ORIGINAL ARTICLE

ASSOCIATION OF CLINICAL DIAGNOSIS WITH HISTOPATHOLOGY IN VARIOUS SKIN DISEASES

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Background: Dermatological diagnosis are mainly clinical; however, skin biopsies are frequently done to support clinical diagnosis when in doubt. Aim of this study is to relate the clinical diagnosis of various dermatological conditions with histopathological diagnosis. **Methods:** In this descriptive prospective study, 223 patients were enrolled from dermatology OPD at Benazir Bhutto Hospital through non-probability consecutive sampling. Patients were diagnosed clinically and skin biopsies of all patients were taken after informed consent and clinical data was sent to a histopathologist. **Results:** Patients between ages of 2–85 years were evaluated. Mean age was 39.65±19.43 years. Out of total 223 patients 112 were males and 111 were females. Clinical diagnosis was same as histopathological diagnosis in 180 (80.7%). Out of 80.7% cases, most common disorder was Eczema, 18 cases (10%). The diseases lying in the inflammatory dermatosis group have highest sensitivity, specificity, PPV and NPV, i.e., 91.2%, 90.8%, 84.1% and 86.8% respectively. The discordance between clinical and histological diagnosis was highest in infectious disease group. The concordance between clinical and histological diagnosis in infectious diseases was just 28%. **Conclusion:** Documenting a histological diagnosis is essential in dermatology as most of the dermatosis have mimicking clinical presentation. The inflammatory lesions have superior clinical and histopathological correlation as compared to infectious diseases and therefore dermatologists should try to biopsy infective dermatosis more often rather than relying on clinical judgment solely.

Keywords: Dermatological diseases; Clinical diagnosis; Histopathological diagnosis

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INTRODUCTION

Globally dermatological diseases are among the few common diseases with increasing worldwide prevalence. These diseases have significant impact on our economy.[1] There are various approaches towards diagnosing and managing dermatological diseases. Diagnosis can be made on clinical assessment, under examination by lens or microscopes or it can be made upon a histopathological evaluation. Some literatures label histopathological diagnosis as gold standard in evaluating underlying pathology and in making accurate diagnosis due to limitations of examination through lens and microscopes.[2]

Skin biopsy is a lengthy process that depends on various steps before reaching the precise diagnosis, i.e., decision concerning the anatomical site and lesion from where the specimen will be collected; choice of biopsy technique; identification, handling and fixation of the specimen; filling in the pathological order; macroscopic analysis of the skin specimen; histological processing and preparation of slides; microscopic study with diagnosis; and interpretation of the histopathologic report etc.[3] In our setups skin diseases are common reason for patients to visit hospitals, since many of these diseases have different clinical presentations with clinical overlaps there diagnosis is difficult to be made on clinical examination alone, therefore skin biopsies are often performed to confirm the clinical suspicion.[4]

Generally, dermatologists do not go for histopathological examination to diagnose inflammatory diseases, benign tumours and skin cysts, depending on the certainty of the clinician or surgeon on it being a benign lesion but to confirm a melanoma and differentiate it from benign pigmented lesions like pigmented seborrheic keratosis they often go for histopathological diagnosis due to clinical similarities. Epidermal cysts may mimic non-clinically diagnosed neoplasms, such as basal cell carcinoma and epidermoid carcinoma.[5–7] Sometimes an experienced clinician may not diagnose the disease correctly hence when doubt exists, pathological examination is necessary.

In order to establish histopathological diagnosis, clinical information is also required in order to guide the histopathologist. Based on the submitted clinical picture histological diagnosis is made. This information is conveyed to pathologist via pathology request form. Although clinicopathological concordance is much higher in dermatological diseases, there is limited literature

available in Pakistan on comparison of clinical diagnosis with histopathological diagnosis. The aim of this study is to correlate clinical diagnosis with the histological diagnosis in various skin diseases.

MATERIAL AND METHODS

This descriptive prospective study was conducted at dermatology OPD of Benazir Bhutto Hospital over a period of 12 months from 1st January to 31st December, 2018. A total of 223 patients were enrolled in this study through non-probability consecutive sampling. Patients between 2–90 years were enrolled in this study. Patients with diseases ranging from inflammatory to malignant skin conditions were included in study.

All patients in this study were examined and a clinical diagnosis was made for each case. At the same time, Skin biopsy of lesions was taken after informed consent and sent to histopathologist for tissue diagnosis along with case history. The histopathological diagnosis was compared with initial clinical diagnosis and results were collected on a specially designed *pro forma* by a post graduate trainee. Linear by linear association test, one sample t-test and diagnostic accuracy (sensitivity, specificity, Positive predictive value and negative predictive value) will be used to analyse the data. Data was stratified according to age of the patients and post stratification results were analysed.

