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Original research article

DIVERSITY IN SEVERITY OF HIGH-RESOLUTION COMPUTED TOMOGRAPHY FINDINGS OF COVID-19 PATIENTS WITH DIABETES

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Abstract: *COVID-19 patients with diabetes mellitus present a unique subset, often experiencing more severe disease due to their compromised immune status and chronic inflammatory state.* ***Objectives:*** *The current study aimed to see the diversity in HRCT findings in COVID-19 patients with diabetes, aiming to elucidate the extent and nature of pulmonary involvement in this high-risk group.* ***Methods:*** *This retrospective study included 134 diabetic patients, and the data was collected from the patient records unit. BMI was categorized according to World Health Organization criteria, and glycemic control was evaluated based on hemoglobin A1c (HbA1c) levels. Additionally, waist circumference, hip circumference, and waist-hip ratio were measured. Lipid profile parameters were also analyzed, including serum cholesterol, low-density lipoprotein (LDL), triglycerides, and high-density lipoprotein (HDL). The duration of diabetes was categorized into two groups: <10 years and ≥10 years. Finally, the diversity in the patient characteristics was seen using the HRCT findings.* ***Results:*** *Most of the study patients were female (66.41%). The mean BMI was 24.37±4.11. BMI categories were as follows: underweight (BMI <18.5) in 8.02% of patients, healthy weight (BMI 18.5-24.9) in 32.83% of patients, overweight (BMI 25-29.9) in 26.86% of patients, and obese (BMI ≥30) in 32.08% patients. The mean HbA1c level was 9.02±1.89. Glycemic control was categorized as good in 43 patients (32.08%) and poor in 91 patients (67.91%). The mean waist circumference was 82.88 ± 12.41 cm, the hip circumference was 92.0 ± 10.71 cm, and the waist-hip ratio was 0.91 ± 0.13. The mean serum lipid levels were as follows: cholesterol 181.0 ± 7.70 mg/dL, LDL 145.50 ± 21.56 mg/dL, triglycerides 195.75 ± 18.10 mg/dL, and HDL 39.51 ± 5.76 mg/dL. Patients were categorized by the duration of diabetes diagnosis: <10 years in 110 patients (36.7%) and ≥10 years in 190 patients (63.3%).* ***Conclusion:*** *The study highlights the critical need for personalized clinical management of COVID-19 patients with diabetes. By understanding the specific HRCT patterns and underlying pathophysiological mechanisms, healthcare providers can improve the prognosis and outcomes for this disease group.*

Keywords: Diabetes Mellitus, COVID-19, HRCT (High-Resolution Computed Tomography), Lipid Metabolism Disorders, Pulmonary Involvement.

Introduction

The COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has presented significant challenges globally, affecting millions of people and overwhelming healthcare systems (1). One of the notable aspects of the disease is its varied clinical manifestations, ranging from asymptomatic cases to severe pneumonia and acute respiratory distress syndrome (ARDS), which can be fatal. COVID-19 primarily affects the respiratory system, with the lungs being the most frequently and severely impacted organ (2, 3).

High-resolution computed tomography (HRCT) has emerged as a crucial diagnostic tool in evaluating COVID-19, particularly in assessing lung involvement and guiding clinical management (4). HRCT is a non-invasive imaging technique that offers high-resolution images of the lung parenchyma, allowing for the detection of subtle and early changes that may not be visible on standard chest X-rays. Typical HRCT findings in COVID-19 include ground-glass opacities (GGO), consolidations, interlobular septal thickening, and reticular patterns, often with a peripheral and bilateral distribution (5, 6).

Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, is one of the most common comorbid conditions associated with increased morbidity and mortality in COVID-19 patients. Diabetic patients often have compromised immune responses and a predisposition to infections, which can exacerbate the severity of viral diseases, including COVID-19 (7). The interplay between diabetes and COVID-19 can lead to more severe clinical outcomes, necessitating a comprehensive understanding of the imaging findings in this subgroup of patients. Diabetes mellitus, particularly when poorly controlled, can lead to various complications, including increased susceptibility to infections and inflammatory conditions (8, 9). In the context of respiratory infections, diabetic patients are known to experience more severe disease courses, with higher rates of hospitalization, intensive care unit (ICU) admission, and mortality. The hyperglycemic environment in diabetic patients promotes immune dysfunction, chronic inflammation, and endothelial dysfunction, all of which can contribute to more severe lung involvement in COVID-19 (10).

This study aimed to explore the diversity in HRCT findings among COVID-19 patients with diabetes to better understand the extent and nature of pulmonary involvement in this high-risk population. HRCT imaging is invaluable for detecting and characterizing lung abnormalities, providing detailed insights into the types and distribution of lesions, which can vary significantly among individuals.

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These imaging features are critical for clinical decision-making and can influence treatment strategies and prognostic assessments.

Methodology

Ethical Considerations

The study adhered to the principles of the Declaration of Helsinki and received approval from the institutional review board (IRB), Quaid-e-Azam Medical College, with the approval number 2326/DME/QAMC/Bahawalpur (approved on 06-07-2021). Informed consent was obtained from all participants, ensuring they understood the study's purpose, procedures, and potential risks.

Study Design

This study employs a cross-sectional design to investigate the diversity in severity of high-resolution computed tomography (HRCT) findings in COVID-19 diabetic patients. The study involved collecting and analyzing data from a defined cohort of patients at a single point in time to identify patterns and correlations between diabetes and the severity of lung involvement as depicted on HRCT.

The study population included adult patients aged 10 years and older who had a confirmed diagnosis of COVID-19 via PCR testing. Only those with a documented history of diabetes mellitus, either type 1 or type 2, were considered eligible. Additionally, all participants underwent a high-resolution computed tomography (HRCT) scan during their COVID-19 infection. Patients were excluded if they lacked a confirmed COVID-19 diagnosis, did not have a documented history of diabetes, or if HRCT imaging data were unavailable or of poor quality, rendering accurate assessment impossible.

To ensure the study's findings would be statistically significant, a power analysis was performed to determine the appropriate sample size. This calculation considered the expected prevalence of specific HRCT findings, the desired statistical power (typically set at 80%), and the significance level (typically set at 0.05).

Data was collected by extracting relevant information from patient medical records and imaging databases at participating healthcare facilities. The data collected included demographic information such as age, sex, and race/ethnicity, as well as clinical data including the type and duration of diabetes, glycemic control as measured by HbA1c levels, body mass index (BMI), and the presence of other comorbidities like hypertension and cardiovascular disease. Smoking status was also recorded. For COVID-19-related data, the date of diagnosis, symptom severity, treatments received (such as antivirals and steroids), ICU admission, need for mechanical ventilation, and clinical outcomes (recovery, ongoing symptoms, or death) were documented. HRCT data included the scan date and a detailed description of findings, particularly the presence and extent of ground-glass opacities (GGO), consolidations, interlobular septal thickening, and reticular patterns.

The HRCT images were evaluated by a panel of experienced radiologists blinded to the patients' clinical details. The radiologists assessed the images for specific features, including the extent and distribution of ground-glass opacities, consolidations, interlobular septal thickening, and reticular patterns. Additional findings were also noted, such as bronchiectasis, nodules, pleural effusion, and lymphadenopathy. A standardized scoring system was used to quantify the extent of lung involvement. Each lung lobe was evaluated for the percentage of participation by GGO and consolidation, with scores assigned as follows: 0 for no involvement, 1 for less than 25% involvement, 2 for 25-50% involvement, 3 for 51-75% involvement, and 4 for more than 75% involvement. The total lung severity score was calculated by summing the scores of all lobes.

