Have Skin Biopsy Results in Adults Been Affected in the COVID-19 Pandemic?

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ABSTRACT The purpose of this study was to assess how skin biopsy results from adults, which occupy an important place in dermatological practice, have been affected by the COVID-19 pandemic. Adult patients aged over 18 presenting to the dermatology clinical of a tertiary hospital between March 12, 2019 and March 11, 2020, and between March 12, 2020 and March 11, 2021, from whom skin biopsies had been taken and who had undergone pathological examination were included in the study. Pre-COVID-19 pandemic data were compared with post-pandemic data. No significant difference was determined between the two periods in terms of age, sex, type of biopsy, preliminary diagnosis numbers, or clinicopathological correlation ($P>0.05$). The diseases most frequently diagnosed through biopsy before the pandemic were psoriasis (13.7%), pseudopelade of Brocq (6.8%), and fibroepithelial polyp (5.5%), compared with psoriasis (9.4%), basal cell carcinoma (BCC) (6.3%), lichen planus (6.3%), and urticarial vasculitis (6.3%) during the pandemic. Diagnoses of BCC and urticarial vasculitis were significantly elevated after the COVID-19 pandemic ($P<0.05$), while no periodic difference was observed in other diagnoses. A rise in the incidence of various diseases, such as urticarial vasculitis, may be indicative of a risk of asymptomatic COVID-19. Further polymerase chain reaction and/or antibody-based investigations should be carried out in order to establish whether dermatological diseases are associated with asymptomatic COVID-19 cases. Determining the clinical and histopathological aspects of COVID-19, which can progress with various cutaneous findings, will be useful in the early diagnosis and treatment of this novel and life-threatening disease.

KEY WORDS: biopsy, clinicopathological correlation, COVID-19, dermatology, pathology

INTRODUCTION

A number of severe pneumonia cases began appearing in the city of Wuhan in Hubei province, China, in December 2019. The pathogen underlying these cases was identified as the novel and highly infectious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which subsequently spread rapidly across the world. The outbreak was subsequently declared a pandemic by the World Health Organization, which named this new type of pathogen coronavirus disease 2019 (COVID-19) (1). The first case in Turkey was observed on March 11, 2020. The Turkish government subsequently imposed various restrictions at different times, aimed at preventing the spread of the infection. Face-to-face education

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in schools was replaced by distance learning. Flexible working was introduced in public offices and institutions. Hairdressers, restaurants, cafeterias, theaters, cinemas, swimming pools, and shopping malls were closed. Citizens were asked to stay away from hospitals except in emergencies. Domestic and international travel was restricted, and individuals aged over 65 and under 18 were obliged to remain at home. Lockdowns were also imposed on all age groups at specific times in the midweek, at the weekends, and on public holidays. The media broadcasts repeated calls for mask-earing, social distancing, and hygiene, and for the public to stay at home (2). However, the numbers of patients requesting appointments with dermatology outpatient clinics and the spectrum of dermatological diseases observed were significantly impacted by the psychological and other side-effects of the pandemic (3).

Skin biopsy is one of the most frequently employed diagnostic tests in dermatology. The diagnosis of diseases of the skin relies not only on clinical findings, but also on histopathological evidence. Diseases that are not always easily diagnosed clinically can be easily identified through their microscopic characteristics (4,5).

The purpose of this study was to perform a retrospective evaluation of how skin biopsy results in adults, with their important place in dermatology practice, have been affected by the COVID-19 pandemic.

PATIENTS AND METHODS

Study design

This single center retrospective-study was approved by the Ethics Committee of Yozgat Bozok University, Yozgat, Turkey (Decision no: 2017-KAEK-189_2021.04.14_10) and by the Ministry of Health Scientific Research Platform (Application form no: 2021-04-06T09_56_31).

The study was conducted at the Yozgat Bozok University Hospital, a tertiary institution. Adult patients aged over 18, presenting to the dermatology clinical between March 12, 2019, and March 11, 2020 (before the COVID-19 pandemic), and between March 12, 2020, and March 11, 2021 (after the COVID-19 pandemic), from whom skin biopsies had been taken and who had undergone pathological examination were included in the study. These patients' skin biopsy reports and the results of polymerase chain reaction (PCR) tests for COVID-19, if these had been performed, were retrieved from the hospital records. Patients with missing clinical data were excluded from the study.

