

Clinicopathological concordance in the diagnosis of skin diseases: a retrospective analysis of 5000 histopathology reports

Fahad Mohammed Al-Saif,^{ab} Salman Abdulaziz Binsufayan,^{ab} Abdulaziz Hasan Alhussain,^a Tuqa Morad Alkaff,^a Hesham Mohammed Alshaikh,^{ab} Mosfer Saeed Aldosari,^{ab} Saud Abdulaziz Binsufayan,^a Rawan Murshed AlTaleb,^a Hend Metia Alotaibi,^{ab} Mohammed Abdulaziz Alshahwan^{ab}

From the ^aDepartment of Dermatology, College of Medicine, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia; ^bDepartment of Dermatology, King Saud University, Riyadh, Saudi Arabia

Correspondence: Dr. Salman Abdulaziz Binsufayan · Department of Dermatology, King Khalid University Hospital, Riyadh 11462, Saudi Arabia · T: +966555999864 · sabinsufayan@gmail.com · ORCID: <https://orcid.org/0000-0002-3065-6794>

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BACKGROUND: The accuracy of clinical diagnoses of skin diseases has not been researched in Saudi Arabia.

OBJECTIVES: Assess concordance between the histopathological and clinical diagnosis in skin diseases.

DESIGN: Retrospective.

SETTING: Academic tertiary care center.

METHODS: Demographic, clinical and pathological data were collected from the medical record for the period 1997-2013.

MAIN OUTCOME MEASURES: Concordance between the pathological and clinical diagnosis.

SAMPLE SIZE: 4268 cases.

RESULTS: Of 4268 biopsies, 2440 (58.1%) were females. The mean age (SD) of patients was 36.9 (17.8) years. The three most common locations from which skin biopsies were retrieved in descending order were the lower extremity (1123; 29.1%), head, neck, scalp and hair (1033; 26.7%) and trunk (853; 22.1%). Overall concordance was 75.9% (partial concordance 47.6%, full concordance 28.3%). Biopsies from the oral mucosa and lips had the lowest concordance (overall 58.5%, full 26.4%) at $P=.004$. Overall concordance was highest for the following three diagnoses: malignant neoplasms, 88%; vesiculobullous diseases 87%; urticarias, erythemas, and purpuras 87%.

CONCLUSION: There is considerable variability in concordance among different histopathological diagnoses. The full concordance between the clinical diagnosis and the pathological diagnosis is low. This is a reflection of the fact that the biopsies were obtained only in cases where the clinical diagnosis was a dilemma.

LIMITATIONS: Single center, retrospective, incomplete medical records, low percentage of biopsies were assessed by dermatopathologists.

CONFLICT OF INTEREST: None.

Dermatologists tend to rely on clinical diagnosis more than other medical specialties, reserving investigations for confirmation in a small number of cases.¹ Approximately 1.3% of patients attending the dermatology clinic need a skin biopsy.¹ Skin biopsy is one of the recognized tools used in the diagnosis of skin diseases, performed mainly to improve the accuracy of diagnosis, evaluate therapy, and assess the prognosis of a wide range of skin diseases.^{2,3} Skin diseases that frequently require skin biopsy include inflammatory dermatoses such as dermatitis and psoriasis and malignancies such as melanomas and epitheliomas.⁴

Although both clinical and histopathological data are critical for the proper diagnosis of several skin disorders, few studies have examined concordance or the agreement between clinical and histopathological diagnoses of skin disorders.^{1,4-6} In these studies, agreement of both diagnoses has ranged between 67% and 87%, depending on the study definition of concordance and whether clinical data were available to the pathologist.^{1,4-7} Additionally, several biopsy-related factors can influence the diagnostic yield of a skin biopsy.^{8,9} Insufficient clinical information on the skin biopsy requisition form is a common finding and is considered an important challenge for accurate histopathological diagnosis.¹⁰⁻¹³ Nevertheless, the clinicopathological concordance of biopsies referred by dermatologists is probably better than those referred by physicians in other medical disciplines.^{7,14,15}

Few studies have provided group-specific clinicopathological concordance of skin diseases diagnosed by dermatologists.^{1,5} Additionally, such concordance has never been examined locally or regionally. The objectives of the current study were to examine the clinicopathological concordance of different skin diseases diagnosed by dermatologists at a tertiary care setting and to examine the effect of biopsy-related factors, various differential diagnoses, and specialization of the pathologist on such concordance.