RESULTS

Overall, 223 biopsies of the patients presenting to dermatology OPD were examined. Minimum age was 2 years whereas maximum age of participants was 85 years with mean age of 39.65±19.43 years. Majority 141 patients were adult (63.2%). Male to female ratio was almost equal, 112 (50.2%) males and 111 (49.8%) were females. Patients were categories in 5 groups with respect to their diseases. The detail descriptive results are mentioned in table-1.

Out of 223 patients 67 different diseases were diagnosed. The most common disease was eczema in 24 patients followed by psoriasis in 19 patients and Pemphigus Vulgaris in 17 patients.

A single case each of actinic prurigo, amyloidosis, Bowen disease, dermatofibroma, ectodermal dysplasia, epidermolysis bullosa, granuloma annulare, haemangioma, keratosis pilaris, linear IgA, LSA, lupus profundus, Madura foot, mastocytosis, deep mycosis, mycosis fungoides, necrobiosis lipoidica, nodular histiocytosis, pityriasis lichenoides chronica, PLEVA, prurigo nodularis, rosacea, seborrheic keratosis, tuberculoid leprosy, urticaria, vasculitic ulcer, verrucous carcinoma and xanthoma were seen and in all cases histology came out to be the same as was the clinical diagnosis.

Bullous pemphigoid, chronic prurigo, cutaneous vasculitis, dermatitis herpetiformis, erythema nodosum, lichen planus pigmentosus, melanoma, pemphigus foliaceus, reactive perforating collaginosis, skin tag, SLE, urticarial vasculitis and vasculitis are the 13 diseases in which clinicohistological concordance was again 100%.

Cutaneous horn, erythema multiforme, LSC and wart are the 4 diseases in which clinicopathological discordance was seen in one patient while in ashy dermatosis, CAD, sweet syndrome and keratoacanthoma clinicopathological concordance was seen in 50% of cases. Same was the percentage in CBDC cases. Clinicopathological concordance was not seen in 2 out of 9 patients (22.2%) in cases of BCC, leishmaniasis and lichen planus, 1 out of 3 patients (33.3%) of bullous impetigo and drug eruptions, 4 out of 12 patients (33.3%) of DLE, 6 out of 24 patients (25%) of eczema, 1 out of 5 patients (20%) of lupus vulgaris and morphea, 3 out of 17 patients (17.6%) of pemphigus vulgaris, 3 out of 19 patients (15.8%) of psoriasis, 2 out of 5 patients (40%) of pyoderma gangrenosum and SCC, 2 out of 3 patients (66.7%) of sarcoidosis.

We divided all 67 diseases into 5 groups. The details of frequency & percentage of clinicopathological concordance in different disease groups is illustrated in table-2.

It is observed in the above table 2 that the percentage of clinicopathological concordance is approximately same in all 5 groups of different skin diseases with *p*-value 0.054. The same relation exists when we stratify our data with age as in children having age less or equal to 14 years *p*-value 0.171, in Youth *p*-value 0.254, in Adults P-value 0.471, in Middle-aged adults *p*-value 0.789, in older adults *p*-value 0.412 and in Seniors *p*-value 0.349. (Table-3)

On the basis of our sample results we can also estimate the minimum percentage of correct diagnosis through clinical examination of different dermatological disease groups which is 83% (*p*-value 0.037) for tumours, 78% (*p*-value 0.03) for inflammatory dermatosis, 64% (*p*-value 0.043) for vesicobullous disorders and 28% (*p*-value 0.044) for infections.

Similarly, the conspicuous disease groups in our sample, i.e., Inflammatory dermatosis, tumours and vesicobullous disorders have sensitivity, specificity, positive predictive value and negative predictive value 91.2%; 90.8%; 84.1% & 86.8%, 78.1%; 99%; 92.6% & 96.4% and 83.8%; 96.2%; 81.6% & 96.8% respectively.

Table-1: Descriptive analysis of qualitative variables in the study

Variable	Categories	Frequency (%)
Sex	Male	112 (50.2)
	Female	111 (49.8)
Age groups	Children (0–14 years)	28 (12.6)
	Youth (15–24 years)	27 (12.1)
	Young Adults (25–35 years)	41 (18.4)
	Middle-age adults (36–55 years)	79 (35.4)
	Older adults (55–64 years)	21 (9.4)
	Seniors (65 or more years)	27 (12.1)
Disease groups (Histopathological Diagnosis)	Inflammatory dermatosis	136 (61)
	Tumours	32 (14.3)
	Infections	12 (5.4)
	Vesicobullous disorders	37 (16.6)
	Miscellaneous	6 (2.7)

Table-2: Frequency and percentage of clinicopathological concordance in different disease groups

