ISSN (Online) 2249-6084 (Print) 2250-1029

International Journal of Pharmaceutical and Phytopharmacological Research (eIJPPR)
[Impact Factor – 0.852]

Journal Homepage: www.eijppr.com

Review Article

Etiopathogenesis of Kushtha Roga W.S.R. to Psoriasis

Satyapal Singh [1*], P.S. Byadgi[2], J.S. Tripathi[3], N.P. Rai[4]
[1]Senior Resident and Research Scholar, Department of Kayachikitsa, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.
[2]Assistant Professor, Department of VikritiVigyan, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.
[3]Professor, department of Kayachikitsa, faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.
[4]Professor and Head, Department of Kayachikitsa, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh, India.

Article info

Article History:
Received 28 September 2014
Accepted 11 November 2014

Keywords:
Ayurveda, Kushtha Roga, Dermatological disorders, Psoriasis, Etiology, Pathogenesis.

Abstract

The main objective of this review is to discuss the different aspects of etiology and pathogenesis of Kushtha Roga with special reference to psoriasis. In Ayurveda Kushtha Roga includes dermatological disorders including psoriasis. Kushtha roga including psoriasis described as one of the most chronic disorders and is very difficult to cure.Several modifying factors including obesity, trauma, infection and a possible deficiency of the active forms of vitamin D3 plays an important role in the development of psoriasis. Psorias is a complex, chronic, multifactorial, inflammatory disease that involves hyperproliferation of the keratinocytes in the epidermis, with an increase in the epidermal cell turnover rate. Environmental, genetic, and immunologic factors appear to play a key role in the pathogenesis of different chronic dermatological disorders especially in psoriasis. The disease psoriasis, most commonly manifests on the skin of the elbows, knees, scalp, lumbosacral areas, intergluteal clefts, and glans penis. In up to 30% of patients, the joints are also affected. Both sciences, ayurveda and modern medical science accepted that diet, activities, environmental, genetic and immunological and psychological factors play key role in the etio-pathogenesis of dermatological disorders.

1. INTRODUCTION

The skin is the largest organ of our body. It is one of the five 'Gyanendriyas' described in Ayurvedic texts, which is responsible for 'Sparsha Gyan' or touch sensation. Most of the skin disorders have been described under the umbrella of Kushtha. Word Kushtha means a pathological condition which despises the skin. Skin is an important organ of communication with the external world. Psoriasis is one of the most common dermatological diseases affecting up to 2.5% of the world's population. It is a non-infectious chronic inflammatory skin disorder clinically characterised by erythematous sharply demarcated papules and rounded plaques covered by silvery micaceous scales. Psoriasis appears to affect men and women equally. Although psoriasis can affect all age groups, the onset of psoriasis tends to peak between the ages of 20 and 30 and between ages fifty and sixty[1].Psoriasis is typically unpredictable in its course, may vary in severity from one episode or flare to another, and often recurs throughout an affected person's life. Symptom presentation can vary significantly from one patient to another. Psoriasis is associated with significant comorbidities and affects patient's quality of life. Psychological factors have traditionally been associated with the onset, development and persistence of skin diseases. Stress is emphasized as one of the major important factors in the initiation and exacerbation of skin diseases. Psoriasis is independently associated with depression and the risk of psychiatric comorbidity increases with the severity of psoriasis[2]. Successful management of psoriasis patients depends on clinician's understanding of the various treatment options as well as their recognition of associated adverse reactions. In Ayurveda kushtha roga is also considered as a Papakarmaja Vyadhi (a disease due to sinful activities).

Corresponding Author:
Satyapal Singh, Senior Resident and Research Scholar,
Department of Kayachikitsa, faculty of Ayurveda,
Institute of Medical Sciences ,Banaras Hindu University ,
Varanasi, Uttar Pradesh, India.
Email: spmairti@gmail.com ; Contact No. +91-9450035793

2. ETIOPATHOGENESIS OF KUSHTHA

2.1 Etiology
The etiology can be broadly grouped into two categories, which are immediate causative factors and distant causative factors.

