# **Original Research**

# PROFILE OF SKIN BIOPSY PATIENTS IN DR. SOETOMO GENERAL ACADEMIC HOSPITAL, SURABAYA, INDONESIA

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# ABSTRACT

Skin biopsy is an important tool used by dermatologists in diagnostic determination. The correlation between clinical and histological features is needed in understanding pathogenesis and formulating the diagnosis of a skin disease with a greatly varied spectrum of histopathological results, while the observable clinical symptoms are highly limited. Skin diseases are still a serious problem worldwide, especially in Indonesia. Based on the Indonesian Health Profile in 2010, skin diseases ranked third out of 10 most diseases in outpatients in hospitals throughout Indonesia. This study was a review of the profile of skin biopsy results in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia from 1 July 2014 to 31 July 2019, which were subjected to anatomic pathology examination. This study was an observational descriptive study using secondary data sources from the medical records at the Communication and Information Technology Installation (ICT) of Dr. Soetomo General Academic Hospital, Surabaya. Based on data searches, the total number of biopsy examinations performed was 1,368 cases. There were more female patients (50.3%) than males (49.7%). The most common skin disorder found was erythropapulosquamous disorder (30%), followed by infection (18%). Other cases consisted of skin tumor (15%), vesiculobullous (13%), connective tissue disease (7%), pigmentation disorders (5%), and vasculitis (5%). Diseases that could not be classified into 7 groups of the biopsy criteria were grouped separately in other diseases (7%).

Keywords: Skin health; skin disease; skin histopathology; disease

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# Hii j nii j tư:

- 1. Profile of skin biopsy results which carried out the anatomical pathology ezamination was reviewed.
- 2. Vhe highest skin biopsy disease group case are erythropapuloss uamous, infection, skin tumor, siculobullous, connective tissue disease, pigmentation disorders, and vasculitis

# INTRODUCTION

Skin biopsy is an important tool used by dermatologists in diagnostic determination (James et al. 2015). The correlation between clinical and histological features is needed to understand pathogenesis and formulating the diagnosis of a disease given the spectrum of histopathological results of each skin disease that varies greatly, while clinical symptoms that can be seen are very limited. Skin disease is a serious problem in worldwide (Veldurthy et al. 2015). Based on the Indonesian Health Profile in 2010, skin diseases ranked third out of 10 highest diseases in outpatients in hospitals throughout Indonesia. This study examined the profile of patients with skin disease that underwent biopsy at Dr. Soetomo General Academic Hospital, Surabaya on July 1, 2014 to July 31, 2019 which were recorded at Hospital Information and Communication Centre.

# MATERIALS AND METHODS

In this study, we used medical records of skin disease patients recorded in the ICT at Dr. Soetomo General Academic Hospital, Surabaya between which was conducted on July 1, 2014 to July 31, 2019. This study was approved by the Health Research Committee of Dr. Soetomo General Academic Hospital under a decree Number 1319/KPEK/VII/2019. Among patients applied to the hospital underwent skin biopsy and had histopathological data that were determined. Histopathological diagnoses were classified based on the criteria indicated in the textbook "Lever's Histopathology of the Skin". According to this classification, the disease groups were indicated as erytrhopapulosquamous, infectious diseases, skin vesiculobullous disease, vascular diseases, tumors. connective tissue diseases, pigmentation disorders and



other disease that consisted of metabolic disease, genodermatoses and other non-specific inflammatory disease. Demographic data of the patients and histopathological diagnoses were retrospectively evaluated. The patients were also analyzed in groups of sex and age.