METHODS

This study was conducted at the Department of Dermatology at King Khalid University Hospital in Riyadh (KKUH), Saudi Arabia. KKUH is an 800-bed tertiary care teaching hospital affiliated with the King Saud University. The hospital is governmentally funded and provides free primary to tertiary healthcare services for Saudi patients from the northern Riyadh area. The study design was approved by the institutional review board of the College of Medicine at King Khalid University Hospital (approval number E-18-3114) and

the procedures followed were in accordance with the Helsinki Declaration of 1975, as amended in 1983. The requirement for informed consent was waived because of the retrospective nature of the study. Data were collected through a retrospective review of the charts and histopathological reports of patients whose skin biopsies were examined at the clinical pathology laboratory of KKUH between 1997 and 2013. Exclusion criteria included lack of clinical or histopathological diagnosis or non-specific clinical or histopathological diagnosis. There were no exclusion criteria based on age, sex, hospital location (inpatient versus clinic), site of biopsy, or type of biopsy.

A data collection sheet was developed to collect data on the age, sex, date and number of biopsy, site of biopsy, type of biopsy, histopathological diagnosis, clinical diagnosis, clinicopathological concordance, and type of pathologist (general or dermatopathologist). The data were collected and reviewed by trained specialists at KKUH. Two dermatology specialists classified histopathological diagnoses into predetermined categories of skin diseases and evaluated the study outcome. The classification of skin diseases was based on ICD-10 and Dermatology (Bologna) textbook.^{16,17} The main study outcome was clinicopathological concordance, which included three groups. Full concordance was defined as identical provisional clinical and histopathological diagnosis.¹ Partial concordance (corroborative) was defined as inclusion of the histopathological diagnosis as one of the clinical differential diagnosis recorded by the dermatologist.¹ Discordance was defined as incompatibility between the histopathological diagnosis and both the provisional clinical diagnosis and the differential diagnosis.¹ Overall concordance was defined as both full and partial concordance combined.

Data are presented as mean and standard deviation for continuous variables and frequencies and percentages for categorical variables. The chi-square test was used to test for significant differences in clinicopathological concordance (overall and full concordance) in relation to the different characteristics of the study biopsies and histopathological diagnoses. All *P* values were two-tailed. A *P* value <.05 was considered significant. IBM SPSS software (release 23.0; IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

RESULTS

Of the 5000 histopathological biopsies, clinicopathological concordance could not be assessed in 648 biopsies because of non-specific histopathological diagnosis (*n*=625), lack of clinical diagnosis (*n*=47), or lack

of histopathological diagnosis (n=8). Additionally, 84 biopsy results were further excluded due to duplicate patient identification number. Finally, 4268 biopsies were included in the final analysis.

Table 1 shows the sociodemographic and clinical characteristics of the patients included in the study. The age ranged between 1 and 97 years, with a mean (SD) of 36.9 (17.8) years. Most (57.9%) biopsies were obtained from adults between 19 and 49 years, followed by older adults (25.9%) and children (16.2%). Most (58.1%) of the biopsies were from female subjects. The most frequent sites of skin biopsies were the lower extremity (29.1%), followed by the head/neck/scalp/hair (26.7%), trunk (22.1%), upper extremity (21.2%), and other sites (4.7%). The most common type of skin biopsies was punch biopsy (82.1%), followed by excisional biopsy (12.5%) and other types of skin biopsies such as shave and incisional (5.4%). The most common histopathological diagnosis was under papulosquamous and eczematous dermatoses (26.2%), followed by benign neoplasms (20.6%); pigmentary diseases (9.1%); urticarias, erythemas, and purpuras (7.4%); rheumatologic and connective tissue diseases (6.2%); infectious diseases (5.9%); malignant neoplasms (4.6%); and other skin diseases (20.0%). Most of the pathologists were general pathologists (83.7%); only 16.3% were dermatopathologists.

