

Effect of the COVID-19 Pandemic on the Diagnosis of Non-Melanoma Skin Cancers: A Retrospective Case Control Study

COVID-19 Pandemisinin Nonmelanom Deri Kanseri Tanısı Üzerindeki Etkisi: Retrospektif Vaka Kontrol Çalışması

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ABSTRACT Objective: The coronavirus disease-2019 (COVID-19) pandemic has caused delays in the diagnosis and treatment of some oncological diseases. This study aimed to reveal the effect of the COVID-19 pandemic on the frequency of diagnosis of non-melanoma skin cancers (NMSC) and the demographic characteristics of patients. **Material and Methods:** Patients aged over 18 years, who were histopathologically diagnosed with basal cell carcinoma (BCC) or squamous cell carcinoma (SCC) between March 12, 2019 and March 11, 2021 were included in the study. The demographic characteristics of these patients, the number of total skin biopsies, and the number of BCC and SCC biopsies were compared between the pre-pandemic and pandemic periods, based on the date of March 12, 2020, when the pandemic measures began to be implemented in Turkey. **Results:** With the pandemic, there was a 26.7% decrease in the total skin biopsies and a 21% decrease in the total NMSC biopsies. Despite a 34% decrease in the number of biopsies for the diagnosis of BCC, a 15.8% increase was observed in the number of biopsies for the diagnosis of SCC. The frequency of excisional biopsies was observed to increase among the patients with BCC and SCC during the pandemic period ($p=0.004$ and $p=0.001$, respectively). **Conclusion:** The number of total skin biopsies and total NMSC biopsies significantly decreased during the pandemic period. The health system should be reorganized to effectively handle pandemics and similar crisis periods, and new strategies should be determined regarding patient education, early diagnosis, and treatment approaches for NMSC.

ÖZET Amaç: Koronavirüs hastalığı-2019 [coronavirus disease-2019 (COVID-19)] pandemisi bazı onkolojik hastalıkların tanı ve tedavisinde gecikmelere neden olmuştur. Bu çalışmada, COVID-19 pandemisinin melanom dışı deri kanserleri (MDDK) tanı sıklığı ve hastaların demografik özellikleri üzerindeki etkisini ortaya koymak amaçlandı. **Gereç ve Yöntemler:** 12 Mart 2019-11 Mart 2021 tarihleri arasında histopatolojik olarak bazal hücreli karsinom (BHK) ve skuamöz hücreli karsinom (SHK) tanısı almış 18 yaş üstü hastalar çalışmaya dâhil edildi. Türkiye’de pandemi tedbirlerinin başladığı 12 Mart 2020 tarihi baz alınarak, pandemi öncesi ve pandemi dönemindeki total deri biyopsisi, BHK ve SHK biyopsi sayıları ve bu hastaların demografik özellikleri karşılaştırıldı. **Bulgular:** Pandemi ile beraber total deri biyopsisi işlemlerinde %26,7, total MDDK biyopsi işlemlerinde ise %21 oranında azalma izlendi. BHK tanısı için yapılan biyopsi oranında %34 oranında bir azalmaya karşın SHK tanısı için yapılan biyopsi oranında %15,8 oranında artış görüldü. Pandemi döneminde BHK ve SHK hastalarında eksizyonel biyopsi sıklığında artış izlendi (sırasıyla $p=0,004$ ve $p=0,001$). **Sonuç:** Pandemi döneminde total deri biyopsi sayısı ve MDDK biyopsi sayısı önemli ölçüde azalmıştır. Pandemi ve benzeri kriz dönemlerine ilişkin, sağlık sisteminde yeniden düzenlemeler yapılmalı ve MDDK’ye yönelik hasta eğitimi, erken tanı ve tedavi yaklaşımları ile ilgili yeni stratejiler belirlenmelidir.

