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REVIEW ARTICLE

Itch in Ethnic Populations

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Racial and ethnic differences in the prevalence and clinical characteristics of itch have rarely been studied. The aim of this review is to highlight possible associations between ethnicity and different forms of chronic itch. We provide a current review of the prevalence of different types of itch in ethnic populations. Genetic variation may significantly affect receptors for itch as well as response to anti-pruritic therapies. Primary cutaneous amyloidosis, a type of pruritic dermatosis, is particularly common in Asians and rare in Caucasians and African Americans, and this may relate to a genetic polymorphism in the Interleukin-31 receptor. Pruritus secondary to the use of chloroquine for malaria is a common problem for African patients, but is not commonly reported in other ethnic groups. In patients with primary biliary cirrhosis, pruritus is more common and more severe in African Americans and Hispanics compared with Caucasians. Racial and ethnic differences in itch and its medical care are poorly understood. Research is needed to examine biological, psychosocial, and lifestyle factors that may contribute to these disparities. ***Key words: pruritus; race; Black; Asian; Caucasian; Hispanics.***

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The prevalence of itch varies significantly across different ethnic populations. Several pruritic conditions occur more frequently in certain ethnic groups and in certain diseases. However, the impact of ethnicity on itch has so far received minimal attention.

The study of chronic itch is complicated, as it is influenced by multiple factors, such as age, environment, social, cultural, level of education and psychological factors. Knowledge of racial differences in pruritic conditions is useful to aid diagnosis and to provide appropriate management. This short review summarizes the differences in skin structure and function and its association with itch in different ethnic populations, and describes itch entities that are specific to different ethnic populations.

DIFFERENCES IN SKIN BIOLOGY AND ITCH

Few studies have examined the differences between skin types in relation to ethnicity and neurobiology of the skin. Differences between ethnic skin types and skin properties may explain racial disparities seen in pruritic dermatologic disorders.

Epidermal structure and function

A recent study has shown that the skin surface and melanocyte cytosol of darkly pigmented skin is more acidic compared with those of type I–III skin (1). Serine protease enzymes, which have significant roles as pruritogens in atopic eczema and other chronic skin diseases, have been shown to be significantly reduced in black skin too, which have significant roles as pruritogens in atopic eczema and other chronic skin diseases (2, 3) and have increased activity in alkaline skin pH (4). Taken together, these epidermal functional differences could explain differences in itch and skin irritation between different skin types.

There have been several studies that indicate that Asian skin is more sensitive to exogenous chemicals, and this may be due to a thinner stratum corneum and a higher density of eccrine glands (5). Japanese cheek skin was found to have a greater number of acid-sensing ion channels (ASICs) and heightened sensory thresholds in comparison with Caucasians. This may explain why Japanese women more frequently report itch and burning sensations after application of cosmetic products (6).

Skin innervation

To the best of our knowledge, no study has examined the differences in the innervation density of the skin between African Americans, Hispanics, and other ethnic populations.

Microscopic evaluation has revealed that black skin contains larger mast cell granules compared with white skin, and differences in structural properties and enzymes of mast cells have been found (7). However, the clinical relevance of these findings to itch is unclear.

Recently, Wang et al. (8) compared the differences in sensory response and neurogenic inflammation to topical capsaicin between four different ethnic populations: African Americans, East Asians, Hispanics and

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Caucasians. Capsaicin is known to induce initial burning sensation as well as itch and is used in alleviating pain and itch via activation of TRPV1 receptor. African Americans, in sharp contrast to the three other ethnic groups, demonstrated a lack of hyperalgesia and neurogenic inflammation. Hispanics were the only group to report significant itching after capsaicin application. It would be of interest to examine whether there are any functional genetic polymorphisms in receptors for TRPV1 that may explain these findings. In addition, these preliminary results may suggest that response to anti-pruritic drugs may differ between ethnic populations, similar to reports of differences in response to pain-relieving medications between different races (9, 10).