#### RESULTS

Based on the study, skin biopsies had been obtained from 1,368 patients. The study population consisted of 688 females (50.3 %) and 680 males (49.7%) (Table 1). Age classifications consisted of children (0-14 years), youth (15-24 years), adults (25-64 years), and seniors (65 years and above). The results concluded that most cases were found in adults (25-64) with 847 cases (61.9%), while the distribution based on gender tend to vary in every group of diseases. The reasons underlying sex -based disparities in the incidence of skin and skin -related diseases remained largely unknown but were likely multifactorial. Factors that might contribute including sex difference in the structure of skin, genetic predisposition, effects of sex hormones, sociocultural behavior, environmental factors (Andersen & Davis 2017), and the difference in immune system in both genders (Klein 2012).

highest The group with the case was 405 erythropapulosquamous with cases (30%) consisting of 209 cases (51.6%) for male and 196 cases for female (48.4%). Most cases in this group were found in adults (25-64 years). An earlier study about skin biopsy also showed a similar result with papulosquamous being the most common case (Khumar et al. 2015). Costa and Bharambe (2010) had also proven that the majority of cases for erythropapulosquamous disease were found in men and the highest percentage was in the 30-40-year age group aligned with the result in Table 1.

The second group was 247 cases of infection (18%). Male was the predominant gender in this group with 161 cases (65.18%), 86 cases were found in females (34.8%), and the group of age that was mainly affected were adults with 161 cases. The result in Figure 3 presented that most cases were bacterial infections. Based on the report of the Indonesian Ministry of Health in 2012, this aligned with the fact that Indonesia still struggles with Hansen's disease or *leprosy* caused by *Mycobacterium leprae*, where the age of onsets varied but mostly appeared in the adult range of age and male predominant (James et al. 2015).

