The Association Between Hidradenitis Suppurativa and Diet: An Update

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ABSTRACT Hidradenitis suppurativa (HS) is a chronic inflammatory skin condition characterized by painful inflammatory lesions, predominantly affecting areas of the skin rich in apocrine glands, such as inguinal, axillary, submammary, and anogenital regions, with an estimated global prevalence between 1%-4%. The treatment of HS is challenging with various treatment modalities employed to control the disease. Since the condition is chronic and life-impairing, many patients have looked for ways to complement their conventional treatment procedures with non-medical interventions, among which dietary interventions have been of particular interest. Researchers have looked for ways to connect the gastrointestinal system with the skin through the ″skin-gut axis concept″ introducing a strong association between the microbiome of the gastrointestinal system and the skin. In addition, diet stimulation of insulin and IGF-1 (insulin-like growth factor 1) may impact signaling pathways playing a role in HS pathogenesis. Patients have tried various dietary interventions to alleviate their symptoms of inflammation and suppuration. Among the different dietary approaches that have been described are paleo, autoimmune, Mediterranean, and elimination diet regimes. Dietary supplements have become the mainstay of lifestyle factors aimed at improving the clinical signs and symptoms of HS. This review aims to synthesize and present the current findings on diet as a modifiable factor in HS, helping the patients to navigate through the data and helping them make informed choices on their healthy lifestyles.

KEY WORDS: hidradenitis suppurativa, skin-gut axis, diet, dietary supplements

INTRODUCTION

Hidradenitis suppurativa (HS), also known as acne inversa, is a chronic inflammatory skin condition characterized by painful inflammatory lesions, predominantly affecting areas of the skin rich in apocrine glands, such as the inguinal, axillary, submammary, and anogenital regions (1-3). The manifestation of HS is usually apparent between puberty and the age of 40, with the estimated global prevalence between 1% and 4% (4,5). The disease is more prevalent in women; however, the clinical picture tends to worsen in men. The clinical presentation ranges from rare, mild inflammatory nodules to widespread abscesses, sinus tracts, and scarring in the axillary, groin, perianal, perineal, and inframammary regions (2,6,7).

The severity of the disease can be assessed with Hurley clinical grading system, modified Sartorius Score (mSS), HS Severity Index (HSSI), and HS Physician's Global Assessment (4). The score most commonly used in clinical practice is the Hurley clinical grading system, which categorizes HS into three stages (8). Hurley stage I is characterized by single or multiple abscesses without sinus tracts and permanent lesions or cicatrization (scarring). The main hallmarks of Hurley stage II include single/multiple, widely separated, and recurrent abscesses with sinus tracts and cicatrization. Stage III is characterized by multiple interconnected abscesses, sinus tracts, and cicatrization that involves an entire anatomical area (9). According to the modified Dessau definition, this disorder is diagnosed clinically: based on typical lesions, the typical sites where the lesions occur, and the chronicity of the disease (at least two recurrences within six months) (2,4). Three processes have been implicated in the pathogenesis of the disease: follicular hyperkeratosis and dilatation, follicular rupture and subsequent inflammatory response, and chronic inflammation with architectural tissue changes (4). The treatment of HS is very challenging; however, various treatment modalities can improve the symptoms and, to a certain extent, control the disease. They can be divided into non-medical and medical modalities. Non-medical options include lifestyle modifications, such as smoking cessation, weight loss, and a healthy diet. Medical modalities can be divided into local and systemic therapy. Local therapy involves topical clindamycin, topical resorcinol, and surgical interventions (wide local excision, incision, and drainage). Systemic therapy includes antibiotics (tetracycline, rifampicin), oral retinoids, hormone therapy (cyproterone acetate and norgestrel oral contraceptive pills, finasteride), immunosuppressants (corticosteroids, cyclosporine) and biologic agents (adalimumab, infliximab). Both local and systemic therapies have been reported as efficacious in disease control (2,10,11). Since the disease is chronic and life-impairing, many patients have looked for ways to complement their conventional treatment procedures with dietary interventions. In the hope of ameliorating the signs of HS, nutritional habits that could prevent flare-ups are of particular interest to patients. With the patients more informed about their condition, questions on dietary interventions have become a standard part of our everyday clinical practice in HS units. Since the relationship between diet and etiology, treatment and prevention of HS is somewhat controversial, and, with a plethora of non-formal forums providing uncorroborated information, it is important that physicians managing HS provide adequate and correct guidance on this topic. This review aims to collect and present data on a diet as a modifiable factor in HS.