Keywords: Basal cell carcinoma; COVID-19; pandemics; skin neoplasms; squamous cell carcinoma

Anahtar Kelimeler: Bazal hücreli karsinom; COVID-19; pandemiler; deri tümörleri; skuamöz hücreli karsinom

Non-melanoma skin cancer (NMSC) is the most common type of skin neoplasms across the world.¹ Its incidence varies according to the region, being re-

ported as 98/100,000 person-years in Europe.² The increase in ultraviolet exposure, developments in diagnostic methods, and increased public awareness

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through cancer screening programs have gradually increased the globally detected incidence of NMSCs, and it has become an important public health problem.^{2,3} Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) constitute 99% of NMSCs, and the former is approximately three to 5 times more common than the latter.²

Coronavirus disease-2019 (COVID-19) is a highly contagious viral infection caused by severe acute respiratory syndrome coronavirus-2. The virus emerged in Wuhan, China, in December 2019 and then rapidly spread all over the world.⁴ It was declared a pandemic on March 4, 2020, by the World Health Organization (WHO), which instituted essential measures for prevention and confrontation.⁵ In Turkey, the first case of COVID-19 was reported on March 11, 2020, and pandemic measures began to be implemented across the country as of March 12, 2020.⁶

The COVID-19 pandemic has placed a great amount of pressure on the health systems of countries globally.⁷ The increasing hospital load and concerns related to the spread of the virus have made it necessary to pass temporary regulations in health services and reduce non-emergency hospital visits. As a result of restrictions on non-emergency medical and surgical applications and patients' avoidance of hospital visits due to concerns of contracting the virus, disruptions have occurred in the diagnosis and treatment of some diseases.⁸ The pandemic has also resulted in delays in the diagnosis and treatment of oncological diseases. A study conducted in the Netherlands showed that the decrease in skin cancer was higher than other cancers during the pandemic.⁹

In this study, we aimed to reveal the effect of the COVID-19 pandemic on the frequency of total skin biopsies, frequency of NMSC diagnoses, and demographic characteristics of the patients.

MATERIAL AND METHODS

This study was approved by the Firat University Non-interventional Clinical Research Ethics Committee (2021/07-46) and performed according to the rules expressed in the Declaration of Helsinki. The

patients aged 18 years and older who underwent skin biopsy between March 12, 2019 and March 11, 2021 and were diagnosed with SCC or BCC based on a histopathological examination were included in the study. The patients were identified by screening the pathological laboratory data. Tumors taken from body parts other than the skin, recurrent tumors, metastatic tumors, tumors that underwent re-excision, and those that could not be definitively diagnosed were excluded from the study. Age, gender, anatomical region, number of tumors, biopsy type, and surgical margin positivity characteristics were recorded. In order to determine the effects of the COVID-19 pandemic on the frequency of NMSC biopsies and the demographic characteristics of patients, March 12, 2019 to March 11, 2020 was considered as the pre-pandemic period and March 12, 2020 (when quarantine measures began) to March 11, 2021 was evaluated as the pandemic period. During the pandemic, temporary arrangements have been made in health services by reducing the capacity of polyclinics, non-emergency patient admissions, and many medical and surgical procedures in our hospital along with the whole world. The accompanying curfews and concerns about contamination in patients also led to a significant reduction in hospital admissions. For this reason, we determined the number of skin biopsy procedures performed for any reason before and during the pandemic to see the effect of pandemic measures on skin biopsy procedures for general purposes. In the second step, in order to determine how NMSC biopsy procedures are affected by total skin biopsy procedures, we evaluated the ratio of the number of NMSC biopsies to the number of patients who were biopsied for any reason.

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (SPSS, version 25.0. Armonk, NY: IBM Corp.) was used for the statistical analyses. Mean±standard deviation values were obtained for numerical variables, and numbers and percentages were used for categorical variables. Kolmogorov-Smirnov test was used to evaluate the parametric distribution of the variables. Student's t-test was used to compare numerical vari-

ables between the groups. The chi-square test was conducted for the analysis of categorical variables. A p value of <0.05 was considered statistically significant.