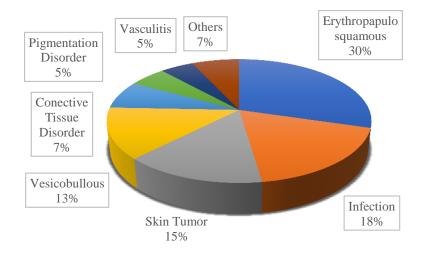


Figure 1. Results of skin biopsies



|                               |        | Age (years) |         |           |           |             |           |           |           |           |           |           |           |           |           |           | 1         |           |           |       |
|-------------------------------|--------|-------------|---------|-----------|-----------|-------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-------|
| GROUPS                        | Gender | 0-<br>4     | 5-<br>9 | 10-<br>14 | 15-<br>19 | 20-<br>24   | 25-<br>29 | 30-<br>34 | 35-<br>39 | 40-<br>44 | 45-<br>49 | 50-<br>54 | 55-<br>59 | 60-<br>64 | 65-<br>69 | 70-<br>74 | 75-<br>79 | 80-<br>84 | 85-<br>89 | τοται |
| Extbrogagulosquamous          | Male   | 6           | 8       | 10        | 10        | 12          | 15        | 15        | 10        | 15        | 19        | 27        | 26        | 16        | 13        | 4         | 1         | 1         | 1         | 209   |
|                               | Female | 5           | 8       | 9         | 7         | 15          | 13        | 12        | 13        | 17        | 26        | 18        | 22        | 17        | 8         | 3         | 3         | ō         | Ô         | 196   |
|                               | Total  |             | 46      | -         | 44        |             | 15        |           | 281       |           |           | 10        | 22        | • •       | Ū         | -         | 34        |           | · ·       | 405   |
| Skin Tumor                    | Male   | 4           | 2       | 6         | 5         | 6           | 3         | 4         | 2         | 4         | 9         | 6         | 9         | 10        | 8         | 7         | 3         | 3         | 1         | 92    |
|                               | Female | 4           | 4       | 8         | 5         | 4           | 10        | 8         | 7         | 8         | 6         | 7         | 8         | 9         | 5         | 7         | 8         | 1         | 0         | 109   |
|                               | Total  |             | 28      |           | 20        |             |           | 110       |           |           |           |           |           |           |           | 43        |           |           | 201       |       |
| Vasculitis                    | Male   | 1           | 2       | 1         | 1         | 2           | 0         | 2         | 0         | 1         | 3         | 3         | 5         | 0         | 1         | 2         | 0         | 0         | 0         | 24    |
|                               | Female | 2           | 0       | 7         | 6         | 7           | 5         | 2         | 0         | 5         | 3         | 3         | 1         | 0         | 0         | 0         | 1         | 0         | 0         | 42    |
|                               | Total  |             | 13      |           | 16        |             |           | 33        |           |           |           |           |           |           |           |           | 4         |           |           | 66    |
| Connective Tissue<br>Disorder | Male   | 1           | 2       | 2         | 1         | 3           | 1         | 3         | 1         | 3         | 5         | 2         | 0         | 1         | 1         | 0         | 0         | 0         | 0         | 26    |
|                               | Female | 1           | 3       | 6         | 4         | 6           | 7         | 5         | 8         | 10        | 14        | 4         | 2         | 1         | 3         | 0         | 0         | 0         | 0         | 74    |
|                               | Total  |             | 15      |           | 14        |             | 67        |           |           |           |           |           |           |           | 4         |           |           | 100       |           |       |
| Pigmentation Disorder         | Male   | 2           | 1       | 11        | 4         | 3           | 5         | 1         | 1         | 1         | 2         | 0         | 0         | 4         | 0         | 2         | 0         | 0         | 0         | 37    |
|                               | Female | 2           | 1       | 7         | 3         | 2           | 4         | 3         | 3         | 2         | 6         | 1         | 1         | 1         | 0         | 0         | 0         | 0         | 0         | 36    |
|                               | Total  |             | 24      |           | 12        |             |           | 35        |           |           |           |           |           |           |           |           | 2         |           |           | 73    |
| Xesicobullous                 | Male   | 5           | 3       | 2         | 5         | 4           | 9         | 3         | 5         | 5         | 12        | 8         | 4         | 5         | 5         | 2         | 3         | 3         | 0         | 83    |
|                               | Female | 4           | 6       | 1         | 5         | 9           | 3         | 7         | 16        | 11        | 5         | 5         | 7         | 11        | 3         | 3         | 2         | 1         | 0         | 99    |
|                               | Total  |             | 21      |           | 23        |             |           | 116       |           |           |           | 6         |           |           |           |           | 22        |           |           | 182   |
| Infection                     | Male   | 3           | 3       | 5         | 11        | 18          | 17        | 12        | 21        | 22        | 15        | 10        | 8         | 5         | 3         | 4         | 2         | 2         | 0         | 161   |
|                               | Female | 1           | 5       | 9         | 5         | 12          | 7         | 7         | 8         | 13        | 2         | 6         | 5         | 3         | 1         | 1         | 0         | 1         | 0         | 86    |
|                               | Total  |             | 26      |           | 46        |             | 161       |           |           |           |           |           |           |           |           | 14        |           |           | 247       |       |
| Other Disease                 | Male   | 7           | 3       | 4         | 4         | 5           | 3         | 3         | 4         | 3         | 1         | 1         | 3         | 3         | 1         | 1         | 1         | 1         | 0         | 48    |
|                               | Female | 0           | 4       | 3         | 7         | 8           | 5         | 6         | 4         | 2         | 0         | 4         | 1         | 1         | 0         | 0         | 1         | 0         | 0         | 46    |
|                               | Total  |             | 21      |           | 24        |             |           |           |           |           | 23        |           |           |           |           |           | 5         |           |           | 94    |
| Total                         | Male   | 29          | 24      | 41        | 41        | 53          | 53        | 43        | 44        | 54        | 66        | 57        | 55        | 44        | 32        | 22        | 10        | 10        | 2         | 680   |
|                               | Female | 19          | 31      | 50        | 42        | 63          | 54        | 50        | 59        | 68        | 62        | 48        | 47        | 43        | 20        | 14        | 15        | 3         | 0         | 688   |
|                               | Total  |             | 194     |           | 19        | 199 431 128 |           |           |           |           |           |           |           |           |           | 1368      |           |           |           |       |

Table 1. Results of skin biopsies by age group and sex

Generally, innate and adaptive immune responses are found higher in female compared to male. These numbers are still correlated to factors from the immune system, such as females with better antibody response to viruses, men with lower CD3<sup>+</sup> and CD4<sup>+</sup> cell counts, CD4<sup>+</sup> to CD8<sup>+</sup> cell ratios, and helper T cell type 1 (Th1) responses than women, women with higher proportions of regulatory T cells and higher cytotoxic T cell activity along with up-regulated expression of antiviral and proinflammatory genes (Klein 2012). The multifactorial cause was why a female could resist varieties of bacterium, viral infections, and parasitic infestation better than male (Ahmed et al. 1985).