Diseases were classified on the basis of pathology results as diseases of the sebaceous, eccrine, and apocrine glands (rosacea), eczema/dermatitis (contact dermatitis, nummular dermatitis, atopic dermatitis, and prurigo nodularis), psoriasis, psoriasiform and pityriasiform dermatoses (psoriasis, pityriasis lichenoides chronica, parapsoriasis, and pityriasis rosea), bullous diseases (pemphigus vulgaris), neutrophilic dermatoses (granuloma faciale, panniculitis, and erythema elevatum diutinum, Sweet's syndrome), benign neoplasms and hyperplasias (fibroepithelial polyp, lentigo simplex, seborrheic keratosis, and nevus), light-induced and ionizing radiation-induced diseases (polymorph light eruption, chondrodermatitis nodularis helicis, and radiation dermatitis), precancerous lesions and carcinomas (actinic keratosis, keratoacanthoma, squamous cell carcinoma, basal cell carcinoma (BCC), and metastatic cancer of the skin (renal cell cancer), pigmentation disorders (post-inflammatory hyperpigmentation), immune, autoimmune, autoinflammatory, and rheumatological diseases (urticaria, lichen planus, discoid lupus erythematosus, morphea, Henoch-Schönlein purpura, urticarial vasculitis, polyarteritis nodosa, livedo vasculitis, pigmented purpuric dermatosis, sarcoidosis, and macular amyloidosis), endocrine, metabolic and nutritional diseases (polymorphic eruption of pregnancy), cutaneous pseudolymphomas and lymphomas (Jessner's lymphocytic infiltration, and mycosis fungoides), cutaneous drug reactions (Stevens-Johnson syndrome, acute generalized exanthematous pustulosis, and fixed drug eruption), diseases due to microbial agents (verruca, lupus vulgaris, and Leishmania), hair follicle and related diseases (pseudopelade of Brocq), and other (hemorrhage, granulation tissue, and nonspecific). Since the International Classification of Diseases-10th Revision (ICD-10) was used for entering diagnoses in the clinic, Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology by Wolff *et al*. was employed in the classification of diseases (6).

Agreement between pathology results and each preliminary diagnosis was evaluated. Clinicopathological correlation was regarded as positive if preliminary diagnoses were in agreement with the pathology results.

Statistical analysis

Data analysis was performed on SPSS 18.0 software. The Mann-Whitney U test and Independent Sample T-test were applied for intergroup comparisons of descriptive statistics (mean, standard deviation [SD], and frequency) and quantitative data, while the Chi-Square test was applied in the comparison of qualitative data. Data were expressed as mean ± SD.

P values less than 0.05 were regarded as statistically significant in all cases.

RESULTS

Skin biopsy was performed in 73 adult patients before the COVID-19 pandemic, 43 (58.9%) women and 30 (41.1%) men. The patients' mean age was 48.07±17.26 years (19-86). Sixty-two (84.9%) patients were aged under 65, and 11 (15.1%) were aged 65 or over. The most common procedure was punch biopsy (93.2%), and the most frequent collection site was the extremities (52.1%). One preliminary diagnosis was established by a dermatologist before pathological examination in one patient, two preliminary diagnoses were established in 19 patients, three in 28 patients, four in 11, five in 8, six in 5, and eight in 1 patient. Correlation was present between preliminary diagnosis before pathology examination and pathological diagnosis in 60 (82.2%) patients. Correlation was found with pathology and the first preliminary diagnosis in 32 patients (43.8%), the second preliminary diagnosis in 13 (17.8%), and the third preliminary diagnosis in 15 (20.5%). Biopsy made no contribution to differential diagnosis in 10 (13.7%) patients, and a diagnosis other than the preliminary diagnoses was finally established in three patients (4.1%) (lentigo simplex, granulation tissue, and pigmented purpuric dermatosis in one patient each) (Table 1).

Table 1. Demographic characteristics and agreement with preliminary diagnoses of adult patients undergoing skin biopsy before and after the COVID-19 pandemic