HIDRADENITIS SUPPURATIVA AND THE "SKIN-GUT AXIS" CONCEPT

The "skin-gut axis" concept introduces a strong association between the microbiome of the gastrointestinal system and the skin. When this axis is disrupted, it can lead to increased intestinal permeability and systemic inflammation, resulting in inflammatory pilosebaceous disorders, such as rosacea, seborrheic dermatitis, acne vulgaris, and, last but not least, HS (5). Furthermore, the gastrointestinal microbiome could be linked with the severity of clinical presentation by its ability to influence systemic inflammation, oxidative stress, glycemic control, and tissue lipid content (5,12). Various dietary components, illnesses, lifestyles, prebiotics, probiotics, antibiotics, as well as some novel biological drugs can alter gut microbiota. This alteration can lead to dysbiosis, which can decrease the gut mucous layer and result in the passage of microbes through the intestinal barrier. Those microbes can then cause the production of toxic products and induce harmful effects by neurotransmitters of the gut microbes or the host. Furthermore, they can produce B-cell hyperresponsiveness, impair T-cell differentiation and, finally, create low levels of IgA secretion. Consequently, dysbiotic gut microbes, toxic products, neurotransmitters, and altered immune cells pass through the circulatory system and change the condition of the skin from healthy to dysbiotic (13).

The gastrointestinal (GI) system and the skin are analogous concerning the functions they possess, thus supporting the existence of a correlation between the skin and gut microbiota. They are both well-vascularized and innervated, since they have powerful immune and neuroendocrine properties. The inner lining of the GI tract and the outer lining of the skin are both lined with epithelial cells that have direct contact with the exogenous environment, thus serving as a link between the inner body and external environment, preventing the entry of harmful microorganisms and particles (14). Due to constant contact with exogenous particles, they also have a high cellular turnover rate, which is important for inhibiting adherence and possible infection with foreign microbiota and particles. It is of great importance that both the GI system and the skin are heavily colonized with different resident microbial species, which are essential for the homeostatic functioning of the organism. Still, when exposed to constant stressors (physical or psychological), they can become an important factor in the pathogenesis of several diseases, some of which have been mentioned above.

The effect of gastrointestinal dysbiosis on the skin has been hypothesized by several authors. According to O'Neill *et al.*, there are three possible scenarios: the gut microbiota can synthesize molecules and factors that could be both beneficial and harmful, enter the circulation and affect distant sites, with free phenol and p-cresol mentioned (15). The second scenario implies that, besides their products, the gut bacteria itself could enter the circulation, most probably through a disrupted gut barrier, and then affect the skin. The third important scenario involves the immune effects and the connection between intestinal dysbiosis and inflammatory skin diseases. Additionally, the authors proposed that the resident microbiota of the skin can have further modulatory effects on immune-related skin disorders that may be related primarily to the gut microbiota (15). In the case of HS, the microbiota of crucial importance are the yeast *Saccharomyces cerevisiae* and bacteriae *Prevotella* and *Porphyromonas* (14).

DIET AS THE RISK FACTOR IN HIDRADENITIS SUPPURATIVA

Several studies have shown that diet may play a role in the manifestation and management of HS. Western diet (food rich in carbohydrates and fats, but low in fibers) can lead to a shift in microbiome composition (an increased ratio of Firmicutes to Bacteroides) and, subsequently, inflammation. This phenomenon has been studied and described in the literature by multiple authors. The study by Guo *et al.* showed that a Western diet reduces the release of antimicrobial peptides in the small intestine, which progresses to dysbiosis and results in the alteration of pro-inflammatory cytokine levels (16). Furthermore, as demonstrated by Birchenough *et al.*, a Western diet reduces the colonic mucosal barrier (a part of the innate immune defense) and contributes to epithelial inflammation (17). In addition, the breakdown products of this type of diet stimulate insulin and IGF-1 (insulin-like growth factor 1) production, which attenuate the FOX01 (forkhead box protein O1) signal pathway and simultaneously increase the mTOR (mechanistic target of rapamycin) signaling pathway. Such modulation results in an increase in keratinocyte desquamation and sebaceous lipogenesis, which may trigger the endogenous release of androgens and ultimately lead to HS (5). Finally, in their study, Molnar *et al.* hypothesized that the high-fat (Western) diet causes dysbiosis, systemic inflammation, and hyperhomocysteinemia in susceptible individuals, which leads to subsequent elevation of pro-inflammatory cytokines, such as IL (interleukin) -1β, IL-6, IL-17, and TNF-α (tumor necrosis factor-alpha). This increase in dysbiosis-led inflammation coupled with a dysregulation of the 1-carbon metabolism results in an increase of matrix metalloproteinases MMP-2, MMP-8, and MMP-9, responsible for tissue matrix remodeling and maintenance of lesions and tracts (18).

