A Review Study Toward Clinical and Histopathological Diagnosis Agreement in Skin Diseases

Sidita Sopjani¹, Bengü Nisa Akay², Aferdita Daka¹

ABSTRACT

Background: It is important to evaluate the agreement between clinical diagnosis and histopathological diagnosis. The aim of this study was to review studies and to calculate the degree of agreement between clinical and histopathological diagnosis. Objective: The aim of this review was to find out the concordance level between clinical and histopathological diagnosis; to find out in which type of pathology concordance was the highest; to identify the types of pathologies for which biopsy was mostly performed and the anatomical region selected for biopsy. Results and Discussion: Review was carried out in accordance with the PRISMA 2020 flow diagram for the selection of articles that met the criteria (years 2005-2021). Articles were found in Google scholar, PubMed, Scopus databases using different keywords. The main criterion was to involve studies that reported data about clinical and histopathological diagnosis. A mean concordance value was calculated and resulted of 72.8 % (95% CI). Conclusion: To our knowledge, our study was the first review done regarding concordance between clinical and histopathological diagnosis in skin diseases with the aim to provide researchers with enriched literature and encourage them to bring about an appropriate systematic review study. Keywords: clinicopathological concordance, skin biopsies, histopathology, clinical diagnoses, histopathological diagnoses; systematic review.

1. BACKGROUND

Histopathology is considered the “gold standard” in the diagnosis of skin diseases (1-3). The choice of technique and anatomical region for biopsy, relevant clinical information and clinical diagnosis affect the accuracy degree of microscopic diagnosis (4). On the other hand, the experience of the pathologist performing the microscopic analysis also affects the accuracy of the diagnosis of skin diseases (1,5-7). When skin lesions can be accessible by dermatologists, biopsy should be considered an appropriate technique (8). It is a fact that the more material is taken from the pathologist, the higher the possibility for accurate diagnosis. However, in some cases, histological signs are so characteristic that even small fragments of skin may be sufficient for diagnosis (1).

Even though many modern techniques have been developed and used in the diagnosis of skin diseases, dermatologists still rely heavily on biopsies for diagnostic purposes, so it is important to calculate the degree of concordance between clinical and histopathological diagnosis and evaluate its accuracy (9,10).

2. OBJECTIVE

The aim of this study was to measure the concordance between clinical and histopathological diagnoses in dermatological cases; to find out in which type of pathology the diagnostic accuracy is the highest; to identify the anatomical region most often selected for biopsy and the types of pathologies for which biopsy was mostly performed.

3. MATERIALS AND METHODS

This research was written in accordance with the Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) statement (11,12). PICO questions were taken as a reference to develop a relevant research question (13). Figure 1 summarized PRISMA 2020 flow diagram: searches of databases and registers only (12).
Search question: In patients with skin diseases, is the clinical diagnosis concordant to the histopathological diagnosis (considered the golden standard)?

Search strategy and selection criteria
A comprehensive search strategy was designed to identify all eligible studies in relation to clinical and histopathological diagnosis. A worldwide literature was examined, and articles of different methodologies were taken in consideration. Articles were retrieved from Google scholar, Embase, Medline, PubMed, Scopus databases using different keywords for the period 2005-2021. Main criterion was the golden standard: histopathology. We included any study that evaluated clinical and histopathological diagnosis concordance without restrictions toward the age, gender, other demographic characteristics of population, study design or test evaluated. There were retrieved 107 articles from different online databases. After reviewing these articles, we found that 48 studies fit our inclusion criteria for qualitative analysis.

Data collection and processing
We analyzed data using Microsoft Office Excel. Firstly, we measured between-study variability (heterogeneity) through I2 test allowing for the theoretically an unimportant heterogeneity across studies. Heterogeneity was considered not important because I2 resulted under 50%. All percentages reported were accompanied by 95% confidence intervals with the minimal and maximal range values. P values less than .05 were statistically significant. Figure 2 and Table 1 summarized data about concordance level of different research.

