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# **ORIGINAL RESEARCH**

# PRECIPITATING FACTORS OF ACNE VULGARIS AT DR. SAIFUL ANWAR HOSPITAL MALANG

Faktor Pencetus Akne Vulgaris di RSUD dr. Saiful Anwar Malang

# Sinta Murlistyarini<sup>1</sup>, Alfonsus Rendy Laksditalia Nugroho<sup>2</sup>, Diane Tantia Sari<sup>3</sup>, Silfia Mandasari<sup>4</sup>

<sup>1</sup>Dermatology and Venereology Department, Faculty of Medicine Universitas Brawijaya / dr. Saiful Anwar Regional General Hospital Malang, Indonesia, <u>sinta husada@yahoo.com</u>

<sup>2</sup>Dermatology and Venereology Department, Faculty of Medicine Universitas Brawijaya / dr. Saiful Anwar Regional General Hospital Malang, Indonesia, <u>rendylaksditalia@gmail.com</u>

<sup>3</sup>Dermatology and Venereology Department, Faculty of Medicine Universitas Brawijaya / dr. Saiful Anwar Regional General Hospital Malang, Indonesia, <u>tantia1702@gmail.com</u>

<sup>4</sup>Dermatology and Venereology Department, Faculty of Medicine Universitas Brawijaya / dr. Saiful Anwar Regional General Hospital Malang, Indonesia, <u>seelvscorpee@gmail.com</u>

Correspondence Author: Diane Tantia Sari, <u>tantia1702@gmail.com</u>, Dermatology and Venereology Department, Faculty of Medicine Universitas Brawijaya / dr. Saiful Anwar Regional General Hospital Malang, 65111, Indonesia

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# ABSTRACT

Background: Acne vulgaris (AV) is an inflammatory disease of the pilosebaceous unit, which often causes stress and disrupts quality of life. Correctly identifying precipitating factors and preventing disease development will holistically increase the effectiveness of acne therapy, enabling better therapeutic outcomes to be achieved. **Purpose:** The objective of this study is to identify the clinical profile and precipitating factors of AV patients who visited Dr. Saiful Anwar Hospital between 2015 until 2017. Methods: This was a descriptive study, using a retrospective case study approach. The sample data was collected from medical records of AV patients from the period of 2015–2017 who met the following inclusion criteria: new AV cases with a complete medical record including gender, age, and precipitating factors. The dependent variable of this study was new AV patients, while the independent variables were the patient clinical profile and precipitating factors. Results: This study included 930 samples, with the number of female patients significantly higher (75.48%) than the number of males. The highest AV prevalence was found in the 15–24 years age group. The most common precipitating factors in females were hormonal issues, stress, and cosmetics; in males, these were stress, genetics, and dietary factors. Conclusion: The incidence of AV at Dr. Saiful Anwar Hospital mostly occurs in the 15–24 years age group, with varying trigger factors. The most frequent AV trigger factor in female patients was hormonal issues; in males, this was stress.

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#### ABSTRAK

Latar Belakang: Akne vulgaris (AV) adalah penyakit inflamasi pada unit pilosebaseus, yang secara kosmetik dapat menimbulkan stress dan mengganggu kualitas hidup. Pengidentifikasian faktor pencetus secara tepat dan menghindarinya akan meningkatkan efektivitas terapi akne secara holistik sehingga tercapai hasil yang lebih baik. Tujuan: Penelitian ini bertujuan untuk mengidentifikasi profil klinis dan faktor pencetus AV pada pasien yang datang berobat ke RSUD dr. Saiful Anwar periode tahun 2015-2017. Metode: Penelitian ini merupakan studi deskriptif. Data sampel dikumpulkan dari data rekam medik pasien AV periode tahun 2015-2017 yang memenuhi kriteria inklusi, yaitu pasien AV baru, dan memiliki rekam medis lengkap, terdiri dari jenis kelamin, usia, dan faktor pencetus AV. Variabel terikat penelitian ini adalah pasien baru AV. Variabel bebas penelitian ini adalah profil pasien dan faktor pencetus AV. Hasil: Penelitian ini mendapatkan 930 sampel pasien AV baru, dengan jumlah pasien perempuan (75,48%) lebih banyak daripada laki-laki. Kelompok usia 15-24 tahun (75,80%) merupakan kelompok usia terbanyak menderita AV. Faktor pencetus AV terbanyak pada wanita adalah hormonal, stres, dan penggunaan kosmetik sedangkan pada laki-laki adalah faktor stres, genetik, dan makanan. Kesimpulan: Insiden AV di RSUD dr. Saiful Anwar banyak terjadi pada kelompok usia 15-24 tahun, dengan faktor pencetus yang bervariasi. Faktor pencetus terbanyak timbulnya AV pada pasien perempuan adalah faktor hormonal, sedangkan pada pasien laki-laki adalah faktor stres.