Overconsumption of the Western diet is known to lead to obesity, insulin resistance, and metabolic syndrome, which are closely linked to the severity and nature of the clinical presentation of HS. According to Hu *et al.*, the crucial element that links HS with insulin signaling and resistance is mTORC1 (mechanistic target of rapamycin complex 1). The Western diet increases insulin signaling via the PI3K/Akt pathway and activates mTORC1, contributing to insulin resistance in 2 ways. When mTORC1is activated, it induces serine/threonine phosphorylation of IRS (insulin receptor substrates) by S6K1 (ribosomal S6 kinase 1) and diminishes its ability to be phosphorylated on tyrosine residues. Subsequently, this results in defective insulin signaling and insulin resistance. Activation of mTORC1 is also a strong contributing factor to lipid synthesis. It activates the transcription factor SREBP-1 (sterol regulatory element binding protein 1), which activates ACC (acetyl CoA carboxylase), an enzyme crucial in regulating fatty acid synthesis. The authors concluded that impaired insulin signaling pathways, increased insulin resistance, as well as chronic inflammation are contributing factors that could lead not only to HS but some other skin diseases, such as acne vulgaris, psoriasis, atopic dermatitis, acanthosis nigricans, and androgenetic alopecia (19).

DIET AS THE MODIFIABLE FACTOR IN HIDRADENITIS SUPPURATIVA

Several different dietary approaches have been described in the literature that could improve the clinical picture of HS.

One of them is the paleo diet (dairy-free, gluten-free, grain-free, legume-free, and nightshade-free, with nightshade-free items being potatoes, tomatoes, eggplants, peppers, and paprika) (20).

Another possible regime is the more strict autoimmune protocol diet. This type follows the paleo diet approach but also includes limitations to eggs, seeds, nuts, and artificial sweeteners (20).

The third option would be the Mediterranean diet. This diet, rich in olive oil (omega-3 fatty acids), has been shown to lead to lower disease severity (21). Omega-3 fatty acids are known for their anti-inflammatory properties. Furthermore, they are found to be significant gene modulators that regulate the expression of proteins related to lipid metabolism and inflammation. Because they act as TLR (Toll-like

receptor) ligands (most notably TLR2 and TLR4), they are able to prevent the inflammatory cytokine cascade. The beneficial effects of omega-3 fatty acids are many. Firstly, they inhibit lymphocyte proliferation and cytokine and antibody production. Secondly, they suppress adhesion molecule expression by decreasing interaction between leukocytes and endothelial cells, thus having an anti-atherosclerotic effect. Finally, they inhibit natural killer cell activity and the subsequent apoptosis of cells (22).

The final diet is the elimination diet regime, which aims to eliminate possible dietary triggers, particularly foods rich in wheat and brewer's yeast (bread, pastries, cakes, wine, beer and cheese) (20).

DOES DIET ALTERATION HAVE AN EFFECT ON HIDRADENITIS SUPPURATIVA?

The study by Dempsey *et al.* showed that diet alteration could improve the signs and symptoms of HS and the quality of life of patients with HS. Out of the 242 patients with HS included, 183 (75.6%) participants made some alterations in their diet. The most common food that patients altered was gluten (48.4%), followed by dairy (43.8%), refined sugars (39.6%), legumes (25.2%), eggs (21.1%), and brewer's yeast (17.0%). The study's results demonstrated a strong association between dietary alteration and improvement of the skin condition, with 65.1% of patients claiming an improvement in HS (23).

The study by Fernandez *et al.* further supports the effect of dietary alteration on HS. Out of 700 patients with HS included in the study, 32.6% identified symptom-exacerbating foods, while 12% identified symptom-alleviating foods. The most commonly reported exacerbating foods were sweets (67.9%), bread/pasta (51.1%), dairy products (50.6%), and high-fat foods (42.2%). Alleviating foods were vegetables (78.7%), fruits (56.2%), chicken (51.7%), and fish (42.7%) (24).