Skin tumor came third with 201 cases (15%), 109 (54.23%) of the cases were female, and 92 (45.77%) were male with most cases appearing in adulthood period. Based on Figure 4, we could observe that this group of diseases consisted of malignant skin tumors and other benign tumors. Malignant skin tumors consisted of melanoma and non-melanoma skin cancers, while other benign tumors consisted of fibroadenoma, hemangioma, and skin tag. Both melanoma and non-melanoma skin cancers were more frequent in male than female with a risky increase in age (Apalla et al. 2017). On the other hand, the other benign tumors dominantly consisted of female's case which included *fibroadenoma* (Greenberg et al. 1998), hemangioma (Glinkova et al. 2004), and a neutral gender case which included skin tag (Pandey & Sonthalia 2021).

The fourth group was vesiculobullous with 182 cases (13%). 99 cases were predominantly females (54.4%) and 83 cases in male (45.6%), while the highest number of cases were found in adults (25-64 years) with 116 cases. A cross-sectional study to evaluate vesiculobullous lesion also presented similar result with the majority of patients presented between 40-49 years old and female patients having a higher number with a male: female ratio of 1:1.27 (Arundhati et al. 2013). In accordance with the difference of immunity among genders, some of the results indicated that females had faster clearance of pathogens but also tend to have a higher susceptibility to inflammatory and autoimmune diseases (Klein 2012). Hormonal and genetic factors also contribute significantly to immune function and disease pathogenesis. Specifically, the expression of X-linked genes and microRNAs, and steroid hormones that affected responses to immunological stimuli differently in male and female (Andersen & Davis 2017). This was shown in groups with autoimmune diseases, such as vesiculobullous and connective tissue disease.

Connective tissue disease was ranked fifth with 100 cases (7%). Based on Figure 6, we can see that most cases in this group consisted of *lupus erythematosus* and *scleroderma* with only 2 cases of dermatomyositis. Therefore, female had a higher number of cases with 74 cases (74%) and 26 cases in male (26%). The highest occurrence for this group was also found in adults (25-64 years). In both *lupus erythematosus* and *scleroderma*, women are more frequently affected.



Scleroderma had a female-to-male ratio between 3:1 up to 14:1.1– 4 and age of onset between 30-50 years (Gottschalk et al. 2014, Odonwodo et al. 2021), while *lupus erythematosus* age of onsets varied between types, but most were included in the adult age (Goldsmith et al. 2012).

Pigmentation disorder came after with a total of 73 cases (5 %), 37 cases for male (50.6%), and 36 for female (49.3%). The age range with most cases was adults with 35 cases, but a high number of cases were also found in childhood with 24 cases. Pigmentation disorder has a diverse age of onset for each disease. Some of those in acquired pigmentation disorder were vitiligo which could appear at any age (childhood to adulthood) and had a high incidence in the second and third decade with age of onset varied between genders (Jan & Masood 2021).

Post-inflammatory hyperpigmentation also varied depending on the etiology of disease, such as acne, impetigo, dermatitis, infection, allergy, and injury (Lawrence & Aboud 2021). A congenital example is *café au lait* that were presented at birth or might even appear early in life, but the size and number of macules might increase with age (Jha & Mendez 2021).

The next group of diseases is vasculitis with a total 66 cases (5 %), consisting of 24 males (36.3%) and 42 females (63.6%). The age of distribution had increased along with age throughout childhood, youth and adulthood, but decreases in the elderly ages. One of the highest cases from this group was *Henoch Schonlein purpura* with 28 cases as seen in Figure 8. Henoch-Schönlein purpura is a vasculitis involving the small vessels that typically affects children. This disease, however, can also be seen in adults and adolescents (Robinson & Hotwagner 2021).