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#### INTRODUCTION

Acne vulgaris (AV) is a chronic inflammatory disease of the pilosebaceous unit that frequently occurs in adolescents (Goh et al., 2019). Acne vulgaris is characterized by pleomorphic lesions, including comedones, papules, pustules, nodules, and cysts, which appear in the predilection area. It most frequently appears on the face, neck, shoulders, upper arms, upper chest, and upper back, as well as in other areas that contain sebaceous glands (Degitz & Ochsendorf, 2017). While self-recovery can be observed in clinical settings, the sequelae can be lifelong with complications of scar formation (Goh et al., 2019). In terms of impacts on psychology and quality of life. AV and its sequelae have a negative effect on the sufferer, generating discomfort, psychosocial and emotional distress, employment difficulties, lack of self-confidence, and even social isolation (Vilar, Dos Santos, & Filho, 2015). The Dermatology Life Quality Index (DLQI) of acne patients is reported to be more detrimental than the

quality of life of psoriatic patients, moreover, the Global Burden of Disease study considered AV to be the third most important disease globally (Tan & Bhate, 2015). Acne vulgaris affects about 85% of adolescents aged between 12 to 25 years old (Lynn et al., 2016). Acne can occur at any age, from infants to the elderly. In European countries, AV has the highest prevalence among people aged 15–17 years, after which it decreases with increasing age (Wolkenstein et al., 2018).

There are several trigger factors of acne, such as genetics, race, stress, hormonal factors, dietary factors, cosmetics, medicinal side effects, physical stress, and smoking habits (Yueng, Indramaya, & Mustika, 2018). The ability to identify the trigger factors appropriately will increase the effectiveness of AV therapy holistically, leading to better outcomes. Effective therapy is needed to prevent patients from encountering various complications that might occur and affect their quality of life. This study accordingly aims to identify the clinical profile and precipitating factors of AV patients who came for treatment at

the Medical Cosmetic Division of the Dermatology and Venereology Outpatient Clinic in Dr. Saiful Anwar Regional General Hospital Malang between January 2015 and December 2017.

# **METHODS**

This is a descriptive study using medical records and descriptive statistics to identify the clinical profiles and precipitating factors of acne vulgaris patients. Data were collected using medical records from 2015–2017. The population in this study were patients with acne vulgaris, while the samples in this study were differentiated based on gender. Approval for this study was received from the Medical Cosmetic Division of the Dermatology and Venereology Outpatient Clinic at Dr. Saiful Anwar Hospital in Malang.

The number of patients visiting the Dermatology and Venereology Outpatient Clinic between January 2015 and December 2017 totaled 24,046 patients; of those, patients who visited the Medical Cosmetic Division numbered 4,725. The population studied in this research were all acne vulgaris cases who came to visit the Dermatology and Venereology Outpatient Clinic between January 2015 and December 2017, for a total of 2,802 patients. The number of samples was determined using the Slovin formula, which recommended at least 351 samples. There were 930 patients who met the inclusion criteria of new cases of AV with complete medical record data available (including gender, age, and AV precipitating factors). Exclusion criteria were incomplete and unreadable medical record data. Data collection was conducted using a purposive sampling technique.