ITCH IN THE GENERAL POPULATION

A cross-sectional study was conducted in Norway, which involved postal questionnaire response from 18,770 adults (11). Eighty-four percent of the sample population was Norwegian, 5% was immigrants from Western countries, and 3% was immigrants from the Indian subcontinent. The presence of itch over the past week in respondents was found to be significantly more in men from East Asia (18%) and Middle East/North Africa (13%) compared with Norwegians (7%). Psychosocial factors, however, are confounding factors as immigrants have different health behaviors and a lower socio-economic status, and these are known to result in increased morbidity (12, 13). On the other hand, in a pilot study investigating chronic itch in the general population, the life prevalence of itch in a sample of the German population ($n = 200$) was found to be 22.6% (14).

DERMATOLOGIC ITCH

Pruritus secondary to dermatologic diseases is the most common cause of itch, and chronic dermatologic itch poses significant morbidity. In a German study, an underlying dermatosis was identified in 42% of 263 patients with chronic pruritus (15). In a study comparing patients with pruritus in Germany and in Uganda, pruritic dermatoses were responsible in 57% (75/132) of the cases in Germany (16). In contrast, in the Ugandan population, dermatoses were responsible for causing itch in 96% (81/84) of the cases.

Several pruritic skin conditions are unique in skin of specific ethnic groups, and some of these will be discussed in more detail below.

Primary localized cutaneous amyloidosis

Primary localized cutaneous amyloidosis consists of primary macular and lichenoid amyloidosis (Fig. 1).

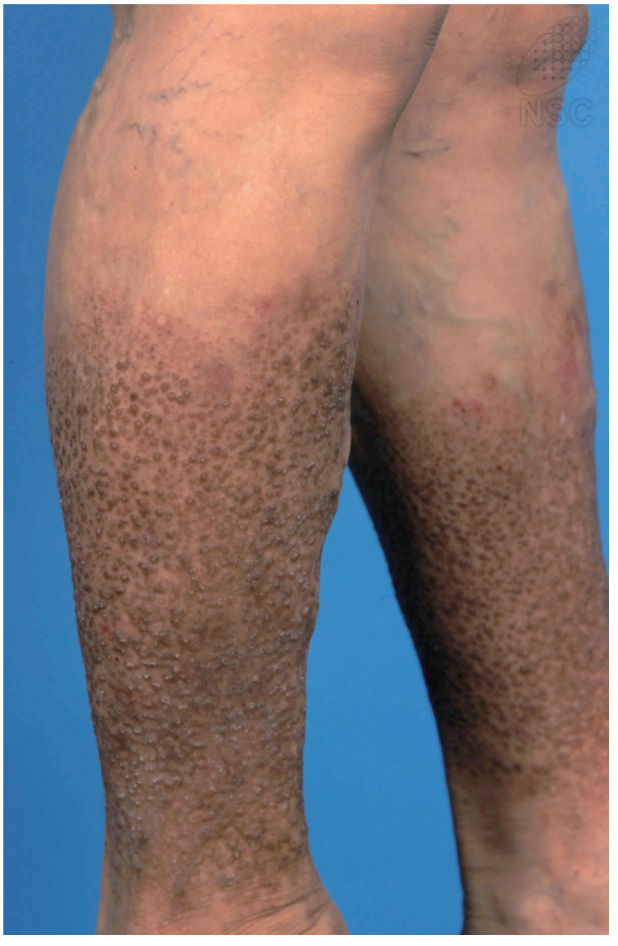

Fig. 1. Brown keratotic papules on the shins and calves of a patient with lichen amyloidosis.

In localized cutaneous amyloidosis, the deposition of amyloid either occurs along reticulin fibers and the basal membrane (peri-reticulary amyloidoses) or along collagen fibers (peri-collagenous amyloidosis) (17). Primary cutaneous amyloidosis has been known to be more common in certain populations, namely Southeast Asians and South Americans (18–21).