Diseases that cannot be classified into the 7 groups (biopsy criteria) are grouped separately in other diseases which consist of metabolic disease, *genodermatoses*, and other nonspecific inflammatory diseases with 94 cases (7 %).

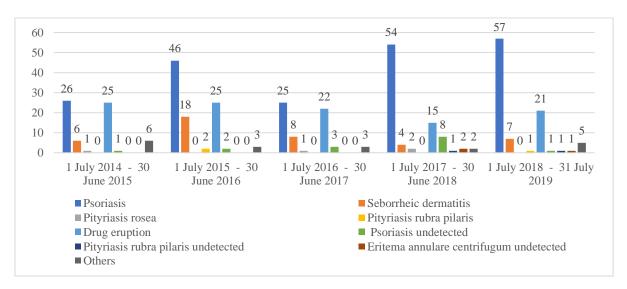


Figure 2. Results of skin biopsies of erythropapulosquamous group

Ertyhropapulosquamous is the first group with the highest number of biopsy cases. Psoriasis is the most common case with 208 cases (51.35%). Drug eruption follows with 108 cases (26.66%). Other diseases are seborrheic dermatitis with 43 cases (10.61%), pityriasis rosea 4 cases (0.98%), and pityriasis rubra pilaris 3 cases (0.74%). There were also other groups of 4.69% consisting of parapsoriasis, *lichen planus, urticaria*, and *prurigo nodularis*. Related study has shown similar result, where psoriasis dominated cases found in the biopsy of papulosquamous group of disease (Hosamane et al. 2016), thus contributing to the fact that this group was dominant in male. It could be caused by genetic predisposition and sociocultural

behavior, where men had a higher chance to smoke and consume alcohol. The age group that showed the highest case were adults that might be caused by psychological stress that frequently happened in that age (Alviariza & Widyawati 2020).

Infection is the second group with the highest number of biopsy cases. The most common diseases were caused by bacterial infection with 191 cases (77.32%) that consisted of Morbus Hansen, cutaneous tuberculosis, and erythrasma followed by yeast and viral infection with 22 cases in each group. Yeast infection consists of zygomycosis, chromomycosis, deep mycoses, and chromoblastomycosis. Viral infection consisted of *verruca vulgaris* as the most



common, *verruca plan*, *condyloma acuminate*, and *molluscum contagiosum*. Next, there was also parasitic infection with 2 cases consisting of scabies and amoebiasis. Based on Figure 3, we can see that most cases were bacterial infections. The data of the Indonesian Ministry of Health in 2012 indicated that one of the most influential bacterial infections was

leprosy which was still considered as a high burden in 14 provinces in Indonesia, while East Java had the highest number of leprosy patients. In adult cases, most patients were male. Although leprosy could occur at all ages, most cases appeared before the age of 35 (James et al. 2015).

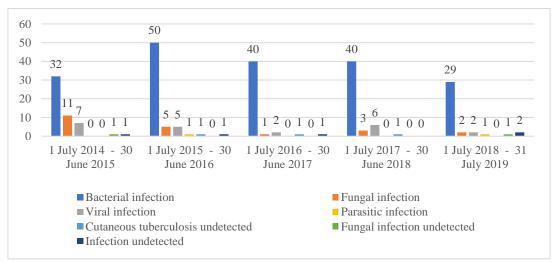


Figure 3. Results of skin biopsies of infection group

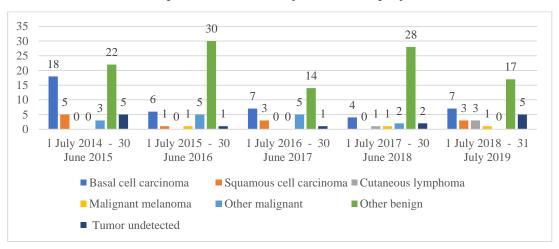


Figure 4. Results of skin biopsies of skin tumor

Skin tumor is the third group which consisted of malignant skin tumors and other benign tumors. The most common malignant tumor in this study was basal cell carcinoma with 42 cases (20.89%), followed by squamous cell carcinoma with 12 cases (5.97%). Also, there were 4 cases of cutaneous lymphoma (1.99%), 3 cases of malignant melanoma (1.49%), and 15 cases of other malignant tumors (7.46%). Apart from malignant tumors, benign tumors were also found and classified as other benign with 111 cases (55.22%) (Figure 4). The other benign tumors were fibroadenoma, hemangioma, and skin tags. Previous research also stated that the incidence of non-melanoma skin cancer

was higher than melanoma. Age, gender, and genetic susceptibility are the most dominant risk factors, and the environmental risk factor was UVR exposure (Apalla et al. 2017).

