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Investigating the Effect of Type II Diabetes on COVID-19 Pneumonia Severity Using Computed Tomography: A Comparative Analysis

Tip II Diyabetin COVID-19 Pnömoni Şiddeti Üzerindeki Etkisinin Bilgisayarlı Tomografi Kullanılarak Araştırılması: Karşılaştırmalı Bir Analiz

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Abstract

The aim of this study was to determine the factors affecting the severity of COVID-19 pneumonia in patients with type 2 diabetes using computed tomography severity scores. Computed tomography findings and pneumonia scores of 136 patients with type 2 diabetes and 136 patients without diabetes (n=272) with positive polymerase chain reaction test between January 2020 and January 2021 were compared using the hospital information system. The number of patients with moderate and severe pneumonia was significantly higher in the type 2 diabetes group (p<0.05). Pneumonia scores were significantly higher in type 2 diabetic patients older than 60 years (p<0.05). No significant correlation was found between pneumonia scores and hemoglobin A1c (p=0.865) and fasting blood glucose (p=0.78). No negative effect of hypertension on pneumonia score was observed in diabetic patients. Pneumonia scores of diabetic patients with renal insufficiency were higher than those of diabetic patients aged <60 years (P<0.05). In conclusion, the present study results revealed that the severity of COVID-19 pneumonia in patients with type 2 diabetes is higher than in healthy subjects. However, there was no significant positive correlation between pneumonia severity, hyperglycemia, and hemoglobin A1c levels in patients with type 2 diabetes.

Keywords: COVID-19, Diabetes mellitus type 2, Computed tomography, Pneumonia.

Özet

Bu çalışmanın amacı tip 2 diyabetli hastalarda bilgisayarlı tomografi skorlarını kullanarak COVID-19 pnömonisinin şiddetini etkileyen faktörleri belirlemektir. Ocak 2020 ile Ocak 2021 tarihleri arasında polimeraz zincir reaksiyon testi pozitif olan 136 tip 2 diyabet hastası ile diyabeti olmayan 136 hastanın (n=272) bilgisayarlı tomografi bulguları ve pnömoni skorları hastane bilgi sistemi kullanılarak karşılaştırıldı. Tip 2 diyabet grubunda orta ve şiddetli pnömoni geçiren hasta sayısı anlamlı olarak daha fazlaydı (p<0.05). 60 yaş üstü tip 2 diyabetik hastalarda pnömoni skorları anlamlı olarak daha yüksek bulundu (p<0.05). Pnömoni skorları ile hemoglobin A1c (p=0.865) ve açlık kan şekeri (p=0.78) arasında ise anlamlı bir korelasyon bulunamadı. Diyabetik hastalarda hipertansiyonun pnömoni skoru üzerine olumsuz etkisi gözlenmedi. Böbrek yetmezliği olan diyabetik hastaların pnömoni skorları <60 yaş diyabetik hastalara göre daha yüksekti (P<0.05). Sonuç olarak çalışma verileri tip 2 diyabetli hastalarda COVID-19 pnömonisinin şiddetinin sağlıklı kişilere göre daha yüksek olduğunu göstermektedir. Tip 2 diyabetli hastalarda pnömoni şiddeti ile hiperglisemi ve hemoglobin A1c düzeyleri arasında ise anlamlı bir pozitif korelasyon saptanmamıştır.

Anahtar Kelimeler: COVID-19, Diyabetes mellitus tip 2, Bilgisayarlı tomografi, Pnömoni.

Introduction

Comorbidities accompanying COVID-19 infection lead to a more severe disease course, prolonged intensive care periods, and increased mortality [1,2]. One of the most common of these comorbidities is Type 2 Diabetes Mellitus (T2DM) [3]. It has been reported that COVID-19 mortality and disease severity are significantly higher in patients with T2DM than in those without diabetes [3]. There are different studies on the effects of hyperglycemia on the clinical outcomes of COVID-19 [4–7]. Patients with T2DM have additional comorbidities such as renal failure and heart diseases [2,3]. These diseases also affect the immune system negatively [2,3]. Aging is another factor that adversely affects the immune system [8]. Computed Tomography (CT) has been the most important imaging method showing the severity of pneumonia during the COVID-19 pandemic, and different scoring systems have been developed to determine the severity of pneumonia [9,10].

In this study, it was aimed to investigate the factors affecting the severity of pneumonia in patients with type 2 diabetes using CT.