Itch is often present in primary localized cutaneous amyloidosis, in both the sporadic and hereditary forms. The prevalence of itch various in different studies: 62% in Singapore (22), 82% in Saudi Arabia (23), and 90% in India (24). The lesions of localized cutaneous amyloidosis commonly occurs over the upper back, outer arms, and the shins and in the study by Salim et al., the most common site of itch was the shins (24).

A study compared the skin innervation density of 30 Hispanic patients with clinico-pathologically proven lichen amyloidosis with 11 healthy Hispanic controls (25). The amount and area covered by nerve fibers in the epidermis and the dermoepidermal junction were found to be significantly higher in healthy skin compared with skin affected by lichen amyloidosis. No difference in innervation density in the papillary dermis was found. An

explanation for these findings may be that the pruritus in lichen amyloidosis is due to damage to the nerve fibers. The cause of this damage, however, is not known.

Molecular studies have recently opened new insights into the pathogenetic mechanisms of pruritus in familial primary localized cutaneous amyloidosis. It has been proposed that when mutant oncostatin M receptor β present on keratinocytes, cutaneous nerves, and specific neurons in the dorsal root ganglia are stimulated by oncostatin M (OSM) or interleukin-31 (IL-31), signaling abnormalities via the OSM type II receptor and/or the IL-31 receptor leads to keratinocyte apoptosis (with subsequent amyloid deposition), reduced number of cutaneous nerves (from possible apoptosis) and, in most individuals, pruritus (26). Lin et al. (27) subsequently identified a point mutation in the IL-31 receptor A gene in a family with hereditary primary cutaneous amyloidosis and this suggests the IL-31 pathway, rather than OSM pathway, is responsible for the pathogenesis of the disease. The distribution of gene polymorphism in different ethnic populations has not been investigated.

Prurigo pigmentosa

Prurigo pigmentosa was first described by Nagashima et al. in 1971 (28). It is characterized by a sudden onset of pruritic erythematous papules that coalesce to form reticulated, mottled patches (Fig. 2) (29). The rash is characteristically localized symmetrically on the upper back, neck, intermammary region and clavicular region; the abdomen, lumbosacral region, and face may sometimes be involved (30). In severe cases, the rash may form edematous and infiltrated plaques that may blister (31, 32). The rash usually resolves within several days to weeks to leave a reticulated, marble-like, post-inflammatory hyperpigmentation that lasts many months or years (29).

Histology of an early lesion of prurigo pigmentosa usually reveals a sparse neutrophilic superficial perivascular and interstitial dermatitis (33). In a fully developed lesion, the infiltrate assumes a lymphocyte-predominant patchy lichenoid pattern and solitary or small clusters of necrotic keratinocytes are commonly seen. In a resolving lesion, histological findings include a sparse lymphocytic infiltrate in the upper dermis, basal necrotic keratinocytes, parakeratosis, and few to many dermal melanophages. Since the first report in 1971, more than 300 Japanese patients with prurigo pigmentosa have been reported (34) and many of the cases involve young adult women. In contrast, after the first non-Japanese case was reported in 1981, only slightly over 60 patients from other countries and races have been reported so far. Of these non-Japanese patients, 23 are from Turkey (34).

In view that prurigo pigmentosa was earlier reported only in Japan, Nagashima (29) suggested that an environmental agent specific to Japan may be involved in the etiology. It was also suggested earlier that a tendency of the Asian skin to yield post-inflammatory hyperpigmentation was important in the recognition of prurigo pigmentosa (35) and this was further supported when other Asian patients from Taiwan (36) and Korea (37) were reported subsequently. However, new cases have been increasingly reported from many parts of the world involving different races over the past decade. A possible reason for the increasing incidence may be that prurigo pigmentosa has been under-recognized in other populations.