Patients were categorized by gender into male and female. Age was divided into several categories, specifically 10–14 years, 15–24 years, 25–34 years, 35–44 years, and  $\geq$  45 years (Wibawa & Winaya, 2019). Precipitating factors of acne vulgaris were defined as possible factors that could trigger acne vulgaris, including cosmetics, hormonal factors, dietary factors, stress, and genetic factors. All data recorded in medical records were obtained by the doctor in charge of taking history.

All outcome variable data were presented in a descriptive model in the form of narratives and tables. Descriptive statistical components, such as percentages, are used to describe the data. This research was conducted at the Dermatology and Venereology Outpatient Clinic of Dr. Saiful Anwar Hospital in Malang and has been approved by the Medical Research Ethics Committee 400/139/K.3/302/2019.

#### RESULTS

There were about 930 new AV patients from January 2015 to December 2017, constituting 3.87% of the total 24,046 patients in the Dermatology and Venereology Outpatient Clinic at Dr. Saiful Anwar Hospital (RSSA) Malang (Table 1). Compared to the total number of AV patients from 2015 to 2017, the percentage of new AV cases was 33.19% from 2,802 patients (Table 2). Most cases of AV were obtained (about 374 new patients) in 2015.

#### Table 1

Number of Cases per Year

Year	Number of Total Patients	Number of New Patients with Acne Vulgaris	Percentage (%)
2015	8,310	374	4.50
2016	7,946	329	4.14
2017	7,790	227	2.91
Total	24,046	930	3.87

#### Table 2

Distribution of Cases in Division of Medical Cosmetics

Year	Number of Total Patients with Acne Vulgaris	Number of New Patients with Acne Vulgaris	Percentage (%)		
2015	1,058	374	35.34		
2016	1,006	329	32.70		
2017	738	227	30.75		
Total	2,802	930	33.19		

Based on the gender distribution of new AV patients in the Division of Medical Cosmetics in the Dermatology and Venereology Outpatient Clinic from 2015 to 2017, most of the data obtained showed that the majority of patients were women, numbering 702 people or 75.48% of the total new AV patients. By contrast, male patients numbered 228 people or 24.51% of total new AV patients (Table 3). As can be seen from Table 4, the age distribution data of the most recent AV patients was found to fall primarily within the range of 15–24 years old (about 704 people or 75.80% of total). The second highest proportion were aged from 25–34 years old (14.41% of total

patients). This was followed by patients aged 10–14 years old (about 55 people, or 5.91%), those aged from 35–44 years old (about 29 people or 3.11%), and seven patients  $\geq$  45 years old (0.75% of total patients).

#### Table 3

Distribution of New Patients with Acne Vulgaris Based on Gender

	N	umber o	Total			
Year	Male					Female
	n	%	n	%	n	%
2015	118	31.55	256	68.45	374	100.00
2016	56	17.02	273	82.98	329	100.00
2017	54	23.78	173	76.21	227	100.00
Total	228	24.51	702	75.48	930	100.00

#### Table 4

Distribution Based on Age

Age (years old)	Total Number	Percentage (%)			
10-14	55	5.91			
15-24	704	75.80			
25-34	134	14.41			
35-44	29	3.11			
$\geq$ 45	7	0.75			
Total	930	100.00			

Based on the identified trigger factors, it was found that the most common trigger was hormonal factors, followed by stress, cosmetics, genetics, and dietary factors (Table 5). Based on gender, the most frequent trigger in female patients was hormonal factors, while the most frequent precipitating factor in male patients was stress (Table 6).

#### DISCUSSION

In this study, it was determined that 930 new AV patients visited the Medical Cosmetic Division at the Dermatology and Venereology Outpatient Clinic at Dr. Saiful Anwar General Hospital Malang between 2015 and 2017. In brief, this was

# 3.87% of the total 24,046 patients who went to the Dermatology and Venereology Outpatient Clinic. New AV patients who visited the Medical Cosmetic Division from 2015 to 2017 represented 33.19% of the total 2,802 AV patients. These were the most recent cases received by the Medical Cosmetic Division of the Dermatology and Venereology Outpatient Clinic at Dr. Saiful Anwar General Hospital Malang. In 2015, there were 374 new AV patients (4.50% of total patients) which represented the highest number of new acne cases within a three-year period. In 2016 and 2017, the number of new AV patients decreased to 329 (4.14%) and 227 (2.91%), respectively. This decrease might be due to the fact that not all AV patients went to the RSSA; instead, they preferred to access treatment in another place (such as private practice doctors, private clinics, online medicine, herbal medicine, etc.).