	Before the COVID-19 pandemic n (%)	**After the COVID-19 pandemic n (%)**	***P***
Sex			0.62
Female	43 (58.9)	35 (54.7)	
Male	30 (41.1)	29 (45.3)	
Age group			0.92
19-65 years	62 (84.9)	53 (82.8)	
Over 65	11 (15.1)	11 (17.2)	
*Mean age	48.07 ± 17.26	49.67 ± 14.93	0.56*
Biopsy type			0.27
Punch	68 (93.2)	55 (85.9)	
Excisional	5 (6.8)	9 (14.1)	
Biopsy area			0.70
Head and neck	19 (26)	15 (23.4)	
Body	16 (21.9)	18 (28.1)	
Extremities	38 (52.1)	31 (48.4)	
Number of pre-diagnoses			1.10
2 ≤	20 (27.4)	27 (42.2)	
2>	53 (72.6)	37 (57.8)	
One	1 (1.4)	5 (7.8)	
Two	19 (26)	22 (34.4)	
Three	28 (38.4)	22 (34.4)	
Four	11 (15.1)	6 (9.4)	
Five	8 (11)	7 (10.9)	
Six	5 (6.8)	2 (3.1)	
Seven	-	-	
Eight	1 (1.4)	-	
Agreement with pre-diagnoses			0.87
Agreement	60 (82.2)	51 (79.7)	
No agreement	13 (17.8)	13 (20.3)	
Agreement with the 1st pre-diagnosis	32 (43.8)	34 (53.1)	
Agreement with the 2nd pre-diagnosis	13 (17.8)	9 (14.1)	
Agreement with 3rd or subsequent pre-diagnoses	15 (20.5)	8 (12.5)	
Undiagnosed			
Different diagnosis	10 (13.7)	8 (12.5)	
	3 (4.1)	5 (7.8)	

Note: *P*>0.05; There is no significant difference according to the Chi-Square test. *P>0.05; There is no significant difference according to the Independent Sample T-test.

Skin biopsy was performed in 64 adult patients after the COVID-19 pandemic, 35 women (54.7%) and 29 men (45.3%). The mean age of these patients was 49.67±14.93 years (21-76). Fifty-three (82.8%) were aged under 65, and 11 (17.2%) were 65 or older. The most common biopsy method was punch biopsy (85.9%), and the most frequent biopsy site was the extremities (48.4%). One preliminary diagnosis was established by a dermatologist before pathology examination in 5 patients, two preliminary diagnoses were established in 22 patients, three in 22, four in 6, five in 7, and six in 2. Preliminary diagnoses were correlated with pathological diagnosis in 51 (79.7%) patients at pathology examination. Correlation was determined with pathology and the first preliminary diagnosis in 34 patients (53.1%), with the second in nine (14.1%), and with the third or other preliminary diagnosis in eight (12.5%). Biopsy made no contribution to diagnosis in eight (12.5%) cases, and a diagnosis other than the preliminary diagnoses was finally established in five patients (7.8%) (inverted follicular keratosis, urticaria, and pseudopelade of Brocq in one patient each, and Jessner's lymphocytic infiltration in two patients) (Table 1).

Diseases diagnosed with skin biopsy and total numbers in adult patients before and after the COVID-19 pandemic are shown in Table 2. The PCR test was applied for COVID-19 on seven patients who underwent biopsy, and previous COVID-19 infection was detected in three of these. These patients' biopsy diagnoses were BCC, rosacea, and Sweet's syndrome. None of these diagnoses was linked to COVID-19 infection due to incompatibility of the test time and symptom duration.

No significant difference before and after the COVID-19 pandemic in adult patients undergoing skin biopsy was observed in terms of age, sex, type of biopsy, site of biopsy number of preliminary diagnoses, clinicopathological correlation, or diagnostic groups ($P>0.05$) (Table 1 and Table 2).

No significant difference was also observed in terms of age, sex, biopsy site, type of biopsy, and number of preliminary diagnoses between the groups with and without clinicopathological correlation before and after the COVID-19 pandemic ($P>0.05$).

The most frequently seen diagnostic groups before the COVID-19 pandemic were psoriasis/psoriasiform/pityriasiform dermatoses (21.9%), immune/autoimmune/autoinflammatory/rheumatological diseases (15.1%), and benign neoplasms/hyperplasias (8.2%), while the most frequently observed groups after the pandemic were immune/autoimmune/autoinflammatory/rheumatological diseases (21.9%), psoriasis/psoriasiform/pityriasiform dermatoses (10.9%), precancerous lesions/carcinomas (9.4%), and eczema/dermatitis (9.4%). Diagnoses of BCC and urticarial vasculitis were significantly elevated after the COVID-19 pandemic ($P=0.04$; 0.04), but no periodic differences was observed in other diagnoses ($P>0.05$) (Table 2).