After evaluating clinicopathological concordance in the diagnosis of skin disorders among all 4268 biopsies,

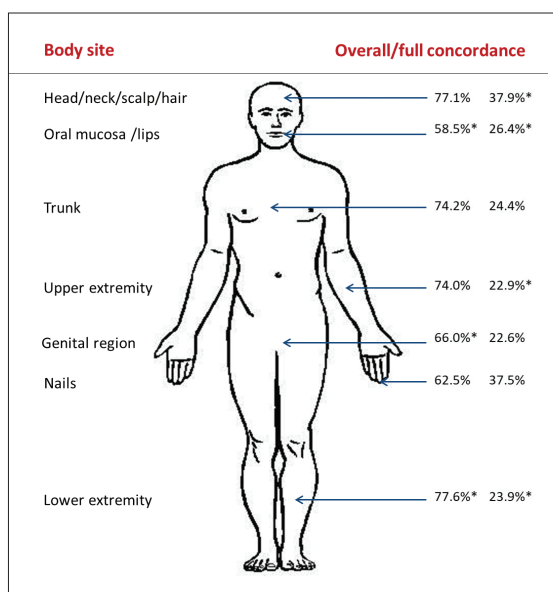


Figure 1. Clinicopathological concordance in the diagnosis of skin disorders by the site of skin biopsy. *Indicate a significantly higher or lower concordance than other body sites

Table 1. Sociodemographic and clinical characteristics of the study biopsies.

Sex	
Male	1758 (41.9)
Female	2440 (58.1)
Patient age (years)	
Children (≤ 18 years)	676 (16.2)
Younger adults (19-49 years)	2416 (57.9)
Older adults (≥ 50 years)	1081 (25.9)
Type of skin biopsy (missing data: n=790, 18.5%)	
Punch	2854 (82.1)
Excisional	435 (12.5)
Others	189 (5.4)
Histopathological diagnoses	
Papulosquamous and eczematous dermatoses	1118 (26.2)
Benign neoplasms	881 (20.6)
Pigmentary diseases	389 (9.1)
Urticarias, erythemas, and purpuras	316 (7.4)
Rheumatologic and connective tissue diseases	265 (6.2)
Infectious diseases	251 (5.9)
Malignant neoplasms	195 (4.6)
Hair, nails, and mucous membranes	153 (3.6)
Adnexal diseases	130 (3.0)
Vesiculobullous diseases	127 (3.0)
Environmental diseases	100 (2.3)
Vascular diseases	82 (1.9)
Metabolic and systemic diseases	71 (1.7)
Genodermatoses	29 (0.7)
Others	161 (3.8)
Drug-related diagnoses	
No	4173 (97.8)
Yes	95 (2.2)
Type of pathologist	
General pathologist	3505 (83.7)
Dermatopathologist	685 (16.3)

Data are number (%) or mean (SD).

Table 2. Clinicopathological concordance in the diagnosis of skin diseases by characteristics of the study biopsies.