Based on gender, female patients were the most common new AV patients who visited the Outpatient Clinic. About 702 new patients (75.48%) were females compared to the 24.51% who were males. This result is in accordance with the research conducted by Wibawa & Winaya (2019) at RSU Indera Denpasar within the period of July 2014 to March 2015, who found that the number of female patients was higher than male patients at 71.20%. This might be because female patients have a higher incidence of acne complaints due to hormonal factors, such as menstrual cycles, hormonal contraception use, and hormone therapy, Moreover, female patients also use cosmetics, which can trigger acne. This is based on the literature review stating that some types of cosmetic treatments such as moisturizers may be comedogenic and acnegenic. In addition, female patients also tend to place more importance on appearance-related factors compared to male patients, which may encourage female patients to come forward for treatment sooner than men (Perera, Peiris, Pathmanathan, Mallawaarachchi, & Karunathilake, 2018).

Table 5		
Trigger Factors of	of Acne	Vulgaris*

00	0				
Veer			Trigger factors		
rear	Cosmetics	Hormonal	Food	Stress	Genetics
2015	167	179	75	195	163
2016	145	225	76	213	135
2017	105	140	58	129	93
Total	417	544	209	537	391

\*One subject can have more than one trigger factor

Ingger Factors of Acne Vulgaris Based on Gender.										
					Trigg	er factors				
Gender	Cosmetics		Hormonal		Food		Stress		Genetics	
	n	%	n	%	n	%	n	%	n	%
Male	48	11.51	42	7.72	56	26.79	124	23,09	111	23.38
Female	369	88.48	502	92.27	153	73.20	413	76,90	280	71.61
Total	417	100.00	544	100.00	209	100.00	537	100.00	391	100.00

Table 6Trigger Factors of Acne Vulgaris Based on Gender\*

\*One subject can have more than one trigger factor

Based on the age distribution data, it was found that 75.80% of new AV patients (704 patients) were aged from 15-24 years old. This data is similar to the results of Wibawa & Winaya (2019) at RSU Indera Denpasar from the period of July 2014 to March 2015. This supports the theory that AV is more common in adolescence. Acne vulgaris affected approximately 80% of patients between 12 and 25 years old without regard to differences in sex and ethnicity (Goh et al., 2019). While the onset of AV varies across age groups, it commonly occurs during puberty and young adulthood and tends to decrease with increasing age (Gollnick, 2015; Wolkenstein et al., 2018); however, persistent and late-onset acne can occur in some patients, for whom acne persists until the fourth and the fifth decade or has its initial onset at advanced age, respectively (Degitz & an Ochsendorf, 2017).

The main acne trigger factor in this study is hormonal factors. However, the trigger factors differ according to gender. Moreover, in line with the theory of AV as a multifactorial disease (Degitz & Ochsendorf, 2017), each patient tends to have more than a single trigger to promote acne. In the current study, the most common trigger factors female patients were hormonal factors in (92.27%), cosmetics (88.48%), and stress (76.90%). By contrast, the most common trigger factors in male patients were dietary (26.90%), genetic (23.38%), and stress (23.09%).