RESULTS

Between March 12, 2019 and March 11, 2021, a total of 256 lesions were diagnosed in 217 patients with NMSC (Table 1). In the evaluation of these patients, 105 of 174 tumors in 151 patients with BCC had been biopsied before the pandemic and 69 during the pandemic, while 38 of the 82 tumors in 66 patients with SCC had been biopsied before the pandemic and 44 during the pandemic (Table 1). The demographic characteristics of the patients diagnosed with BCC and SCC are given in Table 2. Of the patients with BCC, 44% were female and 46% were male, with a mean age of 70.33 ± 1.10 years. Before and during the pandemic, 93% and 91% of BCC tumors were located in the head and neck region, respectively. Of the patients with SCC, 47% were female and 43% were male, with a mean age of 73.88 ± 1.77 years. Before and during the pandemic, 66% and 70% of SCC tumors were located in the head and neck region, respectively. There was no statistically significant difference between the pre-pandemic and pandemic periods in terms of age, gender, and tumor localization among the patients with BCC and SCC ($p > 0.05$) (Table 2). With the pandemic, the rate of excisional biopsies in BCC lesions increased from 71% to 90% ($p = 0.004$). The frequency of excisional biopsies in

SCC increased from 68 to 95%, and the difference was statistically significant between the pre-pandemic and pandemic periods ($p = 0.001$). There was no statistically significant difference in surgical margin positivity in BCC and SCC tumors that underwent total excision ($p = 0.099$ and $p = 0.927$, respectively). In patients with BCC, 92% had a single tumor and 8% had multiple tumors before the pandemic, whereas 78% had a single tumor and 22% had multiple tumors during the pandemic period ($p = 0.019$). In patients with SCC, 94% had a single tumor and 6% had multiple tumors before the pandemic, whereas 76% had a single tumor and 24% had multiple tumors during the pandemic ($p = 0.039$) (Table 2).

The number of total skin biopsies taken for any reason between March 12, 2019 and March 11, 2021 was 1,834. Of these biopsies, 1,058 were performed before the pandemic and 776 during the pandemic. There was a 26.7% decrease in the number of total skin biopsy procedures during the pandemic period. During the pandemic period, 21% decrease was observed in the total NMSC biopsies. While there was a 34% decrease in the biopsies with a diagnosis of BCC during the pandemic, a 15.8% increase was observed in the biopsies with a diagnosis of SCC. With the pandemic, the ratio of total NMSC biopsies over the total skin biopsies increased from 13.5 to 14.6% (Table 1).

DISCUSSION

Although the incidence of NMSC is increasing across the world, it is estimated that the number of newly diagnosed patients remains below the actual figures. WHO estimates that approximately two to three million cases of NMSC may go undiagnosed each year.¹⁰ Recently, worldwide skin cancer screening campaigns have been organized to raise awareness, encourage patients to protect their skin against the sun, and inform them about risk factors and suspicious lesions, which has led to the detection of a higher rate of skin malignancies.¹¹ However, all these positive developments in the diagnosis and treatment of skin cancer have been reversed with the beginning of the COVID-19 pandemic.¹²⁻¹⁵

TABLE 1: Frequency of new diagnoses of BCC and squamous cell carcinoma before and during the pandemic.

	Pre-pandemic	Pandemic	Change, n (%)
Total skin biopsies (n) ^a	1,058	776	-282 (-26.7)
NMSC (n)	143	113	-30 (21)
BCC (n)	105	69	-36 (34)
SCC (n)	38	44	6 (15.8)
Frequency of new NMSC diagnoses (%) ^b	13.5%	14.6%	1.1
BCC ^c	9.9%	8.9%	-1
SCC ^d	3.6%	5.7%	2.1

^aTotal skin biopsies performed for any reasons; ^bRatio of the number of NMSC biopsies to the number of patients who were biopsied for any reason; ^cRatio of the number of BCC biopsies to the number of patients who were biopsied for any reason; ^dRatio of the number of SCC biopsies to the number of patients who were biopsied for any reason; BCC: Basal cell carcinoma; NMSC: Non-melanoma skin cancer; SCC: Squamous cell carcinoma.