	Fully concordant	Partially concordant	Discordant	P value ^a	P value ^b
Sex					
Male	496 (28.2)	850 (48.4)	412 (23.4)	.296	.569
Female	682 (28.0)	1152 (47.2)	606 (24.8)		
Age group					
Children (≤18 years)	220 (32.5)	316 (46.7)	140 (20.7)	.036	.007
Younger adults (19-49 years)	678 (28.1)	1148 (47.5)	590 (24.4)		
Older adults (≥50 years)	270 (25.0)	529 (48.9)	282 (26.1)		
Histopathological diagnoses					
Papulosquamous and eczematous dermatoses	185 (16.5)	686 (61.4)	247 (22.1)	.070	<.001
Benign neoplasms	487 (55.3)	175 (19.9)	219 (24.9)	.548	<.001
Pigmentary diseases	34 (8.7)	194 (49.9)	161 (41.4)	<.001	<.001
Urticarias, erythemas, and purpuras	85 (26.9)	189 (59.8)	42 (13.3)	<.001	<.001
Rheumatologic and connective tissue diseases	54 (20.4)	163 (61.5)	48 (18.1)	.019	<.001
Infectious diseases	64 (25.5)	122 (48.6)	65 (25.9)	.489	.560
Malignant neoplasms	57 (29.2)	114 (58.5)	24 (12.3)	<.001	<.001
Hair, nails, and mucous membranes	68 (44.4)	53 (34.6)	32 (20.9)	.350	<.001
Adnexal diseases	27 (20.8)	68 (52.3)	35 (26.9)	.442	.153
Vesiculobullous diseases	36 (28.3)	75 (59.1)	16 (12.6)	.002	.005
Environmental diseases	11 (11.0)	46 (46.0)	43 (43.0)	<.001	<.001
Vascular diseases	19 (23.2)	28 (34.1)	35 (42.7)	<.001	<.001
Metabolic and systemic diseases	23 (32.4)	38 (53.5)	10 (14.1)	.047	.138
Genodermatoses	8 (27.6)	18 (62.1)	3 (10.3)	.082	.167
Others	50 (31.1)	63 (39.1)	48 (29.8)	.083	.072
Drug-related diagnoses					
No	1200 (28.8)	1967 (47.1)	1006 (24.1)	.831	<.001
Yes	8 (8.4)	65 (68.4)	22 (23.2)		

Data are number (%). P value^a statistical difference in overall concordance in different categories. P value^b statistical difference in full concordance in different categories.

1208 (28.3%) were fully concordant, 2032 (47.6%) were partially concordant (corroborative), and 1028 (24.1%) were discordant. The overall concordance was not different between male and female subjects but was better in children than in adults (P=.036). The overall concordance was slightly better in biopsies obtained from the lower extremity (P=.041) but worse in biopsies

obtained from the genital region and the oral mucosa/lips (P=.024 and P=.004, respectively) (Figure 1). The full concordance was considerably higher in biopsies obtained from the head/neck/scalp/hair (P<.001) but lower in biopsies obtained from the upper extremity, the lower extremity, and the oral mucosa/lips (P=.003, P<.001, and P=.011, respectively). Excisional biopsy

(full 53.6%, partial 17.4%, overall 71%) had lower overall ($P=.012$) but higher full ($P<.001$) concordance compared with punch (full 22.4%, partial 53.3%, overall 75.7%) and other types of biopsy (full 45.5%, partial 27.5%, overall 73%).

There was considerable variability in the overall and full clinicopathological concordances among different histopathological diagnoses (**Table 2**). Compared with other disease categories, the following histopathological diagnoses had significantly better overall concordance: malignant neoplasms (88%, $P<.001$); vesiculobullous diseases (87%, $P=.002$); urticarias, erythemas, and purpuras (87%, $P<.001$); metabolic and systemic diseases (86%, $P=.047$); and rheumatologic and connective tissue diseases (82%, $P=.019$). On the other hand, the following diagnoses had significantly lower overall concordance: pigmentary (59%, $P<.001$), vascular (57%, $P<.001$), and environmental diseases (57%, $P<.001$). Although genodermatoses had the highest overall clinicopathological concordance (90%), the difference from non-genodermatoses was not significant ($P=.082$), probably due to the small number of genodermatoses biopsies ($n=29$). Furthermore, the highest full concordances were observed with benign neoplasms (55%, $P<.001$) and hair, nails, and mucous membranes diseases (44%, $P<.001$), whereas the lowest full concordances were observed with pigmentary diseases (9%, $P<.001$), rheumatologic and environmental diseases (11%, $P<.001$), and connective tissue diseases (20%, $P<.001$). Dermatopathologists (full 21.2%, partial 53.5%, overall 74.7%) had lower full concordance ($P<.001$) but similar overall concordance ($P=.512$) to general pathologists (full 29.4%, partial 46.5%, overall 75.9%). The clinicopathological concordance over the years of the study did not show major differences or special trends (**Figure 2**).