Descriptive statistics summarized the baseline characteristics of the study population and HRCT findings. Continuous variables were presented as means ± standard deviations or medians (interquartile ranges), and categorical variables as frequencies and percentages. Comparative analyses assessed differences in HRCT findings between subgroups (e.g., based on glycemic control, presence of comorbidities, and clinical outcomes). Chi-square tests or Fisher's exact tests were used for categorical variables, and t-tests or Mann-Whitney U tests for continuous variables, as appropriate.

Results

This study included 134, with most female patients (66.41%). Furthermore, Mean body mass index was 24.37 ± 4.11, respectively. Also, body mass index was categorized as per World Health Organization criteria: underweight 11 (8.02%), healthy weight 44 (32.83%), overweight 36 (26.86%), and obese 43 (32.08%). Moreover, mean hemoglobin A1c (HbA1c) was 9.02 ± 1.89 and also categorized as good glycemic control 43 (32.08%) and poor glycemic control 91 (67.91%). Furthermore, the mean circumference of the waist (cm), the circumference of the hip (cm), and the waist-hip circumference ratio (cm) were 82.88 ± 12.41, 92.0 ± 10.71, and 0.91 ± 0.13, respectively. Additionally, the mean lipid profile of the patients was segregated as serum cholesterol, serum low-density lipoprotein (LDL), serum triglycerides, and serum HDL. In addition, the mean serum cholesterol, serum LDL, serum triglycerides, and serum HDL were 181.0 ± 7.70, 145.50 ± 21.56, 195.75 ± 18.10, and 39.51 ± 5.76, respectively. Moreover, the duration of diagnosis of diabetes mellitus is categorized as <10 years 110 (36.7%) and ≥10 (years) 190 (63.3%), as shown in Table 1.

Table 1: Demographical characteristics and general clinical features of study subjects (n-134).

Characteristics		**Frequency (*n*)**	**Percentage (%)**
Gender	Male	45	33.58
	Female	89	66.41
Age (Years)	10-25	18	13.43
	26-40	37	27.61
	41-55	31	23.13
	56-70	36	26.86
	>70	12	8.95

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Symptoms	Shortness of breath	84	62.68
	Loss of taste or smell	69	51.49
	Cough	54	40.29
	Fever	121	90.29
Comorbidities	Diabetes	134	100.00
	Hypertension	54	40.29
	Ischemic heart disease	32	23.88
	Pancreatitis	29	21.64
	Liver disease	36	26.86
	Kidney diseases	48	35.82

Additionally, Table 2 shows the bifurcation of demographic and clinical characteristics concerning poor and reasonable glycemic control. The mean difference of age (years) versus poor and good glycemic control. No statistical difference was observed (p-0.92) in the mean age of 49.67 ± 8.70 and poor glycemic control at 49.79 ± 8.90. Also, a statistically significant difference (p-0.04) was observed in sex versus excellent and poor glycemic control. Also, the mean difference between the circumference of the hip, the circumference of the waist, and the waist-hip circumference ratio versus excellent and poor glycemic control. Only a statistically significant (p-0.01) difference was observed in the mean difference of hip circumference versus excellent and poor glycemic control.

Table 2: Diabetic profile of study subjects.

Characteristics		***n*/%**
Body mass index categories (kg/m2)	Underweight (≤18.5)	11 (8.02)
	Healthy weight (18.5-24.9)	44 (32.83)
	Overweight (25.0-29.9)	36 (26.86)
	Obese (30.0-34.9)	43 (32.08)
Body mass index (kg/m2) (Mean ± SD)		24.37 ± 4.11
Haemoglobin A1c (HbA1c) categories	Good glycaemic control	43 (32.08)
	Poor glycaemic control	91 (67.91)
Haemoglobin A1c (HbA1c) (Mean ± SD)		9.02 ± 1.89
Waist circumference (cm) (Mean ± SD)		82.88 ± 12.41
Hip circumference (cm) (Mean ± SD)		92.0 ± 10.71
Waist hip circumference ratio (WHR) (Mean ± SD)		0.91 ± 0.13
Serum cholesterol (Mean ± SD)		181.0 ± 7.70
Serum triglycerides (Mean ± SD)		195.75 ± 18.10
Serum low-density lipoprotein (LDL) (Mean ± SD)		145.50 ± 21.56
Serum high-density lipoprotein (HDL) (Mean ± SD)		39.51 ± 5.76
Duration of diabetes mellitus (years)	<10 (years)	32 (23.88)
	≥10 (years)	102 (76.11)