Material and Method

Permission was obtained from the Faculty of Medicine Clinical Research Ethics Committee (Decision No:2022-21/177 date:22.11.2022) before the study. Patient consent form was not used because the study was retrospective. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study population and data collection

This retrospective cross-sectional study was conducted in a university hospital. The study groups were selected from unvaccinated patients with pulmonary infiltration on CT of the thorax who were diagnosed with COVID-19 pneumonia by SARS-CoV-2 polymerase chain reaction (PCR) test between January 2020 and January 2021, when the vaccination program had not yet started. Demographic characteristics of the study groups; comorbidities; and clinical, laboratory, and radiological findings of the patients were retrospectively evaluated using the hospital automation system. After the group of patients with T2DM who met the inclusion criteria was formed, a control group was formed of patients with COVID-19 pneumonia without known comorbidities in the same number and age group.

Firstly, the pneumonia scores of T2DM patients and patients without comorbidities were compared. Patients with T2DM were then classified according to their comorbidities and laboratory parameters and compared between their groups.

Inclusion criteria for the T2DM group: Patients diagnosed with T2DM before COVID-19 pneumonia were included. Patients who were not diagnosed with T2DM before COVID-19 pneumonia were not included in the study, even if their fasting glucose and glycated hemoglobin A1c (HbA1c) levels were high.

The inclusion criteria for the control group: Patients with no known comorbidities that could affect the immune system and with normal blood glucose, urea and creatinine levels were included.

Image analysis

Chest CT scans were performed on Toshiba Alexion 16-slice and General Electric (GE) Lightspeed 128-slice CT scanners using standard acquisition protocols. The chest CT images of all patients were evaluated by the same radiologist with more than 20 years of experience using the hospital registry system.

The CT pneumonia severity score is a scoring system that indicates the severity of pneumonia by summing the percentages of the 5 lobes affected. A score between 1 and 5 is given according to the percentage of each of the five lobes affected, and the scores are summed. Scores below 8 indicate mild pneumonia, scores between 8 and 15 indicate moderate pneumonia, and scores between 16 and 25 indicate severe pneumonia [9]. Chest CT findings are categorized as ground-glass opacities (GGO), consolidation, crazy paving, fibrotic bands, and mixed pattern with multiple patterns. Air bronchograms, inverted halo sign, nodules, pleural effusion, mediastinal lymphadenopathy, etc. were also recorded.

Statistical analysis

Descriptive statistics of the variables are presented as mean ± standard deviation, median (min-max), and frequency (n, %). Normality distributions of the variables were assessed using Kolmogorov-Smirnov and Shapiro-Wilk tests. For univariate analysis of the variables in the study, Kruskal-Wallis and Chi-square tests were used, depending on the type of variable and availability of assumptions. Pairwise comparisons of groups with significant differences in the Kruskal-Wallis test were performed using the Mann-Whitney U-test with Bonferroni correction (0.05/group number). Spearman's Rho analysis was used to assess correlations between variables. All data were analyzed using the Statistical Package for Social Sciences for Windows software (IBM SPSS version 25.0, Armonk, NY, USA).

Results

This retrospective study included 272 adult patients (135 males and 137 females. There were 66 males and 70 females in the T2DM group and 69 males and 67 females in the control group for a total of 136 patients. The mean age of the type 2DM group was (63.02±11.98), the mean age in the control group was (62.08±11.05), and the mean age of all study group was (62.55±11.52). In the control group, 94 (69.1%) patients had mild, 37 (27.2%) had moderate, and 5 (3.7%) had severe pneumonia. In the type 2DM patient group, 72 (52.9%) patients had mild, 51 (37.5%) had moderate, and 13 (9.6%) had severe pneumonia. The number of patients with mild pneumonia in the control group and moderate and severe pneumonia in the type 2 DM group was significantly higher (p<0.05), (Figure 1).