Aboud *et al.* reported the benefit of a special diet regime on the clinical picture of HS. Their study included 185 participants. Thirty-seven patients were treated at their center with a brewer's and baker's yeast definitive exclusion diet. The rest of the patients (148) were not treated at their center and did not follow this diet regime. The foods and beverages allowed for consumption were fresh fruits and

Table 1. Diet regimes associated with the improvement of HS

	Description	Improvement of HS	References
Mediterranean diet (rich in omega 3 fatty acids)	fresh fruits and vegetables fish chicken beans extra virgin olive oil	- lower his4 score - lower Sartorius score - lower self-reported disease activity	(21,22)
Elimination regime	no bread no cake no pastries no wine no beer no cheese	- decreased frequency of flare-ups - lower self- reported disease activity	(20,23-25)
Paleo diet	dairy-free gluten-free grain-free legume-free nightshade-free	- subjective reports of symptoms alleviation - subjective reports of decreased flare-up frequency	(20)
Autoimmune protocol	Paleo diet + no eggs no nuts no seeds no artificial sweeteners	subjective reports of symptoms alleviation subjective reports of decreased flare-up frequency	(20)

Table 2. Dietary supplements associated with the improvement of HS

Supplement	Improvement of HS	References
Zinc	- partial and full remission of the disease - decreased expression of inflammatory cell markers	(20,29-31)
Vitamin D	- decrease in number of nodules - decreased frequency of flare-ups	(30,31)
myo-inositol + folic acid + liposomal magnesium	- reduction of Sartorius severity score - improved metabolic profile	(33)

vegetables, white meats, eggs, cereals that do not contain yeast (e.g., rice or com cakes made with puffed cereals), green tea, and coffee. Foods and beverages that were not allowed were bakery products (e.g., pizza, bread, cakes, etc.), soy sauce, vinegar, black tea, beer, wine, fermented cheese, mushrooms, and black tea. Of the 37 patients that followed this diet regime, 26 (70%) reported improved overall well-being and reduced symptoms. Notably, the symptoms recurred after consuming a restricted diet item in 32 of 37 (87%) patients. In the same study, it was observed that symptoms were more severe and flare-ups more frequent in the group of patients not treated with the diet regime. Therefore, the authors concluded that the diet regime reduces local and systemic inflammation. This results in less invasive operative procedures, which maximizes the chances of healing and diminishes the morbidity of surgical excision (25).

Several case reports have showed the beneficial effects of a zero carbohydrate all-meat ketogenic diet consisting of ground beef patties and grass-fed ribeye beef steaks. However, the effects of such an intense diet plan on other organ systems must be considered, since a ketogenic diet can have severe and life-threatening implications.

In addition to diet and a healthy lifestyle, maintaining optimal body weight is important for disease management. As described by Kromann *et al.*, substantial weight loss can significantly reduce disease severity as assessed by flares and the number of affected regions. Furthermore, an overweight body is more prone to increased friction from skin folds and a humid skin milieu, which favors the thriving and growth of microbes and promotes low-grade systemic inflammation, which are the factors leading to the worsening of the clinical picture of HS (26). However, as clinicians, we need to be empathetic when recommending any weight-loss regimes to our patients, taking into account the psychosocial burden of HS and how the inability to afford healthy food choices can lead to more stress and frustration.

A summary of diet regimes associated with the clinical presentation of HS is presented in Table 1.

DIETARY SUPPLEMENTS AND HS

In addition to dietary modifications, dietary supplements have been an area of interest due to their potential anti-inflammatory effect (20). We have witnessed an increasing interest from our patients regarding several substances marketed in "dose form", such as zinc capsules, vitamin D drops, and an oral supplement based on myo-inositol, folic acid, and liposomal magnesium. Zinc inhibits both isoenzymes of 5α-reductase, thus having an anti-inflammatory and anti-androgenic effect (20). Various studies have demonstrated its potent anti-inflammatory ability (20,27-29). Vitamin D studies have shown that its deficiency correlates with HS disease severity. However, a causal relationship cannot be established, as vitamin D deficiency results from chronic inflammation and is not an etiological factor of the disease (30-32). However, due to its anti-inflammatory effect and its positive effects on the immune system, skin homeostasis, and insulin levels, the potential of vitamin D in the treatment of HS must not be neglected. Myo-inositol has insulin-mimetic properties, which may decrease insulin resistance. Folic acid reduces inflammation, decreases insulin resistance, and improves gastrointestinal absorbance. Liposomal magnesium also improves fasting glucose levels and insulin resistance. As an adjuvant to antibiotic therapy, it has been reported to improve the clinical picture and metabolic profile of patients with HS (33).