DISCUSSION

Presentations to hospital decreased during the COVID-19 pandemic that rapidly affected the entire world, for reasons such as stay-at-home calls, lockdowns, restrictions specific to certain age groups, and fear of contracting infectious disease (7-10). One multi-center study reported a 77% decrease in presentations to dermatology clinics soon after the pandemic (7). Another study from Turkey reported a 3.5-fold decrease in dermatology clinic presentations in the first month of the COVID-19 pandemic, and an 8.8-fold decrease in the second month (9). Despite some level of reduction in the number of patients undergoing skin biopsy in the present study, no significant decrease was determined. This may be because of the two hospitals in the province of Yozgat, the city hospital was designated as a pandemic hospital, and the university hospital as a non-pandemic hospital. Kartal *et al*. determined a significant decrease in the frequency of presentations to the dermatology clinic during the pandemic among the pediatric and geriatric populations. Those authors attributed this to fear of contracting infection during hospital visits, in addition to the lockdown (7). While there was no significant difference in the mean ages of patients undergoing skin biopsy in the present study, a slight decrease occurred in patients aged 18-65 after the pandemic, and a slight increase in those aged over 65. The decrease in patient numbers may be due to stay-at-home calls and fear of contracting infection in hospital. Diseases such as skin tumor being more frequently observed at advanced ages may be responsible for the slight increase in the geriatric age group. Turan *et al*. observed that female sex predominated in presentations to the dermatology clinic before the COVID-19 pandemic, while gradual equalization between the sexes occurred after the pandemic (9). Kartal *et al*. also observed that the preponderance in favor of women before the pandemic altered in favor of men after the pandemic (7). Although there was no significant sex difference among patients undergoing skin biopsy in the present study, the female-to-male ratio decreased from 1.43 before the pandemic to 1.21 after it. These findings may indicate a difference between the sexes in terms of pandemic risk perception.

Table 2. The distribution of diagnostic groups and diagnoses in adult patients undergoing skin biopsy before and after the COVID-19 pandemic

Diagnostic groups and diagnoses	Before the COVID-19 pandemic n (%)	After the COVID-19 pandemic n (%)	*P*
Diseases of the sebaceous, eccrine, apocrine glands	*1 (1.4)*	*2 (3.1)*	*0.59*
Rosacea	1 (1.4)	2 (3.1)	0.59
Eczema/Dermatitis	*4 (5.5)*	*6 (9.4)*	*0.51*
Contact dermatitis	2 (2.7)	3 (4.7)	0.66
Nummular dermatitis	0 (0)	2 (3.1)	0.21
Atopic dermatitis	1 (1.4)	0 (0)	1.00
Prurigo nodularis	1 (1.4)	1 (1.4)	1.00
Psoriasis, psoriasiform and pityriasiform dermatoses	*16 (21.9)*	*7 (10.9)*	*0.13*
Psoriasis	10 (13.7)	6 (9.4)	0.60
Pityriasis lichenoides chronica	3 (4.1)	0 (0)	0.24
Parapsoriasis	0 (0)	1 (1.6)	0.46
Pityriasis rosea	3 (4.1)	0 (0)	0.24
Bullous diseases	*1 (1.4)*	*0 (0)*	*1.00*
Pemphigus vulgaris	1 (1.4)	0 (0)	1.00
Neutrophilic dermatoses	*3 (4.1)*	*1 (1.6)*	*0.62*
Granuloma faciale	1 (1.4)	0 (0)	1.00
Panniculitis	1 (1.4)	0 (0)	1.00
Erythema elevatum diutinum	1 (1.4)	0 (0)	1.00
Sweet syndrome	0 (0)	1 (1.6)	0.46
Benign neoplasms and hyperplasias	*6 (8.2)*	*5 (7.8)*	*1.00*
Fibroepithelial polyp	4 (5.5)	2 (3.1)	0.68
Lentigo simplex	1 (1.4)	0 (0)	1.00
Seborrheic keratosis	1 (1.4)	2 (3.1)	0.59
Nevus	0 (0)	1 (1.6)	0.46
Light-induced and ionizing radiation-induced diseases	*2 (2.7)*	*1 (1.6)*	*1.00*
Polymorph light eruption	1 (1.4)	0 (0)	1.00
Chondrodermatitis nodularis helicis	1 (1.4)	0 (0)	1.00
Radiation dermatitis	0 (0)	1 (1.6)	0.46
Precancerous lesions and carcinomas	*3 (4.1)*	*6 (9.4)*	*0.30*
Actinic keratosis	1 (1.4)	0 (0)	1.00
Keratoacanthoma	0 (0)	1 (1.6)	0.46
Squamous cell carcinoma	2 (2.7)	0 (0)	0.49
Basal cell carcinoma	0 (0)	4 (6.3)	**0.04***
Metastatic cancer of the skin (renal cell cancer)	0 (0)	1 (1.6)	1.00
Pigmentation disorders	*1 (1.4)*	*4 (6.3)*	*1.18*
Post-inflammatory hyperpigmentation	1 (1.4)	4 (6.3)	1.18
Immune, autoimmune, autoinflammatory, and rheumatological diseases	*11 (15.1)*	*14 (21.9)*	*0.41*
Urticaria	1 (1.4)	1 (1.6)	1.00
Lichen planus	2 (2.7)	4 (6.3)	0.41
Discoid lupus erythematosus	2 (2.7)	1 (1.6)	1.00
Morphea	0 (0)	2 (3.1)	0.21
Henoch-Schönlein purpura	1 (1.4)	1 (1.6)	1.00
Urticarial vasculitis	0 (0)	4 (6.3)	**0.04***
Polyarteritis nodosa	1 (1.4)	0 (0)	1.00
Livedo vasculitis	1 (1.4)	0 (0)	1.00
Pigmented purpuric dermatosis	2 (2.7)	0 (0)	0.49
Sarcoidosis	1 (1.4)	0 (0)	1.00
Macular amyloidosis	0 (0)	1 (1.6)	0.46
Endocrine, metabolic, and nutritional diseases	*1 (1.4)*	*0 (0)*	*1.00*
Polymorphic eruption of pregnancy	1 (1.4)	0 (0)	1.00
Cutaneous psodolymphomas, and lymphomas	*3 (4.1)*	*2 (3.1)*	*1.00*
Jessner's lymphocytic infiltration	1 (1.4)	2 (3.1)	0.59
Mycosis fungoides	2 (2.7)	0 (0)	0.49