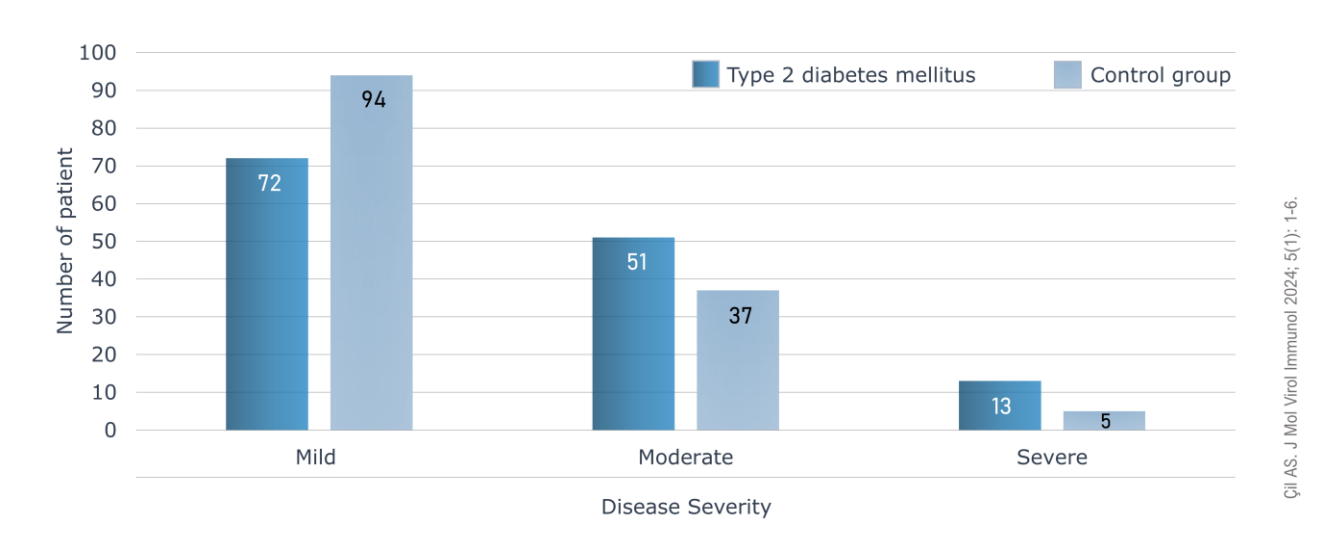

Figure 1. Distribution of mild, moderate, and severe pneumonia in type 2 diabetes and control groups.

When the pneumonia scores of male and female patients were compared, it was found that the pneumonia scores of male patients were higher than those of female patients. The difference between the mean pneumonia scores in the control group was significant (p=0.032), whereas the difference between the scores in the type 2 DM group was not statistically significant (p=0.092) (Table 1).

When the total mean pneumonia scores of both groups were compared without age group, the pneumonia scores of T2DM patients were significantly higher (p<0.001) (Table 2).

When the pneumonia scores were compared according to age groups between the T2DM and control groups, the difference between the pneumonia scores in the 40-49 and 50-59 age groups was not statistically significant, whereas the pneumonia scores of patients with type 2 DM aged 60-69 and over 70 years were found significantly higher, p=0.033 and p=0.019, respectively (Table 2).

In patients with T2DM, neither the HbA1c level (p=0.865) nor the blood glucose level (p=0.78) was significantly correlated with the pneumonia score.

Renal insufficiency was present in 54 patients (39.7%) with T2DM. The mean pneumonia score of patients with renal insufficiency (9.09±4.54) was higher than that of patients with diabetes without renal insufficiency (8.42±4.87). However, this difference was not statistically significant (p=0.357). Pneumonia scores of diabetic patients with renal insufficiency were higher than those of diabetic patients aged <60 years (P<0.05).

No significant difference was found between the pneumonia scores of diabetics with hypertension only and those without comorbidities other than diabetes (p=0.658). Almost all patients with comorbidities other than hypertension and renal failure had more than one comorbidity in the diabetic group. Therefore, a statistical analysis could not be performed by isolating a single comorbidity in these patients. These patients were considered to have multiple comorbidities. Forty (29.4%) of the diabetic patients in the study group had more than one comorbidity. The pneumonia scores of patients with multiple comorbidities (10.86±4.54) were significantly (p<0.001) higher than those of patients with only T2DM (Table 3).

There was no significant difference in the frequency of CT findings between the T2DM and control groups (p>0.05). The most common parenchymal lung findings in both the groups were GGO and consolidations.

Table 1. Comparison of mean pneumonia severity scores according to groups by gender.

Group		Males	Females	p*
Type 2 DM	*mean*	9.43±4.92	7.92±4.46	0.092
	median (range)	9 (1-20)	8 (1-19)	
Control group	*mean*	7.64±3.77	6.48±3.66	0.032
	median (range)	8 (1-17)	6 (1-23)	

*Kruskal-Wallis. DM; Diabetes mellitus.

Table 2. Comparison of mean pneumonia severity scores according to age groups.

Age groups >	40-49	50-59	60-69	70+	Total
Type 2 DM	7.70±4.43	7.32±4.35	9.65±4.83	9.52±4.90	8.69±4.74
Control Group	7.25±5.00	6.57±4.11	7.31±3.28	7.11±3.27	6.81±3.33
p*	0.765	0.464	0.033	0.019	<0.001

*Mann-Whitney U test. DM; Diabetes mellitus.