TABLE 2: Demographic characteristics of the patients with BCC and SCC before and during the pandemic.

Demographic characteristic	Pre-pandemic	Pandemic	p value
BCC			
Age (Mean±SD, minimum-maximum)	69±1.31 (46-93)	72±2.00 (28-96)	0.322
Gender (n, %)			0.168
Female	46 (48%)	20 (36%)	
Male	50 (52%)	35 (64%)	
Localization (n, %)			0.619
Head/neck	98 (93%)	63 (91%)	
Trunk/extremities	7 (7%)	6 (9%)	
Tumor number (n, %)			
1	88 (92%)	43 (78%)	0.019
>1	8 (8%)	12 (22%)	
Biopsy type (n, %)			0.004
Incisional biopsy	30 (29%)	7 (10%)	
Excisional biopsy	75 (71%)	62 (90%)	
Surgical margin (n, %)			0.099
Tumor-negative	47 (63%)	47 (76%)	
Tumor-positive	28 (37%)	15 (24%)	
SCC			
Age (Mean±SD, minimum-maximum)	74±2.33 (36-93)	74±2.71 (38-100)	0.866
Gender (n, %)			0.622
Female	15 (45%)	16 (48%)	
Male	18 (55%)	17 (52%)	
Localization (n, %)			0.651
Head/neck	25 (66%)	31 (70%)	
Trunk/extremities	13 (34%)	13 (30%)	
Tumor number (n, %)			
1	31 (94%)	25 (76%)	0.039
>1	2 (6%)	8 (24%)	
Biopsy type (n, %)			0.001
Incisional biopsy	12 (32%)	2 (5%)	
Excisional biopsy	26 (68%)	42 (95%)	
Surgical margin (n, %)			0.927
Tumor-negative	17 (65%)	27 (64%)	
Tumor-positive	9 (35%)	15 (36%)	

BCC: Basal cell carcinoma; SCC: Squamous cell carcinoma; SD: Standard deviation.

The postponement of non-emergency medical and surgical applications due to the pandemic has caused delays in the diagnosis of many diseases, including dermatological diseases. In a population-based study conducted in Canada, Asai et al. reported a 15% decrease in the total skin biopsies and an 18% decrease in the NMSC biopsies during the pandemic period and noted that the rate of skin biopsies was

lower among the women and elderly, and in certain regions.¹⁴ In our study, we found a 26.7% decrease in the number of total skin biopsy procedures with the implementation of pandemic measures. Thus, more than a quarter of dermatological diseases requiring a biopsy could not be diagnosed. Similarly, we observed a 21% decrease in the number of NMSC biopsy procedures. When the total NMSC biopsies

were compared to the total skin biopsies performed for any reason with the pandemic, a very slight increase was observed in NMSC biopsies from 13.5% to 14.6%, despite a decrease in the number of total skin biopsies. Although this shows that the decrease in the frequency of NMSC biopsies in our center was lower than other skin biopsies, approximately one-fifth of NMSC lesions were not diagnosed during the pandemic period. This may be due to the fact that, during the pandemic, patients with skin tumors are more likely to visit the hospital than patients with other skin diseases, and physicians are less likely to delay surgical procedures for these tumors. Although it shows partial awareness, it has not prevented the decrease in NMSC biopsies in the pandemic.

The decrease in the number of total skin biopsies and NMSC diagnoses during the pandemic period may be related to many factors, most notably the reduction of the capacity of the outpatient clinics and the interruption of patient visits to specialists due to limitations in non-emergency patient admissions. Other important reasons include the reduced number of non-emergency medical and surgical applications and patients' avoidance of hospital visits due to concerns of contracting the virus. NMSC usually occurs in the elderly. Since the course of COVID-19 with higher mortality in the elderly, this population was further discouraged from visiting healthcare centers when needed.