A number of other supplements have been linked to HS, such as curcumin, copper, vitamin B12, ginger, and resveratrol. However, research on these supplements is limited. In our everyday clinical practice, we should be cautious when recommending

supplements that the national health authorities have not approved, as unregulated products can be unsafe for consumption.

A summary of dietary supplements associated with the clinical presentation of HS is presented in Table 2.

CONCLUSION

Even though the pathophysiologic mechanism of HS has not yet been completely understood, it has been shown that diet, especially the Western diet, could contribute to HS, worsening the clinical manifestation and prolonging the drainage from active lesions. Western diet leads to a decrease in antimicrobial peptides and an increase in the Firmicutes/Bacteroidetes ratio. Consequently, there is an increase in inflammation, which leads to matrix remodeling and the formation of tracts. Furthermore, this diet predisposes patients to obesity, diabetes, and metabolic syndrome, thus adding the endocrine factor to this multifactorial disease. Therefore, educating our patients about healthy lifestyles and habits is very important.

References:

1. Weller R, Hunter H, Mann M. Clinical dermatology, 5th edition. Wiley Blackwell, 2015.
2. Lee EY, Alhusayen R, Lansang P, Shear N, Yeung J. What is hidradenitis suppurativa? Can Fam Physician. 2017;63:114-20.
3. Woodruff CM, Charlie AM, Leslie KS. Hidradenitis Suppurativa: A Guide for the Practicing Physician. Mayo Clin Proc. 2015;90:1679-93.
4. Nguyen TV, Damiani G, Orenstein LAV, Hamzavi I, Jemec GB. Hidradenitis suppurativa: an update on epidemiology, phenotypes, diagnosis, pathogenesis, comorbidities and quality of life. J Eur Acad Dermatol Venereol. 2021;35:50-61.
5. Maarouf M, Platto JF, Shi VY. The role of nutrition in inflammatory pilosebaceous disorders: Implication of the skin-gut axis. Australas J Dermatol. 2019;60:e90-e98.
6. Wipperman J, Bragg DA, Litzner B. Hidradenitis Suppurativa: Rapid Evidence Review. Am Fam Physician. 2019;100:562-9.
7. Ballard K, Shuman VL. Hidradenitis Suppurativa. 2021 11. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan.
8. Lovrić I, Brkić J, Ćorluka M, Čović M, Pejić J, Zeljko Penavić J. Two Cases of Hidradenitis Suppurativa Treated with Adalimumab at the Department of Dermatology and Venereology, Clinical Hospital Mostar. Acta Dermatovenerol Croat. 2021;29:108-10.
9. Ovadja ZN, Schuit MM, van der Horst CMAM, Lapid O. Inter- and intrarater reliability of Hurley staging for hidradenitis suppurativa. Br J Dermatol. 2019;181:344-9.
10. Alikhan A, Lynch PJ, Eisen DB. Hidradenitis suppurativa: a comprehensive review. J Am Acad Dermatol. 2009;60:539-61; quiz 562-3.
11. Yhy Hendricks AJ, Hsiao JL, Lowes MA, Shi VY. A Comparison of International Management Guidelines for Hidradenitis Suppurativa. Dermatology. 2021;237:81-96.
12. Bowe W, Patel NB, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis: from anecdote to translational medicine. Benef Microbes. 2014;5:185-99.
13. Mahmud MR, Akter S, Tamanna SK, Mazumder L, Esti IZ, Banerjee S, *et al.* Impact of gut microbiome on skin health: gut-skin axis observed through the lenses of therapeutics and skin diseases. Gut Microbes. 2022;14:2096995.
14. De Pessemier B, Grine L, Debaere M, Maes A, Paetzold B, Callewaert C. Gut-Skin Axis: Current Knowledge of the Interrelationship between Microbial Dysbiosis and Skin Conditions. Microorganisms. 2021;9:353.
15. O'Neill CA, Monteleone G, McLaughlin JT, Paus R. The gut-skin axis in health and disease: A paradigm with therapeutic implications. Bioessays. 2016;38:1167-76.
16. Guo X, Li J, Tang R, Zhang G, Zeng H, Wood RJ, *et al.* High Fat Diet Alters Gut Microbiota and the Expression of Paneth Cell-Antimicrobial Peptides Preceding Changes of Circulating Inflammatory Cytokines. Mediators Inflamm. 2017;2017:9474896.
17. Birchenough G, Schroeder BO, Bäckhed F, Hansson GC. Dietary destabilisation of the balance between the microbiota and the colonic mucus barrier. Gut Microbes. 2019;10:246-50.
18. Molnar J, Mallonee CJ, Stanisic D, Homme RP, George AK, Singh M, *et al.* Hidradenitis Suppurativa and 1-Carbon Metabolism: Role of Gut Microbiome, Matrix Metalloproteinases, and Hyperhomocysteinemia. Front Immunol. 2020;11:1730.
19. Hu Y, Zhu Y, Lian N, Chen M, Bartke A, Yuan R. Metabolic Syndrome and Skin Diseases. Front Endocrinol (Lausanne). 2019;10:788.
20. Silfvast-Kaiser A, Youssef R, Paek SY. Diet in hidra-