Hormonal factors in female patients are commonly associated with menstrual cycles, hormonal contraception, or hormonal therapy (Rocha & Bagatin, 2018; Saint-Jean, Khammari, Seite, Moyal, & Dreno, 2017; Sharma, Dogra, Singh, & Kanwar, 2017). Sharma, Dogra, Singh, & Kanwar (2017) stated that based on the epidemiological pattern of AV in the school-age population in India, recurrence in acne lesions before menstruation was experienced by about 21.10% of women. Saint-Jean, Khammari, Seite, Moyal, & Dreno (2017) further stated that the premenstrual period is often followed by the worsening of acne for many women. During ovulation in the premenstrual phase, elevated progesterone levels transform into testosterone, which stimulates the androgen receptors, mainly in sebocytes; this induces increased sebum quantity, change in sebocyte surface lipid composition, hydration or molecular structure of keratin, and possible effects of prostaglandin through its vasoactive property (Raghunath, Venables, & Millington, 2015). Another explanation regarding the association between menstrual cycle and AV is that hydration induced during the menstrual cycle can lead to constriction in the pilosebaceous orifice between days 16-20 of the menstrual cycle (Hulmani, Bullappa, Kakar, & Kengnal, 2017). External hormonal factors may also trigger or aggravate acne, especially hormones that contain pro-androgen progrestin, in the form of oral preparations, injection, or intrauterine device contraceptives (Rocha & Bagatin, 2018).

In the present study, cosmetics is the second acne trigger factor in female patients. The use of comedogenic and acnegenic cosmetics can cause the occurrence of whiteheads and/or blackheads, and produce acne, respectively. These products contain excess oil that clogs hair follicles and pores, thus leading to blockage of sebaceous glands (Yueng, Indramaya, & Mustika, 2018). Several cosmetic compositions known for their comedogenic properties are isopropyl myristate, lanolin, butyl stearate, stearyl alcohol, and oleic acid (George & Sridharan, 2018). One study by George & Sridharan (2018) assessing 110 acne cases in hospital showed that 40% of patients reported aggravation of acne lesions after using some form of cosmetics; these include applying skin-lightening agents (24.50%), doing facials (14.50%), and using hair oil (9.10%). A study by Perera, Peiris, Pathmanathan, Mallawaarachchi, & Karunathilake (2018) also showed that frequent cosmetic usage has a statistically significant, moderately strong relationship with severity of acne in adolescent females. Conversely, this study can be contrasted with a study by Yueng, Indramaya, & Mustika (2018) in Dr. Soetomo General Hospital Surabaya, which found no association between significant cosmetics (cleansers, moisturizers. facial protection. exfoliators, and decorative cosmetics) and AV degree. This might be due to the small population in that study and the limited number of moderate and severe acne cases, which yielded different results. On the other hand, the appropriate selection of cosmetics can be used as adjunctive treatment for AV. The use of dermocosmetics in the treatment of acne has a role in maintaining a level of improvement in the condition and preventing the appearance of new lesions by targeting specific aspects of acne pathogenesis, increasing the efficacy of another treatment, and managing side-effects of other treatment and potential skin barrier defects (Araviiskaia & Dréno, 2016).

Psychological stress may trigger or exacerbate acne. During emotional stress, several cutaneous neurogenic factors interact with a pathogenic cascade in acne, causing the onset or exacerbation of acne. Stress signals initiate the hypothalamuspituitary-adrenal axis (HPA) and the sympathetic nervous system, which then induce the production of hormones, neuropeptides, and inflammatory cytokines, such as corticotropin-releasing hormone (CRH), melanocortins, and substance P. Secretion of these substances alters the activity of the pilosebaceous which modulates unit. inflammation, proliferation, and sebum production and composition, influencing the chronic course and exacerbation of acne (Jović et al., 2017). Cutaneous microbiota may also be affected by stress mediators (catecholamines) and affects the exacerbation of acne (Borrel et al., 2019). One recent study by Borrel et al (2019) demonstrated that catecholamines can regulate biofilm formation Cutibacterium of acnes (formerly Propionibacterium acnes) and stimulate sebum production by sebocytes. In their study, George & Sridharan (2018) stated that 32.70% of patients reported acne exacerbation during periods of emotional stress. Another clinical study by Di Landro et al (2016) showed that high psychological stress levels were also associated with the occurrence of AV in adult women. This was demonstrated by the prevalence of active working women and the possibility that AV was associated with the work environment or psychological factors. A study by Gül & Cölgecen (2015) showed that adult AV patients are characterized by general psychiatric conditions and somatization tendencies. In line with those

results, studies by Silvia, Panonsih, Purwaningrum, & Rhavika (2019) and Zari & Alrahmani (2017) also showed that psychological stress level has a positive correlation with AV moreover. severity. a recent studv bv Chatzikonstantinou et al (2019) stated that stress management methods using a novel cognitivemanagement based stress intervention, Pythagorean Self-Awareness Intervention (PSAI), is feasible and possibly effective to manage stress for AV. These findings also showed that 93.30% of patients in the intervention group and 26.70% of those in the control group showed improvement in their acne stage after eight weeks of PSAI intervention.