Group	Is the histopathological examination results was the same as clinical diagnosis?		Total
	Yes- N (%)	No- N (%)	
Inflammatory dermatosis	111 (84.1)	21 (15.9)	132
Tumours	25 (92.6)	2 (7.4)	27
Infections	9 (50)	9 (50)	18
Vesicobullous disorders	29 (76.3)	9 (23.7)	38
Miscellaneous	6 (75)	2 (25)	8
Total	180 (80.7)	43 (19.3)	223

Table-3: Comparison of clinicopathological concordance between different disease groups with stratification of patient's age in years

Age groups	Clinical diagnosis matched with Histopathology diagnosis	Clinically diagnosed diseases in groups						*p* value
		Inflammatory dermatosis	Tumours	Infections	Vesicobullous disorders	Miscellaneous	Total	
Children (up to 14 years)	No	3	1	0	3	1	8	0.171
	Yes	13	1	2	3	1	20	
Youth (between 15-24 years)	No	3	0	4	1	0	8	0.254
	Yes	14	1	0	3	1	19	
Adult (between 25 to 35 years)	No	4	0	3	0	0	7	0.471
	Yes	26	3	1	3	1	34	
Middle aged 36–55 years)	No	8	0	1	3	1	13	0.789
	Yes	35	10	5	15	1	66	
Older (between 56 to 64 years)	No	2	1	1	0	0	4	0.412
	Yes	14	1	1	1	0	17	
Senior ≥65 years)	No	1	0	0	2	0	3	0.349
	Yes	9	9	0	4	2	24	
Total	No	21	2	9	9	2	43	0.054
	Yes	111	25	9	29	6	180	

Table-4: Cross tabulation of age groups and different dermatological disease groups

Dermatological diseases groups		Age groups (in years)						Total
		Children (0-14)	Youth (15-24)	Adult (25-35)	Middle-aged (36-55)	Older (55-64)	Seniors ≥65	
Inflammatory dermatosis	Count	16	17	30	43	16	10	132
	% within Diagnosed diseases in groups	12.1%	12.9%	22.7%	32.6%	12.1%	7.6%	100.0%
	% within age in groups	57.1%	63.0%	73.2%	54.4%	76.2%	37.0%	59.2%
Tumours	Count	2	1	3	10	2	9	27
	% within Diagnosed diseases in groups	7.4%	3.7%	11.1%	37.0%	7.4%	33.3%	100.0%
	% within age in groups	7.1%	3.7%	7.3%	12.7%	9.5%	33.3%	12.1%
Infections	Count	2	4	4	6	2	0	18
	% within Diagnosed diseases in groups	11.1%	22.2%	22.2%	33.3%	11.1%	0.0%	100.0%
	% within age in groups	7.1%	14.8%	9.8%	7.6%	9.5%	0.0%	8.1%
Vesicobullous disorders	Count	6	4	3	18	1	6	38
	% within Diagnosed diseases in groups	15.8%	10.5%	7.9%	47.4%	2.6%	15.8%	100.0%
	% within age in groups	21.4%	14.8%	7.3%	22.8%	4.8%	22.2%	17.0%
Miscellaneous	Count	2	1	1	2	0	2	8
	% within Diagnosed diseases in groups	25.0%	12.5%	12.5%	25.0%	0.0%	25.0%	100.0%
	% within age in groups	7.1%	3.7%	2.4%	2.5%	0.0%	7.4%	3.6%
Total	Count	28	27	41	79	21	27	223
	% within Diagnosed diseases in groups	12.6%	12.1%	18.4%	35.4%	9.4%	12.1%	100.0%
	% within age in groups	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

The above table-4 shows that the infectious diseases where percentage of correct diagnosis is very low lies in Youth (15–24 years) followed by adults (25–35 years) where no hurdles to refer from histopathological examination but in the case of Vesicobullous disorders where the percentage of correct diagnosis is not as good. This disease is approximately equally lying in all age groups so we should more research on the evidence (clinical sign and symptoms for diagnosis) of Vesicobullous disorders as we know that biopsy in the age of children (2–14 years and seniors 65 or more years) is not an easy job. Our data also shows that there is relation between age groups and different dermatological disease groups with *p*-value 0.046. In the other hand, our data does not support the hypothesis that there is any relation between different dermatological diseases with patient's sex with *p*-value 0.36.

DISCUSSION

Diagnosis in the field of dermatology is vital for appropriate treatment and cure of disease. Timely diagnosis also lowers the economic burden of treatment as well as reduces the agony of mistreatment.[8]

However, diagnosis needs to be accurate for effectiveness of treatment. As per currently practiced scenarios, diagnosis comprises of detailed history, followed by clinical examination to establish clinical impression. And then this clinical impression is confirmed by histopathological examination.