Cutaneous drug reactions	*1 (1.4)*	*2 (3.1)*	*0.59*
Stevens-Johnson syndrome	0 (0)	1 (1.6)	0.46
Acute generalized exanthematous pustulosis	0 (0)	1 (1.6)	0.46
Fix drug eruption	1 (1.4)	0 (0)	1.00
Diseases due to microbial agents	*4 (5.5)*	*3 (4.7)*	*1.00*
Verruca	2 (2.7)	1 (1.6)	1.00
Lupus vulgaris	2 (2.7)	1 (1.6)	1.00
Leishmania	0 (0)	1 (1.6)	0.46
Hair follicle and related diseases	*5 (6.8)*	*2 (3.1)*	*0.44*
Pseudopelade of Brocq	5 (6.8)	2 (3.1)	0.44
Other	*11 (15.1)*	*9 (14.1)*	*1.00*
Hemorrhage	0 (0)	1 (1.6)	0.46
Granulation tissue	1(1.4)	0 (0)	1.00
Non-specific	10 (13.7)	8 (12.5)	0.95

Note: $^{*}P<0.05$ significantly different according to the Chi-Square test.

Skin biopsy is an economical and practical diagnostic technique in dermatology clinics (11,12). Histopathological examination may sometimes not yield a definite diagnosis. Studies have reported clinicopathological correlation rates of 56.3-89.7% in patients from different age groups (4,5,11,13-16). This variation may be due to a number of factors. One is sufficient information not being provided to the pathologist. Metin and Atasoy reported a correlation rate between preliminary and definite diagnoses of 58.7%, successful clinicopathological correlation rising to 79.1% (5). Rajaratnam *et al*. similarly observed a 55% accurate diagnosis rate in pathology reports in which clinical information was not included, compared with 78% when clinical information was shared (17). Our clinicopathological correlation rates were 82.2% before the COVID-19 pandemic and 79.7% after the pandemic. The role of our inclusion of clinical information and preliminary diagnoses on the pathology request forms is significant in these high figures. In addition to the inclusion of appropriate clinical information, taking the biopsy from the correct lesion is also important in increasing clinicopathological agreement. The taking of biopsies from recent and mature lesions also increases clinicopathological agreement (4). Similarly to the present study, Aslan *et al*. reported no association between clinicopathological correlation and biopsy type and site, while Korfitis *et al*. reported an association between biopsy site and clinicopathological correlation (4,11). The extremities were the most frequent biopsy site in the present study, which is in agreement with Çakır Akay *et al*. (14). Aslan *et al*. performed 84.1% punch and 11.6% excisional biopsies in their study (4). In the present study, pre-COVID-19 pandemic values were 93.2% punch and 6.8% excisional biopsy, compared with 85.9% punch and 14.1% excisional biopsy during the pandemic. The increase in the proportion of excisional biopsies in the COVID-19 pandemic may derive from restrictions on elective surgery in surgical departments and to individuals presenting to the dermatology department rather than surgical departments due to fear of infection in settings such as operating theaters.