2.2 Immediate causative factors
There are seven factors involved in the pathogenesis of Kushtha, according to Acharya Charaka these are Vata, Pitta, Kapha, Tvak, Rakta, Mamsa and Ambu (Lasika)[3]. Charak in Sutrasthana[4] has been cited that Kushtha is a Raktaja Roga. Hence, the factors responsible for the vitiation of these seven components are also considered in the etiology of Kushtha.

2.3 Distant causative factors
Distant causative factors are those which do not involved directly in pathogenesis of disease but they aggravate the actual causative factor and thus play an important role in pathogenesis of disease.These factors are Adibala pravritta vyadhi (Kulaja), Poorva janmakrita and Janmot tarakalaja.

2.4 Kulaja Nidana
Kushtha is Adibala Pravritta Vyadhi[5]. Kushthayukta Shukra and Shonita results in the birth of "Kushthi child"[6].If both Mother and Father are having kushtha, the offspring also becomes a patient of Kushtha as the Shonita and Sukra of the patient were vitiated.

2.5 Poorvajanmakrit
According to Sushruta if the person suffered from kushtha in his previous life and if he takes rebirth then he develops kushtha in his present life also[7].

2.6 Janmottarakalaja
These nidanas can be categorized into, Aharaja–diet and dietetic pattern and Viharaja- faulty lifestyle.

2.7 Aharaja Nidana

Aharaja nidanas include the following:

1. Atisevan and Atyasan
2. Adhyasana and Ajirnasana
3. Vishamashana and
4. Viruddha Ahara

2.8 Atisevana and Atyashana

Atimatra→Amotpatti→Kushthautpatti

Taking excessive Guru and Snigdha Ahara produces Dushti in Rasavaha Srotas[8]. Acharya Charak has also described - "Gurubhojanam Durvipakakaranam"[9]. Guru Ahara also causes Dusti of Mamsavaha Srotas[10]. Excessive Drava causes Dushti of Raktavaha Srotas[11].

2.9 Adhyashana and Ajirnashana

Taking food during incomplete digestion state is called Adhyashana. Intake of food in state of indigestion is Ajirnashana. According to Acharya Charak, taking food in state of indigestion is best known to cause Grahani Dushti[12]. This leads to impairment in normal physiological functions of Grahani as well. Ajirna Adhaysahana causes Agnimandya and Dushti in Malavaha Srotas[13]. Both are cause of Agnimandhya so ultimately produce disease. Both of them also vitiate Rakta[14].If this pathology continues for long time, it may produces Kushtha Roga.

2.10 Vishamashana

Taking food at irregular time and in irregular quantity is termed as Vishamashana. Vishamashana is best known to produce Vishama Agni. In present day life, Hurry, Worry and Curry are becoming universal. In today's life, no one has time to even eat properly.

2.11 Viruddha ahara

Acahrya Charka stated that - **"Virrudha veerya shanam Ninditavyadikaranam"**[15]. All types of Viruddha Ahara do not produce disease because body elements like Dushya and Dehabala (immunity) protect the body from the diseases. Viruddha Ahara specially disturbed the functions of Agni and Srotas as follows.

2.11.1 Effect of Viruddha Ahara on Agni

The Agni mostly gets vitiated by Viruddha type of Ahara. The vitiated Jatharagni does not digest even the Laghu Ahara (food substance easy to digest), resulting in state of indigestion. This indigested food materials turns sour and acts like a poison, which is termed as Amavisha[16].Tridosha get provocated by this type of Amavisha[17].

2.11.2 Effect of Viruddha Ahara on Srotas

In general, food substances and activities (Vihara) which are similar in quality to body humors (doshas) and deleterious to the body elements (dhatus) vitiate the body channels (srotas). The vitiation results in Srotodushti i.e. malfunctioning of Srotas. The symptoms of Srotodushti are as follolws[18]

- Atipravritti
- Sanga
- Siragranthi
- Vimarga Gaman

2.12 Mithyaahara

Improper food habits are another major causative factor of Kushtha. There are certain codes of conducts of eating which when not followed are called Mithyaahara. The codes of conduct of eating have been termed as "Ashta Ahara Vidhi Vishesha Ayatana" and "Dwadashaashanvidhi." Mithyaahara deranges the digestive power of Jatharagni and also cause Dushti of Grahani. Thus the food does not get digested properly leading to production of Ama. As Grahani is also Dushita, Ama undergoes putrefacation which in turn produces Amavisha[19]. So along with Kushtha, other diseases which can be manifested due to Ama, Amavisha, and Grahani Dushti etc. may coexist. Like in Psoriasis, the coexistence of Psoriatic arthritis, Crohn disease, Ulcerative colitis, Dermatogenic enteropathy, Gout, and Diabetes mellitus have been reported.