4. RESULTS AND DISCUSSION
Histopathology was considered helpful in establishing a definitive diagnosis in 84.3% cases (14). Clinical diagnosis alone is not sufficient but should be accompanied by biopsy for more complex cases. Factors such as clinical knowledge, type of biopsy, location of biopsies, number of diagnoses were analyzed by many researchers regarding the concordance between clinical and histopathological diagnosis (10,15). Some researchers found that clinico-pathological agreement can be improved if provided clinical information properly through formulars and clinical photos of the lesions to the doctor (16). Any experienced dermatopathologist agrees with the fact that skin biopsy taken above the waist is easier to interpret, because this way we can avoid abnormalities resulting from blood stasis in the lower extremities (17). Areas of the body affected by constant friction, such as the knees and elbows, are also not preferable for analyzing microscopic abnormalities, as the skin here is thicker. A study identified upper limb as the most common region of biopsies, while the perianal region was considered as the least common (18). Meanwhile, another study reported the lower extremity (29.1%) as

Table 1. Comparative study in clinico-pathological agreement by different authors

<table>
<thead>
<tr>
<th>Various studies</th>
<th>Clinico-histopathological agreement %</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sellheyer K et al., 2005</td>
<td>35</td>
<td>4451</td>
</tr>
<tr>
<td>Yap B et al., 2009</td>
<td>92</td>
<td>400</td>
</tr>
<tr>
<td>Mehta S et al., 2009</td>
<td>65.13</td>
<td>100</td>
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<tr>
<td>D’costa et al., 2010</td>
<td>97.52</td>
<td>161</td>
</tr>
<tr>
<td>Situm M et al., 2011</td>
<td>30.7</td>
<td>12344</td>
</tr>
<tr>
<td>Aslan C et al., 2012</td>
<td>76.8</td>
<td>3949</td>
</tr>
<tr>
<td>Manandhar U et al., 2013</td>
<td>45.33</td>
<td>75</td>
</tr>
<tr>
<td>Sandeep M et al., 2013</td>
<td>65.16</td>
<td>89</td>
</tr>
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<td>Santos I et al., 2018</td>
<td>58.1</td>
<td>1265</td>
</tr>
<tr>
<td>Korfitis C et al., 2014</td>
<td>68</td>
<td>6816</td>
</tr>
<tr>
<td>Hedge VK et al., 2014</td>
<td>87.2</td>
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<tr>
<td>Goyal N et al., 2015</td>
<td>63</td>
<td>795</td>
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<td>Balasubramanian P et al., 2015</td>
<td>59.8</td>
<td>3006</td>
</tr>
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<td>Dutta B et al., 2016</td>
<td>83.39</td>
<td>300</td>
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<td>Sa DK et al., 2016</td>
<td>86.5</td>
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<td>Malik A et al., 2016</td>
<td>61.01</td>
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<td>Kataria U et al., 2017</td>
<td>100</td>
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<td>Kudligi C et al., 2017</td>
<td>96</td>
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<tr>
<td>Lakshmy R et al., 2017</td>
<td>63.6</td>
<td>45</td>
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<td>Gupta P et al., 2018</td>
<td>85.8</td>
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<td>Al Saff MF et al., 2019</td>
<td>75.9</td>
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<td>Daniel BS et al., 2020</td>
<td>54.6</td>
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<td>Ukonu BA et al., 2020</td>
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<td>Venugopal R et al, 2020</td>
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<td>Liu P et al., 2021</td>
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<td>Paul A et al., 2021</td>
<td>74.2</td>
<td>35</td>
</tr>
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Image 1. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only.
the most frequent site of skin biopsy followed by the head/neck/scalp/hair (26.7%), trunk (22.1%), upper extremity (21.2%), and other sites (4.7%) (19).

Skin biopsy is a worthy diagnostic tool in skin issues (20). Several studies emphasized the fact that histopathologic evaluation is the golden standard for diagnosing dermatological disease (21,22). According to Daniel et al. 2020, high rate of clinico-histopathological agreement highlighted the need for skin biopsy in all cases of vesiculobullous diseases (23). Histological diagnosis was provided in 83.3% of all cases and helpful information was collected from dermatologists in 97.2% of all biopsies (24). Several times, dermatologists have been considered as the most responsible and experienced professionals to carry out an appropriate skin biopsy (1,17). Punch biopsy (82.1%) was the most used technique followed by excisional (12.5%), incisional and shave biopsies (5.4%) (19). Punch biopsy is a common and simple diagnostic procedure in dermatology accompanied with few complications, and therefore minor biopsies can be cured without suturing. However, another study recognized the incisional biopsy as the most used technique (24). Although punch biopsy remains the gold standard in the diagnosis of skin cancer, a study concluded that immediate cutaneous diagnostic might improve diagnostic accuracy with less money and time invested (25). Incisional biopsies usually involve part of the lesion, or part of the skin with pathological changes, and part of normal skin to identify the difference between them. Incisional biopsies are of particular importance in diagnosing subcutaneous tissue pathologies but are not suitable for pigmented lesions.