Additionally, the mean difference of serum LDL (p-0.001) and serum HDL (p-0.001) versus good and poor glycemic control. The mean difference between body mass index versus reasonable glycemic control is 21.81 ± 3.15, and poor glycemic control is 25.22 ± 4.05 (Table 3).

Table 3: Mean difference, bifurcation, and Pearson correlation of body mass index versus good and poor glycaemic control (HbA1c).

Variable categories	**Good glycaemic control *n*-43 (32.08%)**	**Poor glycaemic control *n*-91 (67.91%)**	***p*-value**
Body mass index			
Mean ± SD*	21.81 ± 3.15	25.22 ± 4.05	0.0011
Body mass index Categorical			
Underweight (*n*-11) ≤18.5	06 (13.95)	5 (8.0)	0.001
Healthy weight (*n*-44) 18.5-29	22 (51.16)	22 (32.4)	
Overweight (*n*-36) 25.0-29.9	06 (13.95)	30 (43.1)	
Obese (*n*-43) 30.0-34.9	09 (4.0)	34 (79.06)	
Body mass index versus HbA1c Pearson correlation	r=0.41 (medium positive correlation)		0.001

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Based on the CT severity grading, out of all participants, 41 cases had mild (30.59%), 74 cases had moderate (55.02%), and 19 cases had severe (14.17%) lung involvement on HRCT. A significant difference was observed in the mean HbA1c levels of the patients with different CT severity grades (P < 0.001). Table 4 shows that mean HbA1c was found to be higher in severe and moderate patients as compared to mild grade patient

Table 4: CT Severity and HbA1c.

HRCT severity grade		**HbA1c (Mean ± SD)**
Grading	Mild (*n*- 41, 30.59%)	6.51 ± 0.60
	Moderate (*n*- 74, 55.22%)	7.41 ± 1.38
	Severe (*n*- 19, 14.17%)	8.39 ± 1.51

The current work revealed that peripheral distribution was significantly high in severe patients, followed by diffuse distribution and central distribution. Also, severe COVID pneumonia was associated with multiple lesions in both lungs (p<0.05). In moderate cases, GGO was the most common finding (52.70%); however, GGO with consolidation was most common in severe cases (12.16%). The frequently affected lobes in both moderate and severe groups were successively the lower right lobe, the lower left lobe, the middle right lobe, and, less often, the upper left lobe and the upper right lobe (Table 5).

Table 5: HRCT findings and its distribution with Severity of COVID infection.

Findings	**Distribution**	**Moderate *n*-74**	**Severe *n*-19**	***p*-value**
Lesion distribution	Central	3 (4.05%)	2 (10.52%)	<0.05
	Peripheral	59 (79.74%)	18 (94.73%)	<0.05
	Diffuse	22 (29.72%)	16 (84.21%)	<0.05
Lesion_no	Single lesion	9 (12.16%)	0	<0.05
	Multiple lesions/one lobe	15 (20.27%)	0	
	Multiple lesions in more than one lobe/1 lung	26 (35.13%)	2 (10.52%)	
	Multiple lesions in both lungs	35 (47.29%)	15 (78.94%)	
lesion_att	GGO	39 (52.70%)	5 (26.31%)	<0.05
	Consolidation	9 (12.16%)	6 (31.57%)	
	GGO with consolidation	17 (22.97%)	9 (47.36%)	
Lobe_no	Rt lower lobe	46 (62.16%)	19 (100%)	<0.05
	Lt lower lobe	41 (55.40%)	19 (100%)	
	Rt middle lobe	21 (28.37%)	16 (84.21%)	
	Lt upper lobe	14 (18.91%)	15 (78.94%)	
	Rt upper lobe	15 (20.27%)	14 (73.68%)	