2.13 Viharaja Nidan

Acharya Gayadas has been divided the Mithya Viharaja Nidanas into 3 categories viz. Kayika, Vachika and Manasika (improper physical, verbal and mental activities) [20].

2.13.1 Kayika (physical)

Kayika Nidanas include suppression of natural urges, Excessive sun exposure, exposure to air conditioned, work place contradicting with hot and humid environment,Over exertion and over exercises, day sleep, late night sleep and complications of panchakarma therapy.

2.13.2 Vachika (Verbal)

Behavioral misconduct or verbal sinful activities like abusing teachers, deities etc. and verbal antisocial activities are considered as Vachik Nidana (Hetu).These factors bring about psychogenic stress which is of prime importance in the pathogenesis of kushtha (skin diseases). Chinta, Bhaya, Shoka are Vata Prakopaka Nidana and Bhaya, Krodha and Shoka also causes Dushti of Swedavaha Srotas [21]. Chinta causes Dushti of Raktavaha Srotas.

2.13.3 Mansika (Mental)

The diseases, in which no clinical result obtained even after the best treatment were considered as Papakarmaja Vyadhi (disease due to sinful activities). Both Charak[22]and Sushruta[23]have described Kushtha as a most chronic disorder and all acharyas including Bahavaprakash and Madhavakara have included it to be due to Papa-Karma. It indicates that the effective treatment for Kushtha was not available upto the time of Bhavamishra. Even, now a day's skin diseases run a chronic course and dermatologists ultimately end up in making use of corticosteroids to get symptomatic relief.

2.14 Pathogenesis (Samprapti) of Kushtha

The Doshas due to the irrespective Hetus get vitiated and spread throughout the body which inturn vitiates Dhatus and manifests disease.The whole process is known as Samprapti[24]. According to Acharya Charaka 7 Dravyas, when disturbed lead to the genesis of Kushtha[25]. These are 3 doshas namely-Vata, Pitta and Kapha and 4 dushyas namely-Tvaka, Mamsa, Rakta and Lasika (Ambu). After that Kushtha spreads to the entire body by its Prabhava.

Charaka has emphasized the dual part played by Nidana,i.e.simultaneous vitiation of Tridosha and also Shaithilyata in the Dhatus such as Twak, Rakta, Mamsa and Lasika. Thus vitiated Tridoshas gains momentum to vitiate Shithila Dhatus and hence the disease Kushtha gets manifested[26, 46].

Nidana Sevana
↓
Tridosha Prakopa
↓
Twak, Rakta, Mamsa and Ambu Shaithilyata
↓
Further Vitiation of Doshas occurs
↓
These Doshas gets accumulated at the place of Dhatu Shaithilyata
↓
Dosha and dushya samurchhana
↓
Kushtha

Acharya Sushruta described that due to Doshaja and Karmaja Hetus, aggravation of Pitta and Kapha takes place which produce Avarana of Vata which inturn aggravates Vata. Vitiated Vata enters in the Tiryaka Sira with two other vitiated Doshas and their spread leads to further vitiation. After this it reaches to Bahya Rogamarga (Tvak, Rakta, Mamsa, Lasika) and spread throughout the body, producing Mandala at the gathering site of Doshas. If these Doshas are not treated properly. Afterthat they enter into the deeper Dhatus of the body[27,46].

3. ETIOPATHOGENESIS OF PSORIASIS

3.1 Etiology

Exact etiology is still unknown. According to most workers, it is a heredo-familial disease brought on by stress. For long, it was believed to be primarily a disorder of keratinization. However, the successful use of traditional immunosupressants and newer immunomodulatory agents in the treatment of psoriasis led to the belief that psoriasis is primarily a disease of Th1 cell immune

dysregulation. Psoriasis is now considered a multifactorial disorder that has several factors like genetic predisposition, environmental and immunologically mediated inflammation.