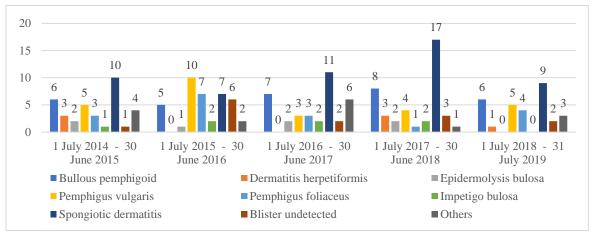
Vesiculobullous disease is the fourth group with spongiotic dermatitis as the most common case with 54 cases (29.67%), followed by bullous pemphigoid with 32 cases (17.58%). The third is pemphigus vulgaris with 27 cases (14.83%). There are also 18 cases (9.89%) of pemphigus foliaceus, and 7 cases (3.44%) of *bullous impetigo, bullous epidermolysis*, and *dermatitis herpetiformis*. A similar result was found in an earlier study, where the most common diseases



found were pemphigus vulgaris and bullous pemphigoid (Arundhati et al. 2013) (Figure 5).

Connective tissue disease is the fifth group. The most common disease was *lupus erythematosus* with 64 cases (64%) (Figure 6). Then, *scleroderma* with 33 cases (33%) and *dermatomyositis* with 2 cases (2%). Biopsy in this group was used to determine prognosis, confirmed the diagnosis and distinguished phases of the disease (Winfield & Jaworsky 2009). Connective

tissue disease is also an autoimmune-related problem that correlates with the state of sex hormones. Women undergo three major endocrinological transitions, namely puberty, pregnancy, and menopause. These endocrinological transitions exert significant effects on immune system. Another factor that contributes as a risk factor is the use of contraceptive pills (Oliver & Silman 2009) (Figure 6).



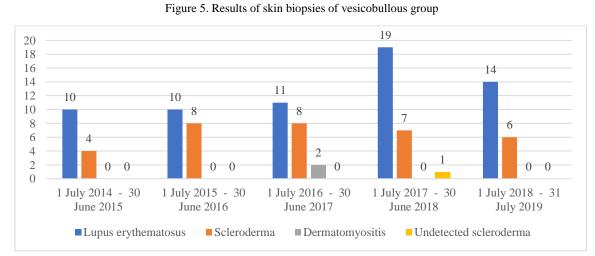


Figure 6. Results of skin biopsies of connective tissue disease

Pigmentation disorder is the sixth group consisting of congenital and acquired pigmentation problems. The most common case is nevus with 30 cases (41.09%) followed by café au lait and vitiligo with 8 cases (10.95%) each. Post-inflammatory hyperpigmentation and lentigo each were found in 6 cases (8.21%) and post-inflammatory hypopigmentation were found in 4 cases (5.47%). Biopsy in this group is often performed to differentiate benign lesions from malignant lesions. One example is malignant lentigo which is melanoma in situ on sun-damaged skin and has a similar character

to solar lentigo in its initial phase, namely light brown pigmented macules (James et al. 2015) (Figure 7).

Vasculitis is the seventh group with Henoch Schonlein purpura as the highest case found with 28 cases (42.42%) followed by pyoderma gangrenosum with 4 cases (6.06%), and leukocytoclastic vasculitis with 2 cases (3.03%). An earlier study shows a slightly different result from this study where leukocytoclastic vasculitis is the highest variant of vasculitis found, followed by Henoch Schonlein purpura and urticarial vasculitis (Gupta et al. 2009) (Figure 8).