The pre-COVID-19 pandemic literature contains a number of inconsistencies in terms of dermatological conditions undergoing skin biopsy. Metin and Atasoy (5) reported the conditions most frequently subjected to skin biopsy as tumors (26%), papulosquamous diseases (10.9%), and nevi (10.3%), while Aslan *et al*. (4) reported inflammatory dermatoses (20.4%), benign tumors (14.6%), and malignant tumors (10.7%) as the conditions most frequently involving skin biopsy, and Çakır Akay *et al*. (14) listed papulosquamous diseases (19.3%), dermatitis (17.6%), and benign skin/cutaneous adnexal tumors (11.6%). These inconsistencies may derive from patient numbers, different patient classifications between studies, demographic and regional variations in diseases seen in dermatology clinics, and inter-clinic variation in skin biopsy application. The conditions most frequently subjected to skin biopsy in the present study were psoriasis/psoriasiform/pityriasiform dermatoses (21.9%), immune/autoimmune/autoinflammatory/rheumatological diseases (15.1%), and benign neoplasms/hyperplasia (8.2%) before the COVID-19 pandemic, and immune/autoimmune/autoinflammatory/rheumatological diseases (21.9%), psoriasis/psoriasiform/pityriasiform dermatoses (10.9%), precancerous lesions/carcinomas (9.4%), and eczema/dermatitis (9.4%). Increased diagnoses of lichen planus and urticarial vasculitis played a role in immune/autoimmune/autoinflammatory/rheumatological disease coming to occupy first place after the pandemic. No significant difference was observed before and after the COVID-19 pandemic in terms of patient numbers in the diagnostic groups. Based on our results, the diseases most frequently diagnosed through biopsy were psoriasis (13.7%), pseudopelade of Brocq (6.8%), and fibroepithelial polyp (5.5%) before the pandemic, and psoriasis (9.4%), BCC (6.3%), lichen planus (6.3%), and

urticarial vasculitis (6.3%) after the pandemic. Diagnoses of BCC and urticarial vasculitis were statistically significantly higher after the COVID-19 pandemic, while no difference was observed in other diagnoses between the two time periods. No change was determined in the prevalence of psoriasis during the pandemic, and it remained the most frequent diagnosis. Psoriasis is a chronic disease with an adverse impact on quality of life. Patients' desire for medical assistance may therefore outweigh the perceived risk of COVID-19. Symptomatic diseases involving widespread lesions and adversely affecting quality of life such as lichen planus and urticarial vasculitis became more prominent during the pandemic. The increase in the numbers of BCC cases may be attributable to restrictions on surgery in surgical branches and to individuals presenting to the dermatology department rather than surgical departments due to fear of infection in setting such as operating rooms.

Various recently reported dermatological manifestations in COVID-19 cases include chilblains/pernio-like lesions, vesicular monomorphic eruptions, urticarial lesions, maculopapular eruptions, acro-ischemia, rash with petechiae/purpuric rash, acute rash reminiscent of symmetrical drug-related intertriginous and flexural exanthema, erythema multiforme-like rash and Kawasaki-like disease, and others (such as mottling, pityriasis rosea-like eruptions, Sweet's syndrome-like eruptions, pustular rash, unspecified rash, and androgenetic alopecia (the Gabrin sign)) (18-22). The pathological mechanisms involved in the emergence of skin lesions in COVID-19 patients are still unclear. Cutaneous manifestations in patients with COVID-19 may be classified into two major groups in terms of pathomechanisms. The first involves clinical features similar to viral exanthems (an immune response to viral nucleotides), while the other involves cutaneous eruptions secondary to systemic outcomes resulting from COVID-19 (particularly vasculitis and thrombotic vasculopathy) (18). Fattori *et al*. examined the skin biopsies of six patients with morbilliform eruption infected with SARS-CoV-2. All six biopsies exhibited differing levels of spongiosis, perivascular inflammatory infiltrates of the dermis, and discrete interface dermatitis in some instances. The presence of the virus was not demonstrated with *in situ* hybridization and immunohistochemistry in any cutaneous specimens (23). Mirza *et al*. reported that the time elapsing from upper airway disease symptoms in COVID-19 to cutaneous findings ranges between three and 38 days, and that approximately one patient in 10 was asymptomatic and presented with cutaneous findings only (21). They therefore suggested that dermatological findings may play an important role in the early detection of cases and control of spread. We observed an increase in urticarial vasculitis cases in the pandemic. These cases had not been subjected to any test for diagnosis of COVID-19. Urticarial vasculitis may be an important finding in terms of asymptomatic infection in COVID-19.