Several risk factors participated in the etiology of psoriasis. These risk factors are discussed below:

3.1.1 Environmental factors

Several evidence indicate that interaction between genes and environment is important in manifestation of disease. Many environmental factors have linked to psoriasis, and have been implicated in initiation of disease process and exacerbation of pre-existing disease[28].

3.1.2 Trauma (skin injury)

Psoriasis at the site of injury is well known (Koebner phenomenon). A wide range of injurious local stimuli, including physical, chemical, electrical, surgical, infective and inflammatory insults have been recognised to elicit psoriatic lesion.

People with psoriasis often notice new lesions 7 to 14 days after the skin is cut, scratched, rubbed, or severely sunburned. This is called the “Koebner phenomenon” and is named after Dr. Koebner who in the 19th century observed that a patient developed new lesions in areas where his horse bit him. This relationship between skin injury and developing new psoriatic lesions has been observed in many patients. Today, a wide range of traumas and skin conditions are known to trigger Koebner phenomenon. Research shows that about 50% of people with psoriasis experience the Koebner phenomenon with development of a psoriatic lesion at the site of a skin injury or in the same place as another skin condition. About 10% of psoriasis patients develop a new psoriatic lesion each time the skin is injured. The likelihood of developing the Koebner phenomenon may increase when psoriasis lesions are already present[29].

3.1.3 Infection

Acute guttate psoriasis is strongly associated with preceeding or concurrent streptococcal infection, particularly of the throat. There is evidence that streptococcal infection may be important in chronic plaque psoriasis, and treatment with rifampicin and peniciline may lead to clearance of skin lesions. One third cases of guttate psoriasis progress to the chronic plaque psoriasis. Guttate and chronic plaque psoriasis share strong HLA association particularly with HLA-Cw6. HIV infection has also been associated with psoriasis[30].

3.1.4 Drugs

There are many drugs reported to be responsible for the onset or exacerbation of psoriasis. Chief amongst these are lithium salts, antimalarials, beta blockers, ACE inhibitors, NSAIDS, and the withdrawal of corticosteroids. Some authors and colleagues have suggested that NSAIDS and beta blockers have little adverse effect but the adverse effect of lithium salts and antimalarials may be severe[31].

3.1.5 Sunlight

Although sunlight is generally beneficial, in small minority of patients, psoriasis may be provoked by the strong sunlight and cause summer exacerbation in exposed skin. Photochemotherapy (PUVA) can be helpfull in these patients.

3.1.6 Metabolic factors

The early onset of psoriasis in the women, with a peak around puberty, changes during pregnancy and provocation of psoriasis by high dose oestrogen therapy potentially indicate a role for hormonal factors in the disease. A questionnaire study has provided data from 65 females who had one or more pregnancies after diagnosis was made. Psoriasis was improved approximately in 40% of the pregnancies, and worsened in 14% .Hypocalcaemia has been reported to occur in severe forms of psoriasis, particularly generalised pustular psoriasis[32].

3.1.7 Psychogenic factors

Considerable clinical evidence exists for the role of psychogenic factors in onset and exacerbation of disease. Seville reported consistent links between major stressfull life events and disease manifestation. Gupta reported more exacervations and worsening of disease related with stress reactivity[33].Someother studies also established the role of psychogenic factors in the initiation/exacervation of psoriasis [48-50].

3.1.8 Alcohol and Smoking

It has long been suspected that both cigarette smokong and alcohol consumption have a detrimental effect on psoriasis. When controlled for confounding variables, studies suggested that alcohol may exacerbate pre-existing disease but does not appear to induce psoriasis. This effect seems greater in men than women. Heavy drinkers tend to have more extensive and inflamed disease. Increased alcohol consumption is a recognized stress response. Excess drinking is undoubtedly also a consequence of disease and leads to treatment resistance and reduces therapeutic compliance[34-35].

3.1.9 Weather

Winter tends to be the most challenging season for people living with psoriasis. Numerous studies indicate cold weather is a common trigger for many people and that hot and sunny climates appear to clear the skin. Cold winter weather is dry, and indoor heat robes the skin of needed moisture. This usually worsens psoriasis. Psoriasis can become even more severe when the stress of the holidays and winter illnesses combine to compromise immune systems.While hot and sunny may help clear psoriasis, air-conditioning can dry out the skin and aggravate psoriasis.