denitis suppurativa: a review of published and lay literature. Int J Dermatol. 2019;58:1225-30.

21. Lorite-Fuentes I, Montero-Vilchez T, Arias-Santiago S, Molina-Leyva A. Potential Benefits of the Mediterranean Diet and Physical Activity in Patients with Hidradenitis Suppurativa: A Cross-Sectional Study in a Spanish Population. Nutrients. 2022;14:551.
22. Balić A, Vlašić D, Žužul K, Marinović B, Bukvić Mokos Z. Omega-3 Versus Omega-6 Polyunsaturated Fatty Acids in the Prevention and Treatment of Inflammatory Skin Diseases. Int J Mol Sci. 2020;21:741.
23. Dempsey A, Butt M, Kirby JS. Prevalence and Impact of Dietary Avoidance among Individuals with Hidradenitis Suppurativa. Dermatology. 2020;236:289-95.
24. Fernandez JM, Marr KD, Hendricks AJ, Price KN, Ludwig CM, Maarouf M, *et al.* Alleviating and exacerbating foods in hidradenitis suppurativa. Dermatol Ther. 2020;33(6).
25. Aboud C, Zamaria N, Cannistrà C. Treatment of hidradenitis suppurativa: Surgery and yeast (Saccharomyces cerevisiae)-exclusion diet. Results after 6 years. Surgery. 2020;167:1012-5.
26. Kromann CB, Ibler KS, Kristiansen VB, Jemec GB. The influence of body weight on the prevalence and severity of hidradenitis suppurativa. Acta Derm Venereol. 2014;94:553-7.
27. Dréno B, Khammari A, Brocard A, Moyse D, Blouin E, Guillet G, *et al.* Hidradenitis suppurativa: the role of deficient cutaneous innate immunity. Arch Dermatol. 2012;148:182-6.
28. Poveda I, Vilarrasa E, Martorell A, García-Martínez FJ, Segura JM, Hispán P, *et al.* Serum Zinc Levels in Hidradenitis Suppurativa: A Case-Control Study. Am J Clin Dermatol. 2018;19:771-7.
29. Brocard A, Knol AC, Khammari A, Dréno B. Hidradenitis suppurativa and zinc: a new therapeutic approach. A pilot study. Dermatology. 2007;214:325-7.
30. Guillet A, Brocard A, Bach Ngohou K, Graveline N, Leloup AG, Ali D, *et al.* Verneuil's disease, innate immunity and vitamin D: a pilot study. J Eur Acad Dermatol Venereol. 2015;29:1347-53.
31. Kelly G, Sweeney CM, Fitzgerald R, O'Keane MP, Kilbane M, Lally A, *et al.* Vitamin D status in hidradenitis suppurativa Br J Dermatol. 2014;170:1379-80.
32. Karagiannidis I, Nikolakis G, Sabat R, Zouboulis CC. Hidradenitis suppurativa/Acne inversa: an endocrine skin disorder? Rev Endocr Metab Disord. 2016;17:335-41.
33. Donnarumma M, Marasca C, Palma M, Vastarella M, Annunziata MC, Fabbrocini G. An oral supplementation based on myo-inositol, folic acid and liposomal magnesium may act synergistically with antibiotic therapy and can improve metabolic profile in patients affected by Hidradenitis suppurativa: our experience. G Ital Dermatol Venereol. 2020;155:749-53.