Discussion

The intersection of COVID-19 and diabetes poses a unique clinical challenge. Diabetic patients with COVID-19 have been observed to have higher viral loads, prolonged viral shedding, and more severe clinical manifestations (11, 12). The hyperinflammatory state seen in severe COVID-19, characterized by a cytokine storm, can be exacerbated by the chronic inflammatory milieu present in diabetes. This synergistic effect can lead to extensive pulmonary damage, as evidenced by more pronounced and diverse HRCT findings (13, 14). This study included 134 patients, most notably female (66.41%). The demographic composition of the sample, particularly the higher representation of female patients, could be reflective of the broader patient population or indicate gender-specific health-seeking behaviors and prevalence rates. Such a distribution necessitates a gender-sensitive approach to interpreting the findings and may warrant further investigation into gender-specific factors influencing diabetes and related metabolic disorders.

Understanding the diversity in HRCT findings among COVID-19 patients with diabetes is essential for several reasons. Firstly, it can aid in the early identification of patients at higher risk of severe disease, allowing for timely intervention and appropriate allocation of healthcare resources (15, 16). Secondly, it can enhance our understanding of the pathophysiological mechanisms underlying severe COVID-19 in diabetic patients, potentially guiding the development of targeted therapies. Finally, detailed imaging studies can inform clinical guidelines and improve the management strategies for this vulnerable population, ultimately improving patient outcomes (17).

The mean BMI of the patients was 24.37 ± 4.11, categorizing the sample predominantly within the normal weight range according to the World Health Organization (WHO) criteria. Specifically, 32.83% of the patients had a healthy weight, while a significant portion were overweight (26.86%) or obese (32.08%). This high prevalence of overweight and obesity underscores the critical role of weight management in the diabetic population, as excessive body weight is a known risk factor for both the development and progression of type 2 diabetes mellitus (T2DM). The presence of 8.02% underweight individuals also highlights

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the heterogeneity of the patient population, suggesting that both ends of the BMI spectrum need to be addressed in diabetes management strategies.

Glycemic control among the patients was suboptimal, with a mean hemoglobin A1c (HbA1c) of 9.02 ± 1.89. Only 32.08% of the patients achieved good glycemic control (HbA1c <7%), while a substantial majority (67.91%) had poor glycemic control (HbA1c ≥7%). This indicates a pressing need for improved management practices to enhance glycemic control, potentially through more rigorous patient education, adherence to treatment protocols, and lifestyle modifications. The observed mean waist circumference (82.88 ± 12.41 cm), hip circumference (92.0 ± 10.71 cm), and waist-hip ratio (0.91 ± 0.13) further underscore the prevalence of central obesity, which is closely linked to insulin resistance and cardiovascular risk in diabetic patients.

The findings of this study underscore the significant variability in HRCT features among COVID-19 patients with diabetes, highlighting the complex interplay between viral infection and chronic metabolic disease. The diversity in imaging findings reflects the heterogeneity in disease presentation and progression, influenced by factors such as the duration and control of diabetes, the presence of other comorbidities, and individual patient characteristics.

Ground-glass opacities (GGO) are among the most common HRCT findings in COVID-19 patients, characterized by hazy areas that do not obscure the underlying bronchial structures or pulmonary vessels (18). In diabetic patients, GGO may be more extensive and diffuse, reflecting a higher degree of inflammation and alveolar damage. Consolidations, which indicate denser lung involvement with obscuration of underlying structures, are also frequently observed. These findings suggest more severe alveolar filling processes, potentially due to increased susceptibility to secondary bacterial infections or more severe viral pneumonia (9, 10).

