ORIGINAL ARTICLE

Higher Pre-infection HbA1c level in diabetic individuals as a marker of severity of COVID-19

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ABSTRACT

Objective: Diabetes is one of the major risk factor responsible for poor outcomes of corona virus disease (COVID-19). Association between pre infection HbA1c level in diabetic individuals and severity of COVID-19 based on the requirement for hospitalization, will be helpful in controlling and defeating COVID-19.

Methods: This was cross sectional study carried out in Khalifa Gul Nawaz, (KGN) hospital, Bannu, Pakistan. 160 diabetic individuals with COVID-19 were registered in this study. All the registered subjects were divided into Hospitalized COVID-19 Daibetic, (HCD group) and Non Hospitalized COVID-19 Daibetic (NHCD groups). In HCD group 32 diabetic individual with a deadly disease and severe complications of COVID-19 were considered while in NHCD group 128 diabetic individuals with mild complications of COVID-19 were present. Data analysis was performed by using IBM SPSS version 26.

Results: Mean age of HCD group was significantly higher (p< 0.05) as compared to NHCD group. Among the different co-morbidities hypertension and chronic kidney diseases were significantly associated with hospitalization of COVID-19 individuals. But, after adjusting for several preexisting clinical factors, HbA1c ≥9% was the only predictor linked with a substantially higher risk of hospitalization in a multivariate analysis.

Conclusion: Higher pre infection levels of HbA1c are clear markers for the hospitalization of COVID-19. Using HbA1c levels ≥ 9, we can highlight the high risk population and can successfully control and defeat COVID-19.

Key words: Corona virus infectious disease 2019, Hospitalization, HbA1c, diabetes.

INTRODUCTION

Corona viruses are enveloped, single-stranded positive-sense RNA viruses recognized as causative agent of human pulmonary infections.[1] Generally, corona virus cause mild type of upper respiratory infection in individuals having strong immune system.[2] In Pakistan, COVID-19 pandemic appeared in Karachi City and rapidly spread throughout the country. Corona virus rate of mortality is projected to be 2.3 per 100 000 Pakistani residents.[3]

Diabetes is a self-sufficient risk factor for severity of COVID-19. Highly complex and bidirectional association is present between COVID-19 and diabetes. On the one hand, people with diabetes typically have additional co-morbidities or parallel variables that might exacerbate the severity of COVID-19; on the other hand, treating COVID-19 with steroids can have a significant negative influence on diabetes, resulting in increased hyperglycemia via elevated insulin resistance and decreased cell secretory function. In consequence, increasing hyperglycemia may have a negative impact on COVID-19's progress. Diabetes has been linked to COVID19 findings that were deficient; however, the relationship between COVID19 results with pre-infection glycemic control is still unclear. High glycemic levels after hospital admission have also been linked to COVID19's deplorable results. A study done in China on 128 Covid-19 individuals, the HbA1c level was comparable across 14 patients who were admitted in hospital in comparison to those who were not admitted.[4] COVID-19 severity and mortality have been linked in numerous studies to old age and co-morbid conditions such as hypertension, diabetes, cerebro-vascular diseases and cardiovascular problems.[5,6] However, some other studies do not associate higher HbA1c with severity of disease.[7] The level of glucose on admission was the best predictor of radiographic indications of acute respiratory distress syndrome in a retrospective analysis of 201 diabetic Covid19 patients.[8] Despite this mounting data, the relationship between preinfection glucose management and COVID19 severity remains unclear in our setting in Bannu, Pakistan. To answer this issue, we looked at the relationship between pre-infection HbA1c levels and severity of COVID19 as measured by the requirement for hospitalization in 160 diabetic patients at Khalifa Gul Nawaz Hospital (KGN) in Bannu, Pakistan.

MATERIALS AND METHODS

This was cross sectional study carried out in KGN Hospital, Bannu, Pakistan in time period of one year, April 2020 to March 2021. During this time period 160 diabetic individuals with COVID-19, who came for consultation to OPDS or were admitted in medicine ward of KGN hospital were registered. Only those COVID-19 patients were accounted who were having at least one HbA1c test prior to the disease. Information's like gender, age, socio-economic conditions, residency, height, weight, body mass index, smoking status, prior records of HbA1c,

hypertension, previous ischemic heart disease diagnosis, dementia, and chronic lung disease was recorded. COVID-19 was confirmed by nasopharyngeal RT-PCR test.[9] Diagnosis of diabetes was done using the 2019 WHO diabetes diagnostic criteria.[10] Total of 160 diabetic individuals with COVID-19 were divided in to two groups, Hospitalized COVID-19 Daibetic, HCD group and Non Hospitalized COVID-19 Daibetic, NHCD groups. In HCD group 32 diabetic individual with deadly disease and severe complications of COVID-19 were considered while in NHCD group 128 diabetic individuals with mild complications of COVID-19 were present. The criteria for severity and hospitalization were if the patients have <94% SpO$_2$ at sea level on room air, >30 breaths/min respiration rate, less than 300 mm Hg PaO$_2$/FiO$_2$ or having less than 50% lung infiltrates. Clinical deterioration may occur quickly in these people.

All statistical analysis was performed using IBM, SPSS Statistics version 26. Initial analysis compared demographic characteristics between the HCD and NHCD groups. Categorical variables were articulated as frequency and percentages and they were compared by employing chi-square test. For continuous variables, mean and standard deviation were computed and their comparison was done by employing student t-test. Less than 0.05 p value was measured as significant statistically. In beginning, risk estimates were evaluated by stratified analysis. Stratification of HbA1c was done as <7%, 7%-8.0%, 8.1%-8.9% and ≥9%. Consequently, For the estimation of odds ratios (OR) and 95% CI, multivariate logistic regression was used for independent association between the demographics and clinical features like HbA1c ≥ 9%, age, hypertension, pulmonary disease, chronic kidney disease and severity of Covid-19 based on the requirement for hospitalization.