3.2 Pathogenesis of psoriasis

Psoriasis is characterized by hyperproliferation and abnormal differentiation of epidermal keratinocytes, lymphocyte infiltration consisting mostly of T lymphocytes and various endothelial vascular changes in the dermal layer, such as angiogenesis, dilatation and high endothelial venule (HEV) formation[36].

The pathogenesis of psoriasis can be summarise in four stages- Abnormal keratinocyte differentiation and hyper proliferation, Infiltration of inflammatory elements, Role of genetic factors and Role of immunological factors.

3.2.1 Abnormal keratinocyte differentiation and hyper proliferation

Multiple growth factors or markers have been shown to modulate keratinocyte differentiation and proliferation and all have implications in the pathogenesis of the disease. Some of these are, epidermal growth factor (EGF) ,transforming growth factor-alpha (TGF-a), keratinocyte transglutaminase type I (TGase K), migration inhibitory factor-related protein-8 (MRP-8), skin-derived antileukoproteinase (SKALP), bone morphogenetic protein-6 (BMP-6), ornithine decarboxylase, activating protein (AP1) and mitogen-activated protein kinase (MAPK) etc.

3.2.2 Infiltration of inflammatory elements

The inflammatory aspect of psoriasis is physically evident by the redness of psoriatic plaques. The biochemical basis for this inflammation stems from several immune modulators, including various cytokines released from keratinocytes and other proteins involved in the inflammatory response, which are increased in psoriasis at both local and systemic level.

Interleukin-12 is a heterodimeric cytokine produced by macrophages. It induces differentiation of CD4 native T cells to Th1 cell and activates natural killer cells. These Th1 cells and activated natural killer cells produce interferon (IFN)-γ, and other type-1 cytokines, such as IL-2 and TNF-α. Interleukin-23 is a more recently described cytokine that is closely related to IL-12 in structure. The dominant role of IL-23 involves the stimulation of a subset of CD4+ T cells (sometimes called IL-17 producing T cells) to produce IL-17. IL-17 is a critical component in the establishment and perpetuation of autoimmune inflammation. IL-17 induces the production of proinflammatory cytokines, predominately by endothelial cells and macrophages. It is believed that IL-17 and IFN-γ synergize to increase production of proinflammatory cytokines by keratinocytes, which is likely important for the development of inflammation in the skin seen in psoriasis[37].

Likewise, pituitary adenylate cyclase activating polypeptide (PACAP) is an inflammatory mediator that is upregulated in psoriatic lesions. Immune cells synthesize PACAP, a regulatory neuropeptide of the VIP family. Its involvement in psoriasis also accounts for the tendency of psoriasis to worsen with stress, because neuropeptides are known for their involvement in skin-nervous system interactions[38].

3.2.3 Role of genetic factors

Psoriasis has been associated with many human leukocyte antigen(HLA) haplotypes. By using linkage analysis and genome-wide association studies, at least nine candidate loci have been identified: 6p (PSORS1), 17q25 (PSORS2), 4q34 (PSORS3), 1q21 (PSORS4), 3q21 (PSORS5), 19p13 (PSORS6), 1p32 (PSORS7), 16q (PSORS8) and 4q31 (PSORS9)[39].

Genetic basis of psoriasis has been accepted for many years, and it is commonly considered as a complex trait. So far, between 10 and 20 chromosome regions have been proposed to harbour psoriasis genes but less than a handful of genes have been

identified. This is due, in part, to their low-risk effects and the limitations in the number of patients and families that have been studied. One locus consistently identified in studies of psoriasis is the class I region of the major histocompatibility locus antigen cluster (MHC). However, it's low penetrance — about 10% — indicates that other genetic and environmental factors are also involved. The identity of psoriasis susceptibility 1 (PSORS1) remains controversial. Although its association with human leukocyte antigen (HLA) Cw6 and psoriasis was reported more than 25 years ago. The extensive linkage disequilibrium across the class I region and its complex evolutionary history has made identification of the susceptibility variant(s) very difficult. Genes within this region lying about 160 kilo bases telomeric to HLA-C, such as corneodesmosin (CDSN) and the α-helical coiled-coil rod (HCR), have been proposed as contenders. A consensus is now begin to emerge, that supports the location of PSORS1as being closer to the region harbouring HLA-C/HLA-B and excluding CDSN and HCR.Other predisposing polygenes might affect the immune system or be involved in keratinocyte differentiation. Common variants in the SLC9A3R1/NAT9 region and loss of a potential RUNX binding site have been described that could potentially affect regulation of the immune synapse. There has also been a report of an association of psoriasis with variant alleles of the lymphoid phosphatase PTPN22[40]. This is also involved in regulation of the immune synapse and an R620W polymorphism is associated with at least four other autoimmune diseases Associations with alleles encoding other components of the immune system such as IL-12 and IL-19/20[41-43].