The effect of diet on AV remains controversial and has been debated in the literature since the early 1900s. Many studies have suggested the association of acne with the glycemic index (GI) and consumption of dairy products. Both of these are suspected to increase insulin-like growth factor (IGF)-1, which stimulates sebocyte proliferation and lipogenesis, as well as increased androgen activity (Kucharska, Szmurło, & Sinska, 2016). A randomized controlled trial conducted by Burris, Shikany, Rietkerk, & Woolf (2018) examined changes in biochemical factors associated with acne in 66 participants with moderate to severe acne, showing that a low Glycemic Index and Glycemic Load diet decreased IGF-1 concentrations, a well-established factor in acne pathogenesis.

The role of genetics in acne pathogenesis has explained by genome-wide already been association studies. Three genomic loci-harboring alleles were identified in the European population and two in the Han Chinese population. These loci are responsible for a component of the TGFB pathway that has a role in the biological mechanism of AV pathogenesis. This finding may indicate a variation affecting the pilosebaceous unit structure that creates a follicular environment prone to bacterial colonization, resulting in inflammation (Petridis et al., 2018). A study by Mina-Vargas et al (2017) also supports the hypothesis that acne is an inherited trait influenced by the action of multiple loci with small effect. In addition to TGF<sup>β</sup>, two other metabolic pathways known to be involved in acne susceptibility are PI3K (which is responsible for insulin metabolism and has a role in the interplay between androgens, insulin, IGF, and acne) and DDB (which has a role in androgen metabolism and inflammation). Research conducted by Vilar, Dos Santos, and Fiho (2015) additionally found that a genetic

history of AV is significantly more common in the AV group compared to the non-acne group.

This was the first epidemiologic study to report on the clinical profile of AV patients at the Dermatology and Venereology Outpatient Clinic of Dr. Saiful Anwar General Hospital Malang. This study provided descriptive data that can act as reference material for further research related to acne vulgaris at Dr. Saiful Anwar Hospital, especially those related to the modification of trigger factors for AV.

#### **Research Limitations**

The key limitation of this study was its descriptive study design, which prevented the statistical analysis of which trigger factors are significant or insignificant in influencing the occurrence of acne vulgaris. Another limitation of this study was that the data description regarding the type of AV and its treatment could not be reported due to data limitations and incompleteness in the medical records. Based on the study results, AV incidence remained high and the most frequent trigger factors of AV in female and male patients were different and varied. The implications for policy that could be suggested based on the study results is that the present research can help to provide data for the purpose of establishing a protocol regarding risk factors for acne vulgaris.

# CONCLUSION

The number of AV patients at the study site from 2015–2017 was 930; Most AV them were female within the range of 15–24 years old. The most common trigger factors for AV in female patients were hormonal factors, stress, and cosmetics, while those for male patients were stress, genetics, and dietary factors. It is concluded that the trigger factors of AV are still varied.

# **CONFLICT OF INTEREST**

The author declare that no conflict of interest in this study.

#### AUTHOR CONTRIBUTIONS

SM1 contributed as the research supervisor and person in charge, while ARLN, DTS, and SM2 contributed to data collection, analysis, and reporting, as well as journal submissions.