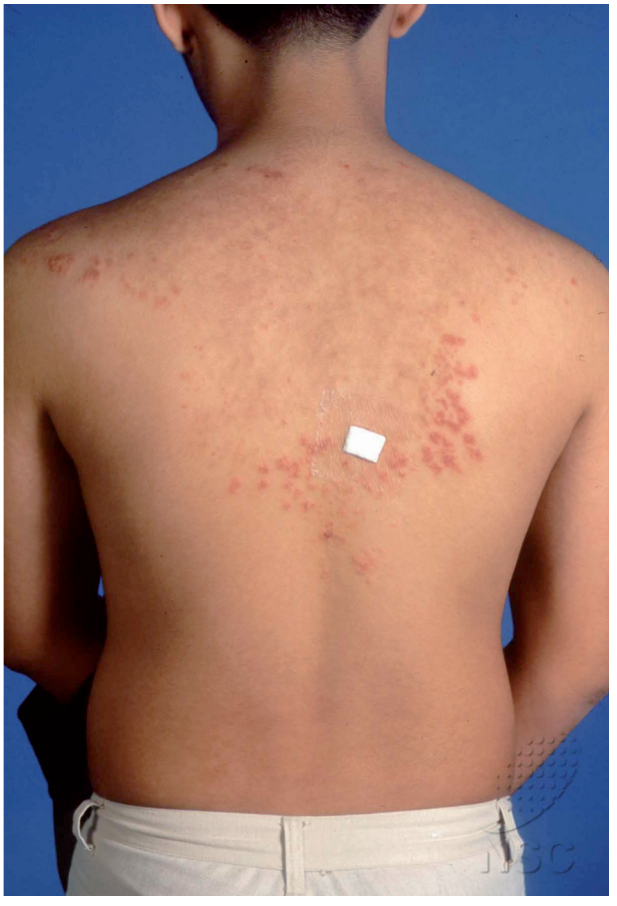

Fig. 2. Erythematous papules that coalesce to form a reticulated pattern and resolve with post-inflammatory hyperpigmentation. The dermatosis is characteristically localized symmetrically on the upper back.

Atopic dermatitis

Black children with atopic dermatitis (AD) were found to be six times more at risk of having severe AD compared with their white counterparts. Difficulties of assessment of erythema due to skin pigmentation might mean that severe cases are not being detected and appropriately treated early on (38). Although it has not been reported, one of the authors (GY) has noted that African Americans have a predominantly extensor involvement of their atopic dermatitis compared with other ethnic groups (Fig. 3).

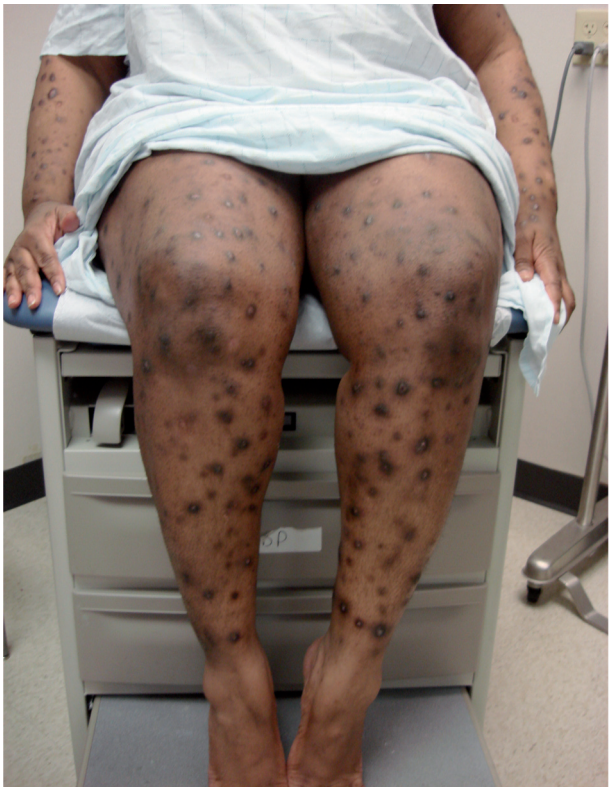

Fig. 3. Pruritic papules and prurigo nodules on shins and extensors of forearms of a patient with atopic dermatitis. These are commonly seen in African American patients.