Various studies listed differently top pathologies with the highest agreement of clinico-histopathological diagnosis. Maximum clinicopathological agreement was recorded in pigmentary skin disorders, followed by infectious inflammatory dermatosis. In a study of Aslan C et al. 2012, inflammatory dermatosis had the highest compliance 93.9% out of all pathologies (10). Pigment disorders had a concordance rate of 87.82% (24). Another study reported benign melanocytic nevi as the pathology with the highest agreement within 89% to 94% (14). Lakshmy R. et al., 2017 observed 100% concordance for indeterminate and tuberculosis cases (26).

Furthermore, Dutta et al., 2016 stated a concordance of 91.6% in 24 cases of cutaneous tuberculosis (27). Other pathologies were benign and cystic lesions. Cysts had a clinico-pathological agreement of 74.82% in an Indian study (18). Similarly, other studies observed a high concordance of benign and cystic lesions over 80% (4,28). Papulosquamous and eczematous dermatoses (26.2%) was found to be the most typical skin disorder, followed by benign neoplasms (20.6%); pigmentary diseases (9.1%); rheumatologic and connective tissue diseases (6.2%); infectious diseases (5.9%); malignant neoplasms (4.6%); and other skin diseases (27.4%) (19). The algorithm of clinical, histopathological, and immunohistochemical criteria resulted helpful in the early diagnosis of mycosis fungoides increasing rate of diagnostic accuracy from 64.2% to 91% (29). A histopathological review reported the findings compatible with mycosis fungoides diagnosis in 64.2% of cases (30). On top of that, epidermotropism was identified as a histopathological feature in more than 75% of cases of mycosis fungoides (31). Regarding dysplastic nevus, clinical and histopathological concordance was found 30.7% in a ten-year period study (29).

When the concordance level is low, clinico-pathological agreement may be compromised (10,32). Mis diagnosing of the cases is produced because of non-agreement between diagnosis. A study noticed a misdiagnosis in the case of seborrheic keratosis which clinically was diagnosed as benign nevi (28). Similarly, some dermatological cases were clinically diagnosed as acquired nevus, angiookeratoma, dermatofibroma, and pyogenic granulomas, meanwhile histopathological diagnosis identified a premalignant lesion (18). Additionally, an observation that was diagnosed as molluscum contagiosum during histopathology examination, its clinical diagnosis was Milia (32).

The figure 2. and table 1. summarized studies that reported agreement between clinical and histopathological diagnosis (4,9,10,14–16,18,19,20,22,23,27,32–47). Confidence level was 95%. Kataria U. 2017; D’Costa et al., 2010; Kudligi C et al., 2017 reported the highest overall clinico-pathological agreement with respective values of 100%, 97.52 % and 96 % as stated from the figure 2 (33–35). The overall mean concordance of 29 studies was 72.8%.

Ukonu B. et al., 2020 concluded a 77.4% concordance between clinical and histopathological diagnosis and had the highest variance of values (36). Dutta B.et al., 2016; Tamas C. et al., 2021; Hedge VK, et al., 2014; Gup ta et al., 2018 and Yap FB. et al., 2009 recorded high concordance as well (27,21,37,32,20). Aslan C. et al., 2012 found the clinicopathological consistency to be 76.8% (10). Meanwhile, Sellhejer C. et al., 2005 and Situm M. et al., 2011 reported the lowest consistency of all articles about 35% and 30% respectively (4,40). Furthermore,
many studies observed an insignificant impact of age, gender, tests, diagnostic tests on concordance rate (45).

The purpose of this study was to identify overall agreement toward clinical and histopathological diagnosis as well as the evaluation of pathologies where biopsy was necessary and the anatomical area where the material had to be taken. Studies that reported high prevalence between clinical diagnosis and histopathological diagnosis stated a higher diagnostic accuracy. The mean agreement resulted 72.8%, giving so a positive answer to our research question at the beginning of the study. Similarly, in a high prevalence study, the diseases lying in the inflammatory dermatosis group had highest sensitivity and specificity, i.e., 91.2% and 90.8%, respectively (48). Another rapid diagnostic test which gave effective results was immediate cutaneous diagnosis which had a sensitivity for squamos epithelial lesions of 98.7% (95% CI: 93.0-100%) and a specificity of 92.6% (95% CI: 87.4-96.1%) (38).

5. CONCLUSION

The number of articles included in the review was not sufficient. A higher number of studies would generate a clearer picture about the agreement between clinical and histopathological diagnoses. But in larger studies set, the data are not homogeneous, do not have the same comparative basis due to the diversity of components and the methodology used. To our knowledge, our study is the first study that highlighted agreement between clinical and histopathological diagnosis in skin issues. This paper aimed to provide researchers with enriched literature and encourage them to bring about an appropriate review study.

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REFERENCES

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