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#### REFERENCES

Araviiskaia, E., & Dréno, B. (2016). The role of topical dermocosmetics in acne vulgaris. Journal of the European Academy of Dermatology and Venereology, 30(6), 926– 935.

https://doi.org/https://doi.org/10.1111/jdv.135 79

- Borrel, V., Thomas, P., Catovic, C., Racine, P.-J., Konto-Ghiorghi, Y., Lefeuvre, L., ... Feuilloley, M. G. J. (2019). Acne and stress: impact of catecholamines on cutibacterium acnes. *Frontiers in Medicine*, *6*, 1–13. https://doi.org/10.3389/fmed.2019.00155
- Burris, J., Shikany, J. M., Rietkerk, W., & Woolf, K. (2018). A low glycemic index and glycemic load diet decreases insulin-like growth factor-1 among adults with moderate and severe acne: a short-duration, 2-week randomized controlled trial. *Journal of the Academy of Nutrition and Dietetics*, 118(10), 1874–1885.

https://doi.org/10.1016/j.jand.2018.02.009

- Chatzikonstantinou, F., Miskedaki, A., Antoniou, C., Chatzikonstantinou, M., Chrousos, G., & Darviri, C. (2019). A novel cognitive stress management technique for acne vulgaris: a short report of a pilot experimental study. *International Journal of Dermatology*, 58(2), 218–220. https://doi.org/10.1111/ijd.14227
- Degitz, K., & Ochsendorf, F. (2017). Acne. Journal of the German Society of Dermatology, 15(7), 709–722. https://doi.org/10.1111/ddg.13278
- Di Landro, A., Cazzaniga, S., Cusano, F., Bonci, A., Carla, C., Musumeci, M. L., ... the Group for Epidemiologic Research in Dermatology Acne Study Group. (2016). Adult female acne and associated risk factors: results of a multicenter case-control study in Italy. *Journal of the American Academy of Dermatology*, 75(6), 1134–1141. https://doi.org/10.1016/j.jaad.2016.06.060
- George, R. M., & Sridharan, R. (2018). Factors aggravating or precipitating acne in Indian adults: a hospital-based study of 110 cases. *Indian Journal of Dermatology*, 63(4), 328– 331. https://doi.org/10.4103/ijd.IJD\_565\_17

- Goh, C., Cheng, C., Agak, G., Zaenglein, A. L., Graber, E. M., Thiboutot, D. M., & Kim, J. (2019). *Acne Vulgaris*. In K. G. Edmonson & K. J. Davis (Eds.), Fitzpatrick's Dermatology (9th ed.). USA: McGraw-Hill Education.
- Gollnick, H. P. M. (2015). From new findings in acne pathogenesis to new approaches in treatment. *Journal of the European Academy of Dermatology and Venereology*, 29(Suppl 5), 1–7. https://doi.org/10.1111/jdv.13186
- Gül, A. I., & Çölgeçen, E. (2015). Personality traits and common psychiatric conditions in adult patients with acne vulgaris. *Annals of Dermatology*, 27(1), 48–52. https://doi.org/10.5021/ad.2015.27.1.48
- Hulmani, M., Bullappa, A., Kakar, S., & Kengnal, P. (2017). Knowledge, attitude and practice towards acne vulgaris among acne patients. *International Journal of Research in Dermatology*, 3(1), 107–112. https://doi.org/10.18203/issn.2455-4529.intjresdermatol20170797
- Jović, A., Marinović, B., Kostović, K., Čeović, R., Basta-Juzbašić, A., & Bukvić Mokos, Z. (2017). The impact of pyschological stress on acne. Acta Dermatovenerologica Croatica: ADC, 25(2), 1133–1141.
- Kucharska, A., Szmurło, A., & Sinska, B. (2016). Significance of diet in treated and untreated acne vulgaris. Advances in Dermatology in Dermatology and Allergology, 33(2), 81–86. https://doi.org/10.5114/ada.2016.59146
- Lynn, D., Umari, T., Dellavalle, R., & Dunnick, C. (2016). The epidemiology of acne vulgaris in late adolescence. *Adolescent Health, Medicine and Therapeutics,* 7, 13–25. https://doi.org/10.2147/ahmt.s55832
- Mina-Vargas, A., Colodro-Conde, L., Grasby, K., Zhu, G., Gordon, S., Medland, S. E., & Martin, N. G. (2017). Heritability and GWAS analyses of acne in australian adolescent twins. *Twin Research and Human Genetics*, 20(6), 541–549. https://doi.org/10.1017/thg.2017.58
- Perera, M. P. N., Peiris, W. M. D. M., Pathmanathan, D., Mallawaarachchi, S., & Karunathilake, I. M. (2018). Relationship between acne vulgaris and cosmetic usage in Sri Lankan urban adolescent females. *Journal* of Cosmetic Dermatology, 17(3), 431–436. https://doi.org/https://doi.org/10.1111/jocd.12 431
- Petridis, C., Navarini, A. A., Dand, N., Saklatvala, J., Baudry, D., Duckworth, M., ... Simpson, M. A. (2018). Genome-wide meta-analysis