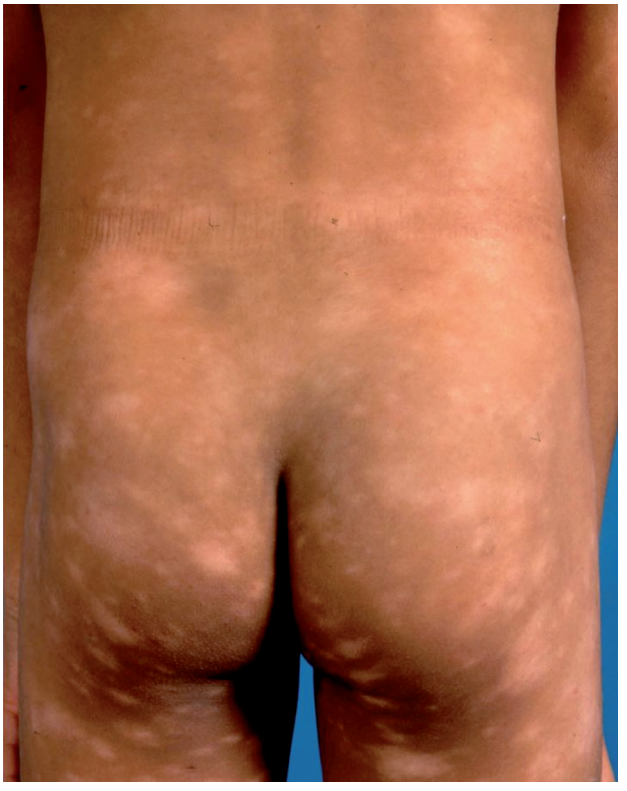

Fig. 4. Hypopigmented mycosis fungoides is more commonly seen in dark-skinned individuals and pruritus is present in many cases.

Keloids

Keloids are known to occur more commonly in Asians and African Americans compared with Caucasians (39). In a study performed in Singapore involving 28 patients, 86% of the patients experienced itch and 46% experienced pain (40). Abnormalities of small nerve fiber function were also found in the same study through the assessment of allodynia and alloknesis and the use quantitative thermosensory testing.

Hypopigmented mycosis fungoides

A rare variant of mycosis fungoides (MF) is the hypopigmented form that typically presents with scattered irregular hypopigmented patches on non-sun exposed areas of the body (41) (Fig. 4). Hypopigmented MF is usually seen in dark-skinned individuals and a large proportion of patients are children (42, 43). Many of the patients also report pruritus (43), and this may be a consequence of the infiltrating and cytotoxic activities of T cells around the basal epidermal region where itch-conducting unmyelinated C-fibers are abundant.

Lichen planus pigmentosus

Lichen planus pigmentosus (LPP) is an uncommon variant of lichen planus clinically characterized by the insidious onset of slate-gray to brownish-black hyperpigmented patches, which present most frequently in a diffuse manner and occur on the face and neck (44). The disease is most frequently reported in Indian patients. Bhutani et al. (45) first delineated the clinical and histopathologic features of LPP in 40 Indian patients in 1974, and subsequently Kanwar et al. (44) reviewed the characteristics of LPP in 124 Indian patients. Smaller series and cases were also described in Middle Eastern populations (46), Japanese (47), Koreans (48), Caucasians (49), and Latin Americans (50). Pruritus has been reported in approximately 33–62% of the patients in various studies (44, 45, 50), but it is generally not severe in comparison with typical lichen planus.

