DM cases before the pandemic, thus illustrating the effects of SARS-CoV-2 on glucose metabolism [20]. A systematic review and meta-analysis of 40 million participants resulted in the diagnosis of 200000 cases of diabetes with a relative risk of 1.62 in patients affected with COVID than with the non- COVID affected population [4]. Subgroup analysis of these patients suggested the risk of developing diabetes was also increased regardless of age, gender, type of diabetes, follow-up time, or level of COVID-19 severity, although undifferentiated diabetes did not have a significant relative risk. These results remained significant even after accounting for the possibility of unmeasured confounding factors.

Conclusion

Detection of new cases of diabetes during post pandemic period has increased. COVID-19 infection emerged as a significant risk factor for development of diabetes in addition to the conventional factors like age, smoking and family history. Community level screening activities has to be intensified, for strengthening secondary prevention of diabetes mellitus.

Declarations

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Nil

Conflict of Interest

The authors have no conflicts of interest to declare

All authors accept and agree with the UN's Declaration of Human Rights

Authorship Criteria

Conception and design of the work: SS, KK and CS; Acquisition of data: SS; Analysis, and interpretation of data: SS, KK and CS; Drafting the work and revising it critically for important intellectual content: SS, KK and CS; Final approval of the version to be published: SS, KK and CS.

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