In this study, we evaluated the concordance of clinical and histopathological diagnosis. In 80.7% cases the clinical diagnosis was found in accordance with histopathological diagnosis, which was comparable to studies done earlier, in which this was 90.5% and 76.5% respectively.[4,9]

García-Solano *et al*. demonstrated that histopathologic diagnoses made in skin specimens referred by a dermatology service are more specific (77%) than biopsies referred by non-dermatological services (41%).[10]

In another study, around 7.7% cases of atypical tumour patients decided to re-appraisal as the histopathological findings did not correlate with clinical findings. The cases which were reviewed due discordance with clinical findings included melanocytic and non-melanocytic tumours, skin lymphomas and inflammatory skin disease.[11]

In a recent study, histopathological findings were matched with the first three diagnosis made by dermatologist clinically. It concluded that clinicopathological concordance increased up to 79.1% when there was cooperation between dermatologist and pathologist. They also concluded that the patients going to biopsy were teen, young and adults only.[12]

Another study shows that SK-like melanomas wrongly diagnosed in about 40% cases of benign tumour. Diagnostic accuracy improved 60.9–68.1% through dermoscopy. Sensitivity and specificity of clinical investigation was 61.9% and 61.1% whereas with dermoscopy 74.5% and 59.6%.[13]

In another study 68016 biopsies were examined, out of which the commonest site 38.3% was head and neck. The average age of the patients included in this study was 54.58±0.26 years. Microscopic examination helped in 83.29% cases in diagnosis. The consensus of the clinical and microscopic diagnosis was observed in 68% cases.[14] In another study the sensitivity of clinical diagnosis keeping skin excision as gold standard was observed as BCC 63.9%, SCC 41.1% and CM 33.8%. The sensitivity of BCC was observed higher for trunk, shoulders and face as compared to other sites.[15] Experience is also a keen factor for correct diagnosis in different skin diseases as supported by a study which compared three groups. First group included two dermatologists having >10 years' experience, second group having two 3–5 years' experienced senior registrar (dermatologists) and in third group six registrar (dermatologist) were included. The results showed that the first group had better skills to correctly diagnose cutaneous malignant melanoma having diagnostic accuracy 80%, sensitivity 91% and PPV 86% in contrast with 62% and 56% sensitivity in the second and third group. This study also showed that thin and intermediate thickness melanomas were difficult to diagnosis irrespective of the clinical experience of dermatologists.[16]

In another study, the diagnostic accuracy of skin malignancies was discussed and it concluded that there is need for biopsy even in undoubted cases of skin malignancies. The results revealed that the diagnostic accuracy of provisional diagnosis of suspected skin malignancy keeping biopsy as gold standard was 54% with the highest accuracy of the site head and neck 67%. The diagnostic accuracy of SCC (squamous cell carcinoma) was 48.7% with sensitivity 90.5% and specificity 75.3% whereas diagnostic accuracy of BCC (basal cell carcinoma) was lower 40% with sensitivity 66.6% and specificity 85.6%.[17]

In another study, in 82.3% of cases histological diagnosis was the same as the first diagnosis made after clinical examination whereas in 16.7% cases the final diagnosis was the one which is mentioned on second or third place through clinical examination while in just 0.008% cases dermatologist have no idea of disease which revealed from biopsy.[4] Wide range of clinical lesions were analysed in this study similar to spectrum of diseases discussed in our study. In our study eczema, DLE and neoplasms showed adequate clinical and histopathological concordance.

However, fewer dermatological diseases were not concordant, major proportion of which was patients of psoriasis.

A good clinical description of the lesion does correlate with histopathology of lesion, if appropriately given. Among the discordant cases in this study, when the clinical description was used to formulate a set of differential diagnosis, in 19.3% cases the clinical description did not correlate with the final diagnosis. Cerroni *et al.* suggested that adding clinical photographs improved the diagnostic accuracy by dermatopathologists**.** With advancement in technology, adding clinical images could be used as a valid tool to improve diagnosis.[18]

A few studies have also been conducted to evaluate the diagnostic accuracy of skin diseases by physicians by comparing the clinical to the histological diagnosis. One of these studies measured the diagnostic yield of non-dermatologists between 34–45% and that of dermatologists being 71% and 75% for inflammatory dermatoses or neoplasms and cysts, respectively.[19] Another study found 76.8% of pathological diagnoses to be consistent with the ones given by the dermatologists, whereas a third one measured a clinicopathological agreement of up to 92% with this success being attributed by the author to the close cooperation between the dermatologist and the pathologist.[9,20] All of these results are comparable to our study.

CONCLUSION

Detailed history and clinical examination play a key role in dermatological diagnosis. However, we must go for histopathological confirmation of any dermatosis when in doubt. The inflammatory lesions have superior clinical and histopathological correlation as compared to infectious diseases and therefore dermatologists should try to biopsy infective dermatosis more often rather than relying on clinical judgment solely.

AUTHORS' CONTRIBUTION

SN: Data collection, literature review. NW: Conceptualization, data interpretation. AM: Data analysis, write-up, proof reading.

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