implicates mediators of hair follicle development and morphogenesis in risk for severe acne. *Nature Communications*, 9(1). https://doi.org/10.1038/s41467-018-07459-5

- Raghunath, R. S., Venables, Z. C., & Millington, G. W. M. (2015). The menstrual cycle and the skin. *Clinical and Experimental Dermatology*, 40(2), 111–115. https://doi.org/10.1111/ced.12588
- Rocha, M. A., & Bagatin, E. (2018). Adult-onset acne: prevalence, impact, and management challenges. *Clinical, Cosmetic and Investigational Dermatology, 11*, 59–69.
- Saint-Jean, M., Khammari, A., Seite, S., Moyal, D., & Dreno, B. (2017). Characteristics of premenstrual acne flare-up and benefits of a dermocosmetic treatment: a double-blind randomised trial. *European Journal of Dermatology*, 27(2), 144–149. https://doi.org/10.1684/ejd.2016.2952
- Sharma, R., Dogra, S., Singh, A., & Kanwar, A. (2017). Epidemiological patterns of acne vulgaris among adolescents in North India: a cross-sectional study and brief review of literature. *Indian Journal of Paediatric Dermatology*, 18(3), 196–201. https://doi.org/10.4103/ijpd.ijpd 82 16
- Silvia, E., Panonsih, R. N., Purwaningrum, R., & Rhavika, D. R. (2019). Perbandingan tingkat stres akne vulgaris ringan dengan akne vulgaris berat pada mahasiswa pendidikan dokter fakultas kedokteran Universitas Malahayati. Jurnal Ilmu Kedokteran dan Kesehatan, 6(1), 43–48. https://doi.org/10.33024/jikk.v6i1.2286
- Tan, J. K. L., & Bhate, K. (2015). A global perspective on the epidemiology of acne. *The British Journal of Dermatology*, 172(Suppl 1), 3–12. https://doi.org/10.1111/bjd.13462
- Vilar, G. N., Dos Santos, L. A., & Filho, J. F. S. (2015). Quality of life, self-esteem and psychosocial factors in adolescents with acne vulgaris. *Anais Brasileiros de Dermatologia*, 90(5), 622–629. https://doi.org/10.1590/abd1806-4841.201533726
- Wibawa, I. G. A. E., & Winaya, K. K. (2019). Karakteristik penderita acne vulgaris di Rumah Sakit Umum (RSU) Indera Denpasar periode 2014-2015. Jurnal Medika Udayana, 8(11), 1–4.
- Wolkenstein, P., Machovcová, A., Szepietowski, J. C., Tennstedt, D., Veraldi, S., & Delarue, A. (2018). Acne prevalence and associations with lifestyle: a cross-sectional online survey

of adolescents/young adults in 7 European countries. *Journal of the European Academy of Dermatology and Venereology*, *32*(2), 298– 306. https://doi.org/10.1111/jdv.14475

Yueng, M. Z., Indramaya, D. M., & Mustika, A. (2018). Relationship between diet, cosmetics and degree of acne vulgaris in dermatovenereology outpatients at Dr. Soetomo General Hospital, Surabaya. *Althea*  *Medical Journal*, 5(4), 161–167. https://doi.org/10.15850/amj.v5n4.1496

Zari, S., & Alrahmani, D. (2017). The association between stress and acne among female medical students in Jeddah, Saudi Arabia. *Clinical, Cosmetic and Investigational Dermatology, 10,* 503–506. https://doi.org/10.2147/CCID.S148499