SYSTEMIC ITCH

Systemic disease is a frequent cause of chronic pruritus. In a survey comparing patients with pruritus in Germany and in Uganda, systemic diseases were the underlying cause in 47% (36/132) of the German patients (16). In marked contrast, systemic diseases were not found in any of the 84 Ugandan patients (81 had pruritic dermatoses and 3 had pruritus of unknown origin). Accounting for this vast difference, it was postulated that Ugandan patients with severe systemic diseases do not have a survival period that allows the initiation of itch (51).

Ethnic disparities are noted in a number of pruritic systemic diseases, as described below. Of note, uremic

pruritus, which is the most common cause of systemic itch, seems to have similar prevalence among different ethnic groups. The prevalence of uremic pruritus in patients on hemodialysis in Japan was similar to Western countries (43% compared with 36–50%) (52).

Primary biliary cirrhosis

Primary biliary cirrhosis (PBC) is an uncommon chronic cholestatic liver disease that primarily affects young and middle-aged Caucasian women. It has traditionally been the model for the study of pruritus, itching being the index symptom in the majority of patients and affects nearly 70% of PBC patients by 10 years after diagnosis (53). A prevalence rate of 55% was found among 180 patients with PBC in a US study (54). In a retrospective study performed in Singapore, in which most patients were Chinese (32 out of 34), 17.6% (6/34) had pruritus at presentation (55). In a US study aimed to examine differences in the severity of liver disease between Caucasian and non-Caucasian patients with PBC, 79% (58/73) of non-Caucasian patients had a history of pruritus compared with 51% (237/462) of Caucasians (56). In addition, African Americans and Hispanics were found to have more severe pruritus and more advanced disease at presentation compared with Caucasians.

Pruritic papular eruption in HIV infection

Pruritus is an important source of morbidity in HIV-infected patients (57). Pruritic papular eruption (PPE) is the most common cutaneous manifestation in HIV-infected patients (58) and is characterized by chronic pruritus and symmetric papular eruptions on the trunk and extremities, with the absence of other definable causes of itching in an HIV-infected patient (59). PPE seems to be much less common in the developed countries of Europe and North America (60). The prevalence of PPE in HIV-infected patients in various studies was 10% (37/358) in Brazil (61), 18% (52/284) in Zaire (60), and 46% (62/134) in Haiti (62).

In the study conducted in Zaire, 51% (33/284) of the HIV-infected patients reported PPE as the initial manifestation of their disease and the authors concluded that the presence of an unexplained generalized pruritic papular eruption is highly indicative of HIV infection in African patients (60). In the Haitian study (62), PPE was the presenting symptom in 79% (49/62) of the patients, often appearing months before the diagnosis of HIV. In contrast, in a small Thai study, PPE was the initial presentation in only 25% (5/20) of the cases (63). The reported positive predictive value of PPE for HIV infection was 82–87% (60), and PPE thereby plays an important role in diagnosing HIV infection in populations in which its incidence in HIV is high and where serologic testing for HIV is not easily available.

Diabetes mellitus

Diabetes mellitus is the most common endocrine disease and it has a worldwide distribution. Itch has not been considered to be associated with diabetes except in localized forms of itch associated with candida and intertrigo infections (64). In a large study, generalized pruritus without apparent cause was present in 3% (8/300) of diabetic patients, but this was not significantly more than controls (65). However, in a recent large-scale study in Japan involving more than 2500 diabetics, 11% of diabetics compared with 2% of matched controls had truncal pruritus; the truncal pruritus was also found to be highly associated with diabetic polyneuropathy (66). In a study from India, the prevalence of itch was similar, occurring in 10% (10/100) of the patients (67). In contrast, in a Kuwaiti study, the prevalence of itch was 49% (52/106), accounting for the second most common cutaneous manifestation in the patients (68).