3.2.4 Role of immunological factors

Immunologic phenomena recently have been proved to be a major factor in the pathogenesis of the psoriasis.The current understanding of the molecular pathogenesis of psoriasis assigns central importance to an interaction between acquired and innate immunity.

Psoriasis is now considered an example of an autoimmune disease mediated by a T helper type 1 cell (TH1-type immune) response. T helper (Th) 17 cells, a novel T-cell subset, have been implicated in the pathogenesis of psoriasis and other autoimmune inflammatory diseases.T lymphocytes are key pathogenic contributors in psoriasis. Resolution of skin disease has been induced by agents that target activated T cells or T cell co-stimulation, andby administration of cytokines that decrease type 1 T cell activation[44].

Both innate and acquired immune changes are thought to be responsible for the development of psoriatic plaques. Different types of helper T subsets, dendritic cells, plasmacytoid dendritic cells as well as Langerhans cells have been found to play a role in psoriasis. The successful use of T-cell immunosuppressant cyclosporin A in the treatment of psoriasis led the concept that T cell activation is a key event in psoriasis. This study was further strengthened with the successful use of anti-T cell specific drugs in the form of anti-CD3 and -CD4 monoclonal antibodies in treatment. There is also the possibility that psoriasis may be an organ-specific autoimmune disease with similarities to rheumatoid arthritis and multiple sclerosis. Recent use of so-called "etio-pathogenetic" drugs like methotrexate, and alefacept suggests autoimmunity as a major factor in pathogenesis of psoriasis[45].

4. DISCUSSION

Dermatological disorders described in modern medicine many be compared to Kushtha Roga. It is considered as one of the most chronic disorder which is very difficult to cure. Dietetic, behavioural, environmental, genetic, and immunologic factors appear to play an important role in the pathogenesis of Kushtha roga including psoriasis. Psoriasis is a complex, chronic, multifactorial, inflammatory disease that involves hyperproliferation of the keratinocytes in the epidermis, with an increase in the epidermal cell turnover rate. The disease most commonly manifests on the skin of the elbows, knees, scalp, lumbosacral areas, intergluteal clefts, and glans penis. In up to 30% of patients, the joints are also affected.[47]

Kapha disturbance leads to immunological variations which favours the development of psoriasis. Due to pitta disturbance there is a development of hyperproliferation of the keratinocytes in the epidermis. An increase in the epidermal cell turnover rate is because of vitiated Vata.

Ayurveda recognised the role of psychological factors in the pathogenesis of different skin disorders. In this context Acharya charaka stated that the skin has an eternal relationship with the mann (psyche/mind). Therefore, psychological stress due to any cause directly or indirectly leads to negative impact on mann, which inturn leads to initiation/ exacervation of pre-existing skin disease. Several studies on psoriasis revealed that there is a strong relation exist between the psychological stress and psoriasis.

5. CONCLUSION

The present review has mainly focused on different aspects of etiopathogenesis of Kushtha Roga and psoriasis. Other dermatological conditions also share many stigmatizing effects of psoriasis because of their visibility and the ignorance on the part of both by the general public and some healthcare providers.Thus, Patients of the skin disorder always experience physical, mental and socio-economic embarrassment in the society. This embarrassment leads to mental stress which further causes aggravation of pre existing disease. In this way here an attempt has been made to present a collective knowledge on etiopathogenesis of Kushtha Roga and psoriasis. In a nut shell dietetic, behavioural, environmental, genetic, and immunological factors appear to play an important role in the pathogenesis of Kushtha roga including psoriasis.

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