An increase in presentations to the dermatology clinic during the COVID-19 pandemic has also been reported for patients with pityriasis rosea (3,7,9). Some authors have hypothesized that SARS-CoV-2 may reactivate latent infections such as HHV-6/7 and herpes zoster by behaving as a transactivator agent (24,25). Pityriasis rosea-like cutaneous eruption was described in an adult case from Iran (26). A digitate variant was detected in a male patient of advanced age admitted to hospital with severe COVID-19 disease. Mild diffuse epidermal spongiosis, spongiotic vesicles containing lymphocytes, and Langerhans cells were observed at skin biopsy. The papillary dermis was described as slightly edematous. The presence of a lymphohistiocytic infiltrate was also observed in the upper dermis (27). The frequency of pityriasis rosea in adult patients undergoing biopsy was 4.1% before the pandemic in the present study, but no cases were diagnosed during it. Pityriasis rosea is a benign papulosquamous disease. It is also self-limiting even if not treated. The condition is characterized by a "herald patch" followed by scaly oval patches on the trunk and proximal extremities, resulting in a "Christmas tree" appearance. Accompanying collarette scaling is frequently reported (6). Diagnosis can be based on these characteristics without histopathological examination. Biopsy is not performed on patients with pityriasis rosea with a typical clinical appearance in our clinic, which may explain why pityriasis rosea was not diagnosed during the pandemic.

Limitations

The principal limitations of this study were its retrospective nature, the fact it was conducted in a single center, the absence of some dermatological disease groups, and the low numbers of some dermatoses. In addition, this study examined the effect of the COVID-19 pandemic on skin biopsy results during a one-year period. However, new results may emerge as the pandemic continues.

CONCLUSION

Sex, age, biopsy type, biopsy site, number of prediagnoses, clinicopathological correlation appear not to be statistically affected in adult patients undergoing skin biopsy before and after the COVID-19 pandemic, but different results may occur with the

continuation of the pandemic. Moreover, a rise in the incidence of various diseases, such as urticarial vasculitis, may be indicative of a risk of asymptomatic COVID-19. Further polymerase chain reaction and/or antibody-based investigations should be carried out in order to establish whether dermatological diseases are associated with asymptomatic COVID-19 cases. Determining the clinical and histopathological aspects of COVID-19, which can progress with various cutaneous findings, will be useful in the early diagnosis and treatment of this novel and life-threatening disease.

References:

1. Guo YR, Cao QD, Hong ZS, Tan YY, Chen SD, Jin HJ, *et al*. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak - an update on the status. Mil Med Res. 2020;7:11.
2. New Coronavirus Disease (COVID-19). https://covid19bilgi.saglik.gov.tr/tr/. Accessed July 20, 2020.
3. Kutlu Ö, Metin A. Relative changes in the pattern of diseases presenting in dermatology outpatient clinic in the era of the COVID-19 pandemic. Dermatol Ther. 2020;33:e14096.
4. Aslan C, Göktay F, Mansur AT, Aydıngöz IE, Güneş P, Ekmekçi TR. Clinicopathological consistency in skin disorders: a retrospective study of 3949 pathological reports. J Am Acad Dermatol. 2012;66:393-400.
5. Metin MS, Atasoy M. The importance of clinical and histopathological correlation in the diagnosis of skin diseases: An eleven years' experience. Ann Med Res. 2019;26:304-8.
6. Wolff AK, Jonhson RA, Saavedra AP, Roh EK (2017). Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology (8th ed.). New York, Mc Graw Hill.
7. Kartal SP, Çelik G, Sendur N, Aytekin S, Serdaroğlu S, Doğan B, *et al*. Multicenter study evaluating the impact of COVID-19 outbreak on dermatology outpatients in Turkey. Dermatol Ther. 2020;33:e14485.
8. Gisondi P, Piaserico S, Conti A, Naldi L. Dermatologists and SARS-CoV-2: the impact of the pandemic on daily practice. J Eur Acad Dermatol Venereol. 2020;34:1196-201.
9. Turan Ç, Metin N, Utlu Z, Öner Ü, Kotan ÖS. Change of the diagnostic distribution in applicants to dermatology after COVID-19 pandemic: What it whispers to us? Dermatol Ther. 2020;33:e13804.
10. Kwatra SG, Sweren RJ, Grossberg AL. Dermatology practices as vectors for COVID-19 transmission: A call for immediate cessation of nonemergent dermatology visits. J Am Acad Dermatol. 2020;82:e179-80.
11. Korfitis C, Gregoriou S, Antoniou C, Katsambas AD, Rigopoulos D. Skin biopsy in the context of dermatological diagnosis: a retrospective cohort study. Dermatol Res Pract. 2014;2014:734906.
12. Elston DM, Stratman EJ, Miller SJ. Skin biopsy: Biopsy issues in specific diseases. J Am Acad Dermatol. 2016;74:1-16.
13. Uçak H, Uçmak D, Akkurt ZM, Sula B, Türkçü G, Arıca M. Clinicopathologic correlation of skin biopsies in pediatric patients who consulted to dermatology outpatient clinic of a university hospital. Dicle Med J. 2014;41:526-8.
14. Çakır Akay GA, Erdoğan FG, Umudum H. Retrospective Evaluation of Clinicopathological Consistency of Skin Biopsies in Adult Patients. J Ankara Univ Fac Med. 2018;71:207-11.
15. Afşar FŞ, Aktaş S, Diniz G, Ortaç R. The Role of Biopsy in Pediatric Dermatopathology. Turkderm. 2011;45:137-9.
16. Çölgeçen E, Şahin S, Gürel G, Aytekin B. Clinicopathological Corrrelation of Skin Biopsies in Pediatric Patients. J Ankara Univ Fac Med. 2020;73:234-8.
17. Rajaratnam R, Smith AG, Biswas A, Stephens M. The value of skin biopsy in inflammatory dermatoses. Am J Dermatopathol. 2009;31:350-3.
18. Kaya G, Kaya A, Saurat JH. Clinical and Histopathological Features and Potential Pathological Mechanisms of Skin Lesions in COVID-19: Review of the Literature. Dermatopathology (Basel). 2020;7:3-16.
19. Wollina U, Karadağ AS, Rowland-Payne C, Chiriac A, Lotti T. Cutaneous signs in COVID-19 patients: A review. Dermatol Ther. 2020;33:e13549.
20. Kanitakis J, Lesort C, Danset M, Jullien D. Chilblain-like acral lesions during the COVID-19 pandemic ("COVID toes"): Histologic, immunofluorescence, and immunohistochemical study of 17 cases. J Am Acad Dermatol. 2020;83:870-5.
21. Mirza FN, Malik AA, Omer SB, Sethi A. Dermatologic manifestations of COVID-19: a comprehensive systematic review. Int J Dermatol. 2021;60:418-50.
22. Wollina U, Chiriac A, Karadag AS. The Dermatological Spectrum of Coronavirus Disease-19 Disease: Cutaneous Signs for Diagnostics and Prognosis and an Expanded Classification. Open

Access Macedonian Journal of Medical Sciences. 2020;8:294-303.

23. Fattori A, Cribier B, Chenard MP, Mitcov M, Mayeur S, Weingertner N. Cutaneous manifestations in patients with coronavirus disease 2019: clinical and histological findings. Hum Pathol. 2021;107:39-45.
24. Ciccarese G, Parodi A, Drago F. SARS-CoV-2 as possible inducer of viral reactivations. Dermatol Ther. 2020;33:e13878.
25. Dursun R, Temiz SA. The clinics of HHV-6 infection in COVID-19 pandemic: Pityriasis rosea and Kawasaki disease. Dermatol Ther. 2020;33:e13730.
26. Ehsani AH, Nasimi M, Bigdelo Z. Pityriasis rosea as a cutaneous manifestation of COVID-19 infection. J Eur Acad Dermatol Venereol. 2020;34:e436-7.
27. Sanchez A, Sohier P, Benghanem S, L'Honneur AS, Rozenberg F, Dupin N, *et al*. Digitate Papulosquamous Eruption Associated With Severe Acute Respiratory Syndrome Coronavirus 2 Infection. JAMA Dermatol. 2020;156:819-20.