Helminthic infections

A number of infectious diseases cause itch and such diseases are prevalent in certain regions of the world. Onchocericasis is a major health problem, particularly in Africa, and approximately 18 million people are currently infected with this parasite. Onchocerciasis is currently endemic in 30 African countries, Yemen, and isolated regions of South America. A study to assess the true public-health importance of onchocercal skin disease throughout the African region was conducted in 7 centers (3 in Nigeria and 1 each in Ghana, Cameroon, Tanzania and Uganda) and involved 5459 subjects (69). A strong correlation was found between the prevalence of itching, which affects 42% of the population aged 20 years, and the level of endemicity, which was measured by the prevalence of onchocercal skin lesions.

In a study conducted in the USA involving 30,930 subjects, the seroprevalence of *Toxocara* was 13.9% and this was higher in non-Hispanic blacks (21.2%) compared with non-Hispanic whites (12%) and Mexican Americans (10.7%) (70). Increased *Toxocara* seropositivity was found to be associated with low level of education of the head of household, poverty, elevated blood lead concentrations, and dog ownership.

Chloroquine-induced itch

Chloroquine has been used widely in the management of malaria and auto-inflammatory skin diseases, such as lupus erythematosus. One major side-effect of chloroquine use is itch, and this is significantly more common in Africans compared with Caucasians (71). In Africa, up to 60% of adults experienced generalized and severe pruritus (72) and 65% of patients developed itch after

taking chloroquine for malaria (73). In a recent questionnaire survey of university students from Mozambique, the lifetime prevalence of chloroquine-induced pruritus was 30% (158/525) (74). Chloroquine-induced itch appears to be less common in children compared with adults (20.3% vs. 12.8% in a study carried out in Kenya) (75). With regards to lupus patients, in a Spanish study, 38.5% (40/104) treated with anti-malarial therapy (chloroquine and hydrochloroquine) developed possible drug-induced itch and another 5.8% (6/104) developed aquagenic pruritus (76).

The cellular and molecular mechanisms mediating chloroquine-induced itch has recently been elucidated (77). *Mrgprs*, a family of G protein-coupled receptors expressed exclusively in peripheral sensory neurons, have been identified as receptors for chloroquine on itch-selective neurons. *Mrgpr* genes are highly polymorphic, which may suggest that variability in *Mrgpr* underlies the ethnic variation in chloroquine itch (78).

Pruritus in pregnancy

Pruritus, which is a common complaint during pregnancy, may be physiologic, or may herald a flare of a pre-existing dermatosis or the onset of a specific dermatosis of pregnancy (79).

Intrahepatic cholestasis of pregnancy (ICP) is a cholestatic disorder characterized by pruritus, elevated serum aminotransferases and bile acid levels, with onset in the second or third trimester of pregnancy, and spontaneous relief of signs and symptoms within 2–3 weeks after delivery (80, 81). There was a high incidence of ICP in Chile and Bolivia in the 1970s, occurring in 16% and 9% of pregnancies, respectively (82, 83). Significantly higher incidences were noted in the Araucanos Indians in Chile (28%) and the Aimara Indians of Bolivia (14%) compared with other ethnic groups. The incidence of ICP, however, has decreased considerably in these two countries, and in Chile, the rate was approximately 4% in 1995 and 1.5–4% more recently (84, 85). In comparison, the incidence of ICP in Scandinavian and Baltic countries was 1–2%, while in other regions of Europe, Asia, North America and Australia, the incidence was less than 1% (84, 86–88). The low incidence in Europe had remained stable for many years (88). In a retrospective study conducted in the UK, the prevalence of ICP was 0.6% in the white population, compared with 1.5% in Asians of Pakistani origin and 1.2% in Asians of Indian origin (89). The authors concluded that the prevalence of ICP was significantly higher in Asians of Pakistani and Indian origin compared with the Caucasian population.

CONCLUSION

The prevalence of itch in various conditions varies across different ethnic groups and skin types, and this may be due to biological ethnic differences in the skin. Although there have been few studies directly comparing the prevalence of itch between various ethnic populations, there is good evidence that such racial disparity exists in various conditions. Further research is needed to examine the biological, psychosocial and lifestyle factors that may contribute to these disparities.

The authors declare no conflict of interest.

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