In our study, when we evaluated NMSC separately, we observed a 34% decrease in the number of biopsies with a diagnosis of BCC diagnoses, but there was a 15.8% increase in the number of biopsies with a diagnosis of SCC diagnoses. In the literature, there are only few studies on the frequency of BCC and SCC diagnoses during the pandemic.^{15,16} Marson et al. detected 51% and 25% reductions in BCC and 44.1% and 21% reductions in SCC within the first 3 months and 6 months, respectively. The authors also observed a delay of 1.9 months in the diagnosis of BCC and approximately 2.1 months in that of SCC. They concluded that although there was a return to the pre-pandemic values in the later stages of the pandemic, some cases were still undiagnosed, and the de-

crease in the BCC diagnosis was greater compared to SCC.¹⁶ We consider that the significant decrease in the diagnosis of BCC is due to the slower growth of these tumors compared to SCC, unpredictability of malignancy suspicion by patients and non-specialists, and the consequent decrease in referrals to specialist physicians. However, contrary to the decrease in the incidence of BCC, we observed a 15.8% increase in the incidence of SCC. Abbassi et al., evaluating rearrangements in the management of NMSCs in a tertiary hospital in the UK during the first wave of the pandemic, reported a 10% decrease in the diagnosis of BCC and a 10% increase in the diagnosis of SCC which is consistent with our findings.¹⁵ In another study, despite the decrease in BCC during the pandemic, an approximately 2-fold increase in the number of SCC was observed.¹⁷ The reason for the increase in the number of SCC during the pandemic period is unknown. Firstly, since SCC is a tumor that grows more rapidly than BCC, it is expected that there will be less reduction in biopsy procedures compared to BCC. Therefore, SCC is less neglected by patients and easier to recognize by physicians.¹⁶ Secondly, surgical procedures for diagnosis and treatment may be postponed in primary and secondary care hospitals during the pandemic. Therefore, the referral of patients to our hospital, which is a tertiary center, may cause a misleading increase in SCC. Lastly, COVID-19 is a virus that affects many systems. Human papillomavirus, Epstein Barr virus, human herpesvirus 8, Merkel cell polyomavirus, hepatitis B virus, hepatitis C virus, and human T lymphotropic virus Type 1 are viruses that have been shown to have an oncogenic effect.¹⁸ Whether COVID-19 has an oncogenic effect similar to these viruses and whether it plays a role in the tumorigenesis and progression of SCC is an issue that needs to be clarified, and long-term studies are needed.

Delays in the diagnosis and treatment of NMSC may reduce the chance of successful treatment with medical therapy or simple surgical methods, leading to more aggressive surgical interventions and increased mortality and morbidity. SCC is responsible for a significant portion of NMSC-related deaths.¹⁹

The delayed diagnosis of SCC has been shown to lead to disease progression and increased metastasis rates.^{20,21} While a short-term delay in the diagnosis and treatment of low-risk BCC tumors can be tolerated, high-risk BCC lesions, including those located in high-risk areas, poorly demarcated lesions such as morpheaform BCC, aggressive histopathological subtypes such as infiltrative BCC, presence of perineural invasion, recurrent lesions, immunosuppression, and radiotherapy history can result in cosmetic and functional problems, significantly increasing the morbidity.²

We did not observe any difference between the pre-pandemic and pandemic periods in terms of gender, age, and tumor localization in patients with NMSC. However, we found that the number of patients with BCC and SCC presenting with a single tumor significantly decreased during the pandemic; thus, the diagnostic delay in patients with solitary tumors was higher than in those with multiple tumors. This may be because multiple skin tumors are more frightening and lead patients to seek more medical advice.