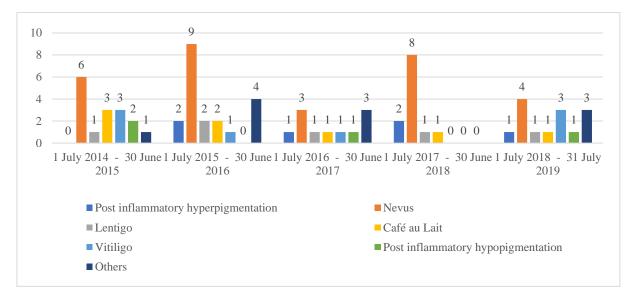
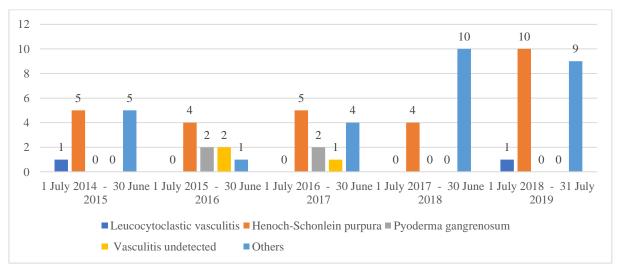
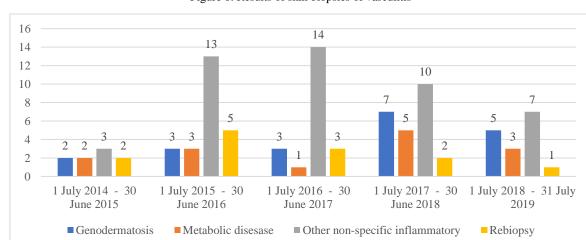


Figure 7. Results of skin biopsies pigmentation disorder





#### Figure 8. Results of skin biopsies of vasculitis

Figure 9. Results of skin biopsies of other disease



In this group, Biopsy was used mainly for diagnosis confirmation (Johnson et al. 1983). This group consisted of 48 males and 46 females, with 21-30 years old as the highest age group that underwent biopsy. This group consisted of genodermatoses with 20 cases (21.27%), 14 cases of metabolic disease (14.89%), and other nonspecific inflammatory diseases with 13 cases (13.82%). 13 cases showed the need to be rebiopsied. Genodermatoses consisted of ichthyosis and *xeroderma pigmentosum*. Metabolic disease consisted of amyloidosis (Figure 9).

## Strength and limitation

Vj e stud{ provides insigjt into tje prohile oh smin biops{ results in a large academic j ospital in Kadonesia, y j icj can j elp improve tj e diagnosis and treatment oh smin diseases in tje countr{OVj e stud{ covers a substantial period oh hive {ears, y j icj can provide a more comprej ensive understanding oh tj e prevalence and distribution oh smin diseases in tj e regionOVj e stud{ is based on data hrom a single j ospital, y j icj ma{ not be representative oh tj e entire population in Kadonesia0

# CONCLUSION

Based on the study, skin biopsies had been obtained from 1,368 patients consisting of 688 females (50.3 %) and 680 males (49.7%). Age classifications were children (0-14 years), youth (15-24 years), adults (25-64 years), and seniors (65 years and above). This study indicated that most cases were found in adults (25-64) with 847 cases (61.9%). The group with the highest case was erythropapulosquamous with 405 cases (30%) followed by infection with 247 cases (18%). Other cases consisted of skin tumor with 201 cases (15%), 182 cases of vesiculobullous group (13%), 100 cases of connective tissue disease (7%), 73 cases of pigmentation disorders (5%), and vasculitis with 66 cases (5%). Diseases that could not be classified into the 7 groups (biopsy criteria) were grouped separately in other diseases which consisted of metabolic disease, genodermatoses and other non-specific inflammatory disease with 94 cases (7%).

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# **Conflict of interest**

None0

#### **Funding disclosure**

Pone0

#### Author contribution

Cll autj or contribution anal{sis data, collected data, consepsual tj e design stud{0TCCRY C y as y rite tj e manuscript0

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