DISCUSSION

We report an overall 76% clinicopathological concordance in a wide range of skin diseases diagnosed by dermatologists at a tertiary care hospital over more than 15 years. This finding is generally similar to previous studies that assessed the accuracy of clinical diagnoses established by dermatologists with a subsequent biopsy confirmation. The concordance in these studies ranged between 67% and 87%.^{1,4,5,7} For example, an evaluation of 3949 skin biopsies over 10 years in a hospital in Turkey showed that pathological diagnoses were concordant with clinical diagnoses in 76.8% of the cases.⁵ Additionally, a review of more than 6700 skin biopsies over 3 years in a hospital in Greece showed that the pathological diagnoses were concordant with

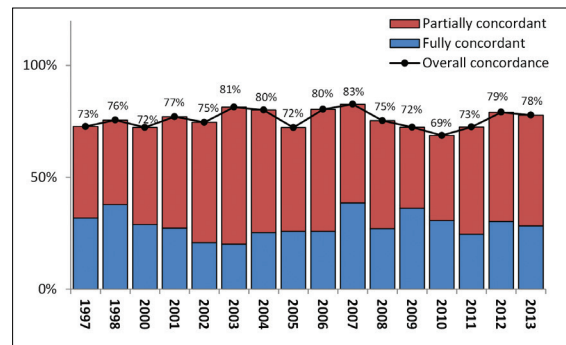


Figure 2. Trend of clinicopathological concordance in the diagnosis of skin disorders.

the clinical diagnoses in 68% of the cases.⁴ Moreover, a review of 371 skin biopsies over a year in a hospital in India showed that pathological diagnosis was concordant with provisional diagnosis in 67.4% of the cases, concordant with one of the clinical differential diagnosis in 19.1% of the cases, and discordant with either provisional or differential clinical diagnosis in 13.5% of the cases.¹

The definition of clinicopathological concordance used in this study was similar to that used by Sa and Kumar, which differentiated between partial and full concordance.¹ A similar strategy of defining concordance was used by Sellheyer and Bergfeld but without such differentiation.⁷ However, the definition of clinicopathological concordance by other studies was slightly different. For example, Aslan et al defined clinicopathological concordance as definite or descriptive pathological diagnosis that is concordant with the clinical diagnosis.⁵ Additionally, Korfitis et al recognized four groups of clinicopathological concordance based on similarity of histological diagnoses with specific clinical diagnosis, disease category, and being a subset of or partially overlapping with the proposed clinical diagnoses.⁴ Since all the above definitions used histopathological reports as gold standard, the variability in defining concordance appeared to have a minimal impact on the findings of these studies, which reported relatively comparable concordances.^{1,4,5,7} Interestingly, in this study, the full concordance was low across all types of biopsies and all locations and was approximately one-third of the overall concordance (28% versus 76%), and it was even less than 20% in some diseases such as malignant neoplasms; urticarias, erythemas, and purpuras; and vesiculobullous diseases. This probably reflects the clinical nature of these diseases, which could have variable presentations and multiple differential diagnosis. Additionally, clinicians usually get biopsies only in cases where the diagnosis was a dilemma, and some derma-

tologists do not require biopsy in presentations that are typical of certain diseases and only reserve biopsy to investigate diseases that have several differential diagnoses.

As demonstrated by our study results, there is higher overall concordance in children compared to adults as well as higher overall concordance in all types of biopsies taken from the lower extremity as compared to other sites. In both instances, this could be due to higher incidence of certain diseases that are easier to diagnose, clinically as well as histopathologically, in specific age groups or with predilection for special sites respectively.