In our study, we found that the excision rate increased from 71% to 90% in BCC and from 68% to 95% in SCC, but there was no change in surgical margin positivity. Abbassi et al. observed a 158% increase in the excision rates during the peak period of the first wave of the pandemic and noted a decrease in the rate of close and positive surgical margins.¹⁵ On the contrary, in another study, an increase in surgical margin positivity was observed in NMSC during the pandemic.¹⁷ In the consensus guidelines for melanoma management during the COVID-19 pandemic period, it is recommended that suspicious lesions can be excised by general practitioners/local multidisciplinary teams with a surgical margin of 2 mm.²² However, there is no consensus yet on the management of NMSC in the pandemic. Few studies in the literature and our study show an increase in the tendency of physicians to perform the excisional biopsy.¹⁵ A punch or shave biopsy is generally used as the first-line diagnostic method in the diagnosis of NMSC. According to the National Comprehensive Cancer Network 2017 guidelines, tumors smaller

than 20 cm located on the trunk and extremities and those smaller than 10 mm in the cheek, forehead, scalp, neck, and pretibial region are classified as low-risk NMSC. Low-risk NMSC tumors can be treated with certain topical agents, such as 5-fluorouracil and diclofenac gel; non-excisional surgical methods, such as cryotherapy, electrodesiccation, and curettage; or simple total excision. Although the possible reason for the increase in BCC and SCC excision procedures may be the surgeons' decision to perform direct excision in order not to waste time, it should be kept in mind that increasing rates of total excision may lead to increased morbidity such as extensive surgical wound, delayed wound healing, secondary infections, scar development, and poor cosmetic results in some certain cases with low-risk NMSC tumors that can also be treated more comfortably with non-surgical treatment modalities.²³ Increasing excisional biopsy procedures may also result in increased unnecessary excisions in non-malignant lesions biopsied with suspicion of malignancy.

The major limitation of our study is its single-center design. Multicenter studies with a larger patient series are needed to clarify whether the increase in the SCC diagnoses reflects a true increase in the number of cases. Studies evaluating the long-term frequency of NMSC before the pandemic will provide more accurate data in revealing whether there is a trend of change independent of the pandemic in the incidence of NMSC. Since this study was conducted in the first year of the pandemic period, it is insufficient to reveal the long-term effects of pandemic restrictions on the frequency of NMSC diagnosis. Another important limitation of the study is the inability to distinguish between factors arising from the restrictions in the health system or the decrease in patient admissions. Longer-term studies comparing different pandemic restraint practices may guide in this regard.

Although oncological diseases were intended to be excluded from restrictions applied to outpatient clinic presentations, there was still a significant decrease in the number of new NMSC diagnoses. In order to prevent a delay in the diagnosis of such diseases, alternative methods such as teledermatology

should be used more effectively in crises, patient awareness should be increased by attaching more importance to social information studies on NMSC, and patients' access to specialist physicians in case of suspicious lesions should be facilitated.

CONCLUSION

During the COVID-19 pandemic, there was a decrease in the number of total skin biopsies and the number of total biopsies with diagnosis of NMSC. The health system should be reorganized to effectively handle pandemics and similar crisis periods, and new strategies should be determined concerning patient education, early diagnosis, and treatment approaches for NMSC.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Esmâ İnan Yüksel, İlknur Çalık, Dilek Canat; **Design:** Esmâ İnan Yüksel, İlknur Çalık; **Control/Supervision:** Esmâ İnan Yüksel, Betül Demir, Dilek Canat; **Data Collection and/or Processing:** Esmâ İnan Yüksel, İlknur Çalık; **Analysis and/or Interpretation:** Esmâ İnan Yüksel, Demet Çiçek, Betül Demir, Dilek Canat; **Literature Review:** Esmâ İnan Yüksel, Dilek Canat; **Writing the Article:** Esmâ İnan Yüksel, İlknur Çalık; **Critical Review:** Demet Çiçek, Betül Demir, Dilek Canat; **References and Fundings:** Esmâ İnan Yüksel; **Materials:** İlknur Çalık, Esmâ İnan Yüksel.

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