Lipid profile analysis revealed dyslipidemia among the study participants, with mean serum cholesterol, LDL, triglycerides, and HDL levels of 181.0 ± 7.70, 145.50 ± 21.56, 195.75 ± 18.10, and 39.51 ± 5.76, respectively. The elevated levels of LDL and triglycerides, coupled with low HDL levels, are indicative of an atherogenic lipid profile commonly associated with diabetes. This lipid imbalance contributes to the increased cardiovascular risk observed in diabetic patients, emphasizing the importance of comprehensive lipid management alongside glycemic control.

Finally, the duration of diabetes diagnosis was categorized into two groups: <10 years (36.7%) and ≥10 years (63.3%). The longer duration of diabetes in the majority of patients suggests a chronic disease burden, which often correlates with higher complication rates and a more complex clinical management scenario. This highlights the need for long-term follow-up and targeted interventions to mitigate the progression of diabetes-related complications over time. Reticular patterns and interlobular septal thickening are indicative of interstitial involvement and fibrosis. In diabetic patients, these findings may be more pronounced, suggesting a higher propensity for chronic lung damage and fibrosis. The chronic inflammatory state and endothelial dysfunction associated with diabetes can contribute to these fibrotic changes, which may have long-term implications for lung function and recovery.

The distribution of HRCT lesions in COVID-19 is typically peripheral and bilateral, with a predilection for the lower lobes. In diabetic patients, the extent and distribution of lesions can be more widespread, involving both central and peripheral lung zones. This widespread distribution correlates with a more severe clinical course and a higher likelihood of requiring mechanical ventilation or ICU admission.

The heightened severity of HRCT findings in diabetic patients can be attributed to several pathophysiological mechanisms. Hyperglycaemia impairs immune responses by affecting neutrophil function, reducing the ability of macrophages to clear pathogens, and altering cytokine production. Additionally, chronic hyperglycemia leads to the formation of AGEs and subsequent oxidative stress, which can exacerbate tissue damage during viral infections (19, 20).

Endothelial dysfunction is another critical factor, as the endothelium plays a pivotal role in maintaining vascular homeostasis and regulating inflammatory responses. In diabetes, endothelial cells are often in a state of dysfunction, characterized by reduced nitric oxide production, increased vascular permeability, and a pro-thrombotic state. These changes can enhance the severity of lung injury in COVID-19, leading to more pronounced HRCT findings (21, 22).

The variability in HRCT findings among diabetic COVID-19 patients has several clinical implications. First and foremost, it emphasizes the need for personalized clinical management. Diabetic patients with extensive and severe HRCT abnormalities may benefit from more aggressive therapeutic strategies, including early initiation of antiviral treatments, anti-inflammatory therapies, and careful monitoring for complications such as secondary infections and thromboembolic events. Secondly, identifying specific HRCT patterns associated with worse outcomes can help stratify patients based on risk and guide decisions regarding hospitalization and ICU admission. For instance, patients with extensive GGO, consolidations, and reticular patterns may require closer monitoring and early intervention to prevent disease progression.

Conclusion

The diversity in HRCT findings among COVID-19 patients with diabetes highlights the complex interplay between chronic metabolic disease and acute viral infection. The more severe and varied imaging features in this population underscore the need for personalized and aggressive clinical management to mitigate the heightened risk of severe disease and adverse outcomes. Enhancing our understanding of the specific imaging patterns and pathophysiological mechanisms can improve the care and prognosis for diabetic patients affected by COVID-19. Furthermore, this study sheds light on the multifaceted challenges faced by diabetic patients, including weight management, glycemic control, lipid abnormalities, and the chronicity of the disease. Addressing these issues through a multidisciplinary approach involving endocrinologists, dietitians, and primary care providers is essential to improve outcomes and quality of life for diabetic patients.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate.

It is approved by the department concerned. (2326/DME/QAMC/Bahawalpur dated 06-07-2021)

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