Although there are many types of skin biopsies, dermatologists usually prefer punch biopsy due to easy technique and minimal bleeding. This was very obvious in this study and in a previous study where more than 80% of the biopsies were punch biopsy.⁵ Several biopsy-related factors can affect the ability of the pathologist to reach correct diagnosis of skin diseases.^{8,9} These include the proper indication, the correct choice of biopsy site and technique, and appropriate methods of tissue fixation and processing.⁸ With the exception of excisional biopsy, the effect of biopsy technique on concordance in the present study was minimal. As stated earlier, although excisional biopsy had a better full concordance, it also had a lower overall concordance compared with other types of biopsy. This finding can be explained by the documentation of a single rather than multiple differential diagnosis by the dermatologist in specific situations, for example, excluding malignancy for suspicious pigmented lesions, and diagnosing subepidermal lesions. Additionally, the better full concordance of excisional biopsy may reflect the fact that it provides the pathologist with sufficient tissues to examine. Indeed, inadequate specimens have been reported as one of the most important challenges for dermatopathologists to reach accurate diagnosis.¹² Previous studies either did not examine the impact of biopsy-related factors on concordance or showed controversial findings.^{1,4-7} For example, Aslan et al failed to show any association between biopsy type and concordance, whereas Korfitis et al showed a significant association between biopsy site and concordance.^{4,5}

The most common histopathological diseases observed in this study were papulosquamous and eczematous dermatoses and benign neoplasms, which accounted for close to half of the cases. This was comparable to other studies that examined all types of skin diseases.^{1,5} The current findings showed a considerable variability in the full and overall clinicopathological concordances among different histopathological diagnoses. Very similar to our findings, Aslan et al found

higher concordance with bullous diseases, connective tissue diseases, metabolic diseases, hereditary disorders, and inflammatory dermatoses but considerably lower concordance with pigmented and environmental diseases.⁵ Likewise, Sa and Kumar found that skin tumors and vesiculobullous diseases had the highest full and overall concordances.¹ The explanation of this variability in concordance is not straightforward, because it depends on several disease-specific factors such as the sensitivity and the specificity of the histopathological findings, dermatologist-specific accuracy in clinical diagnosis, the completeness and the quality of clinical information provided to the pathologist, the biopsy request rate (referral rate) of different diseases, and early versus late presentation of certain diseases.

In our study, the clinical provisional or differential diagnosis was sent with the biopsy to the pathologist and concordance was evaluated by trained dermatologists. Previous studies showed that providing high-quality clinical information with the biopsy improves histopathological diagnostic accuracy, whereas blinding pathologists to the clinical data of biopsies referred by dermatologists or other physicians was associated with marked reduction in the rate of clinicopathological concordance.^{5,6,13} Furthermore, it has been reported that without basic dermatology knowledge, the clinicopathological concordance of skin diseases diagnosed by non-dermatological physicians is compromised.⁷ Therefore, it is extremely important that dermatologists work closely with pathologists to optimize the significance of biopsy results.⁸ Meanwhile, however, dermatopathologists and general pathologists in our study had similar overall concordance. Additionally, the observed lower full concordance and higher partial concordance among dermatopathologists compared to general pathologists may possibly be elucidated by their wider range of clinical dermatology knowledge that guide them to be more selective or more inclusive of certain differential diagnosis depending on the situation.

This study is the first study to examine clinicopathological concordance in a wide range of skin diseases in Saudi Arabia and the region. Additionally, it used a large sample size, a standard definition of concordance and disease classification, trained data collectors and qualified concordance evaluators. Nevertheless, we acknowledge few limitations. As it is a single center retrospective study, the findings should be generalized with caution. Concordance could not be assessed in approximately 13% of the biopsies. However, this was similar to other studies that showed results between 11% and 25% of the biopsies.^{4,5} Moreover, a considerable part of the data regarding the clinical setting was missing in the

medical records and only a minority of cases were evaluated by dermatopathologists. Nonetheless, this study will contribute to future multicenter prospective studies exploring a detailed relationship between clinical and histopathological diagnoses, including inter-evaluator concordance.

In conclusion, we report an overall 76% clinicopathological concordance in a wide range of skin diseases diagnosed by dermatologists at a tertiary care hospital

in Saudi Arabia. There is considerable variability in concordance among different histopathological diagnoses. With the exception of excisional biopsy, the impact of biopsy technique on concordance was minimal. Biopsies obtained from the genital region, oral mucosa/lips, and nails had a lower concordance compared to other body sites. These findings should enlighten dermatologists about clinical diseases that would most likely benefit from biopsy request.

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