Table 3. Comparison of pneumonia scores in patients with T2DM according to the comorbidities.

Comparisons	Pneumonia scores		p*
Type 2 DM vs "Type 2 DM+HT"	8.42±4.87	8.75±4.48	p=0.658
Type 2 DM vs "Type 2 DM+CRF"	8.42±4.87	9.09±4.54	p=0.357
Type 2 DM vs "Type 2 DM+MC"	8.42±4.87	10.86±4.54	<0.001

* Mann-Whitney U test. DM; Diabetes mellitus. HT; Hypertension. CRF; Chronic renal failure. MC; Multiple comorbidities.

Discussion

This retrospective study investigated the effect of T2DM on the severity and radiological findings of COVID-19 pneumonia by comparing the CT pneumonia scores and radiological findings of patients with T2DM with those of patients without known comorbidities in the control group. Demographic, clinical and laboratory findings that may influence CT pneumonia scores in patients with T2DM were evaluated.

Previous studies have reported that COVID-19 pneumonia is more severe in patients with T2DM [1–3]. In this study, the pneumonia scores of T2DM patients aged over 60 years were higher than those of the control group. In this study, unlike other studies, it was observed that the severity of pneumonia in patients with T2DM aged 40-49 and 50-59 years was similar to that in the control group. This difference may be a finding of the present study group and may indicate that the negative effect of T2DM on the immune system becomes more pronounced, especially after the age of 60.

The weakening of the immune system with age is known as immune ageing [11]. Many previous studies have reported that age increases the severity of COVID-19 pneumonia and is the major risk factor for mortality [8,11]. Similarly, in this study, pneumonia was found to be more severe in older patients in the whole study group, more so in T2DM patients. The greater severity of pneumonia in older patients with T2DM suggests that immune senescence progresses more rapidly in T2DM.

In this study, no significant positive correlation was found between blood glucose levels and HbA1c values and pneumonia scores. Similar to the present study, some previous studies have reported that there was no correlation between pneumonia severity and fasting blood glucose and HbA1c levels [12–14]. These data in the present study group suggest that the negative effect of high blood glucose levels on the immune system in patients with T2DM occurs over a long period of time. As a matter of fact, some authors consider T2DM as a chronic, low-grade inflammatory disease that affects the immune system over a long period of time [15]. On the other hand, some studies have argued that hyperglycemia acutely affects the clinical findings of COVID-19, that there is a direct relationship between hyperglycemia and COVID-19 prognosis, and that control of hyperglycemia positively affects the prognosis of the disease [5–7]. It has been reported that hyperglycemia suppresses the immune system and increases the production of inflammatory cytokines, thereby adversely affecting the course of the disease [5–7]. In addition, it has been argued that high blood glucose levels increase the number of angiotensin converting enzyme 2 (ACE2) receptors and that the virus infects cells through this receptor [16]. The differences between the studies may be due to regional and ethnic differences in the study groups, as well as individual factors that positively or negatively affect the immune system. However, it is not entirely clear how hyperglycemia affects the immune system in viral pneumonia [14].

Previous studies have shown that COVID-19 pneumonia has a more severe clinical and radiological course in patients with chronic renal failure than in normal subjects [17,18]. In this study, although the pneumonia scores of T2DM patients with renal failure were higher than those of T2DM patients without renal failure, they were not statistically significant.

Although some studies have claimed that HT increases the severity of COVID-19 pneumonia, the general opinion is that there is no relationship between HT and COVID-19 pneumonia [19]. In this study, no significant difference was found between the pneumonia scores of patients with HT and T2DM and those of patients with T2DM alone.

Although the pneumonia scores of diabetics with multiple comorbidities were significantly higher than those with T2DM alone, the extent to which each comorbidity affected the pneumonia score could not be determined in this study. More prospective and randomized controlled trials are needed in this regard.

The results of this study highlight the importance of assessing different risk factors and comorbidities for viral pneumonia in T2DM patients with order to determine appropriate treatment approaches for patients.

This study has some limitations. As this was a retrospective study, it was not possible to follow the patients' clinics and recovery processes. In addition, the study design may have made it difficult to confirm the causal relationships. As the immune system can be affected by many individual and environmental factors, other factors may have influenced the results.

Conclusion

The severity of COVID-19 pneumonia in T2DM patients is higher than in normal subjects.

The negative effect of T2DM on the immune system becomes more pronounced after the age of 60. There is no significant positive correlation between the severity of pneumonia and hyperglycemia and HbA1c levels in patients with T2DM.

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