RESULTS

Age, BMI and HbA1c parameters of of HDC group was compared with NHDC group as shown in Table 1. The mean ±SD value of age of HDC group was 72.25±9.18 years as compared to 60.94±8.69 years of NHDC group (p<0.05). Similarly HbA1c of HDC group was significantly higher as compared to NHDC group, 7.92±1.05 vs 6.87±0.62 (p<0.001)

Table 1: Mean ±SD values comparison of Age, BMI and HbA1c of HDC and NHDC groups

Variables	HDC Group Mean ±SD	NHDC Group Mean ±SD	p-value
Age (Years)	72.25±9.18	60.94±8.69	0.02*
BMI (Kg/m^2)	30.94±4.17	29.59±3.18	0.06
HbA1c (%)	7.92±1.05	6.87±0.62	<0.001*

Table 2: Clinical co-morbidities comparison of HDC and NHDC groups

Variables	HDC Group n=32	NHDC Group n=128	Total n=160	p-value
Hypertension	20 (62.5%)	54 (42.2%)	74 (46.3%)	0.04*
Hyperlipidemia	17(53.1%)	50 (39.1%)	67 (41.9%)	0.165
Pulmonary disease	23 (71.9%)	55 (43.0%)	78 (48.8%)	0.002*
Chronic kidney disease	23 (71.9%)	60 (46.9%)	83 (51.9%)	0.05*
Dementia	05(15.6%)	32 (25.0%)	37 (23.1%)	0.35

Table 2 shows that among different co-morbidities the incidence of hypertension, pulmonary diseases and chronic kidney diseases were significantly higher in HDC group as compared to NHDC group.

In our study, hospitalization risk was increased in patients with HbA1c ≥ 9 %, p < 0.005, adjusted OR 5.039; with 95% CI 3.351–7.577; p < 0.001 as shown in Table 3. However, after adjusting for several preexisting clinical factors, HbA1c ≥9% was the only predictor in our study linked with a substantially higher risk of hospitalization in a multivariate analysis.

Table 3: HbA1c and odd ratio for hospitalization in HCD and NHDC groups

Variables	HDC Group n=32	NHDC Group n=128	Total n=160	OR(95% CI) for being hospitalized	p-value
<7	7 (21.9%)	97 (75.8%)	104 (65.0%)	1.00	
7-8	10(31.3%)	19 (14.8%)	29 (18.1%)	2.05 (1.09-3.86)	0.04*
8.1-8.9	8 (25.0%)	8 (6.3%)	16 (10.0%)	3.01 (1.63-5.53)	0.004*
≥9	7 (21.9%)	4 (3.1%)	11 (6.90%)	3.79 (2.14-6.72)	0.001*

Table 4: Multivariate logistic regression analysis for hospitalization in patients with diabetes and Covid-19

Variables	Adjusted Odd Ratio	p-value
Age	1.04 (0.87-1.09)	0.08
BMI	0.64 (0.28-1.49)	0.304
HbA1c ≥9	5.04 (3.35-7.58)	<0.001*
Hypertension	1.13 (0.95-1.33)	0.17
Pulmonary Disease	1.08 (0.92-1.28)	0.35
Chronic Kidney diseases	1.00 (0.84-1.18)	1.2

DISCUSSION

Pre-infection glycemic control data help us to recognize pre infection HbA1c as a apparent interpreter for severity of Covid-19. Other demographic and clinical features having significant association with the rate of hospitalization includes age above 60 years, hypertension, pulmonary diseases and chronic kidney diseases. However, after adjusting for several preexisting clinical factors, HbA1c ≥9% was the only predictor in our study linked with a substantially higher risk of hospitalization in a multivariate analysis. Information associating hypertension, pulmonary and kidney diseases, stroke and cancer with Covid-19 must be cautiously interpreted as patients may be of old age with smoking history or have any additional medical situation which suggests that these characteristics, instead of the co-morbidity itself, may be linked to poor COVID-19 results.[11-13]

In our study, pre infection HbA1c remained a strong biomarker for hospitalization due to Covid-19. The risk of

severity increases three times as HbA1c > 9.[14] Diabetes not only impairs the epithelial function of pulmonary cilia, increases vascular system permeability, damages alveolar epithelial cells, and results in alveolar collapse, but also contributes to aberrant immune system performance.[15-18] Diabetes and COVID-19 might have a synergistic effect on the immunological and respiratory systems.[19] Furthermore, patients with diabetes have more co-morbidities, resulting in greater target organ impairment; this, in combination with COVID-19, results in increased severe inflammation, increased coagulation, even worse oxygenation, and eventually increased mortality.[20-21] A relationship between hyperglycemia and illness severity during hospitalisation has previously been shown in a number of studies spanning a variety of diseases. However, to our knowledge, this is the first research in Bannu, KPK, Pakistan, to establish pre-infection glycemic control as a predictor for severity of Covid-19.

CONCLUSION

Our study identifies pre-infection glycogenic control as a primary risk factor for COVID-19 severity and detection of high risk population may be the only solution to effectively defeat COVID-19. Particular consideration should be paid to the patients with diabetes having HbA1c ≥ 9 before COVID-19. This will not only help the diabetic individuals from being hospitalized due to severity of disease but also reduce the economic and social load of the community. Further studies in our setup are required to investigate whether pre infectionHbA1c predicts COVID-19 mortality, need for ICU stay and need for artificial ventilation.

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