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CURRENT SCENARIO OF DERMATOPHYTOSIS IN INDIA

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Doctoral Thesis

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This PhD thesis is dedicated to my father,
Dr. Bhanu S. Verma, dermatologist, mycologist, leprologist and Founder Professor of Dermatology & Venereology Department of Dermatology in M. S. University of Baroda, India. Without his blessings and presence in my life, I would not have been where I am today.

ACKNOWLEDGEMENTS

Latin 'Tempus fugit 'meaning 'Time flies' is the most appropriate phrase that comes to my mind as I begin this acknowledgement. It seems like just yesterday that Prof. Jacek Szepietowski casually asked me if I would consider doing PhD in mycology. We were in Tehran, Iran for an international society of dermatology congress and the question excited me. The epidemic like situation of superficial dermatophytosis was almost 6 years old in India and I had just delivered a talk on the menace of dermatophytosis in India. We were just realizing how a commonly taken for granted disease like 'tinea' would gain such tremendous importance in the dermatological community in India. Prof. Szepietowski was aware of the scenario and my interest in the area, had heard my lectures even in Wroclaw and other places in the world where we often met. His suggestion to do a doctorate on this topic was therefore a very sage idea and also a very generous one since this was no idle suggestion. He said he was willing to be my guide, supervisor, advisor. I knew that mycology was one of his preferred subjects and I thought it was an opportunity worth grabbing with both hands.

I seem to have lost count of the number of phone calls and emails exchanged between the two of us. That just goes to show the sincerity, dedication and the spirit of good will of a perfect gentleman in Prof. Jacek Szepietowski. We have known each other since 2008 and one of the first things that impresses anyone that meets him is his international approach, his interest in global dermatology, his selflessness, kindness and the positive energy that emanates from him. Today, as I am getting ready to finalise my submission of relevant work officially to the university, I take this opportunity to profusely thank Prof. Szepietowski for his friendship. I use the word 'friendship' because he has been friend who is now also a 'philosopher' and 'guide' to me, facilitating my path along the way, encouraging and guiding wherever and whenever required. I realized that if there is one person who I really need to thank from the bottom of my heart, it is Prof. Szepietowski. Thank you, for everything. The international relationships that he fosters will always be a huge asset to all the organisations that he is involved in.

I have been wary of sharing with people that I have been pursuing PhD because I myself had doubts on whether it would be possible to finish such a daunting task sitting thousands of kilometers away. However the acknowledgements would be incomplete without thanking some of my dermatology colleagues and friends who helped indirectly as well as directly in supporting my interest in superficial dermatophytosis, especially against the backdrop of topical steroid abuse. The executive committees of IADVL, Indian Association of Dermatologists, Venereologists and Leprologists of past three years gave their constant support to ITATSA (IADVL Task force Against Topical Steroid Abuse) which I headed for two years. Thank you all very much. Members of the task force that need a special mention include Drs. Koushik Lahiri, Abir Saraswat, Rajetha Damisetty and Kiran Nabar for constantly sharing ideas and opinions. I learnt a lot from them. A special thanks to two of my close friends who have spent hours upondering over issues related to dermatophytosis in the past four years. Prof. Archana Singal of University College of Medical Sciences, New Delhi and Dr. Resham Vasani, an astute and dedicated dermatologist, thank you very much for being a part of my journey. A whole team of German mycologists headed by Prof Pietro Nenoff needs to be acknowledged. I thank them for their zeal and enthusiasm in helping us in so many ways with their knowledge of mycology and microbiology in general. Interaction with them for over two and half years, has been mutually beneficial to learn and teach so many aspects of this particular dermatophyte and the havoc that it has wreaked. Thank you all.

As in many other things, people closest to one's heart always tend to get ignored, albeit unintentionally. A mere 'Thank you' sounds too hollow. I want to thank my wife and son, Ishita and Udit from the bottom of my heart, who have often been ignored often due to my preoccupation of writing and traveling. Thank you for bearing with an obsessive husband who seemed to care more about a fungus than you, but you know that is not true!

I seem to have been especially lucky on two counts in this endeavor. Firstly, I was able to follow this passion of doing a PhD at the age of 58 years of age when it all started. And even more importantly, I have been able to share this excitement with my parents who are in their 90s. Their encouragement and blessings drive me constantly. At this point it may be worth mentioning that my father completed his PhD in mycology from St. John's Institute of Skin, London in 1962, I think I have made him proud and happy by this PhD.

LIST OF PUBLICATIONS - DOCTORAL THESIS

1. **Shyam Verma**, Rengarajan Madhu
   The great Indian epidemic of superficial dermatophytosis: an appraisal.
   Indian J. Dermatol. 2017; 62: 227-236
   Impact Factor (IF) 2017: 1.338

2. **Shyam Verma**, Resham Vasani, Radomir Reszke, Łukasz Matusiak, Jacek C Szepietowski
   Prevalence and clinical characteristics of itch in epidemic-like scenario of dermatophytoses in India: a cross-sectional study.
   J Eur. Acad. Dermatol. Venereol. 2020;34:180-183
   Impact Factor (IF) 2018: 5.113

3. **Shyam Verma**, Resham Vasani, Radomir Reszke, Łukasz Matusiak, Jacek C Szepietowski
   The influence of superficial dermatophytoses epidemic in India on patients' quality of life.
   Adv. Dermatol. Allergol. 2020;
   doi: https://doi.org/10.5114/ada.2019.90088
   Impact Factor (IF) 2018: 1.757

TOTAL IMPACT FACTOR (IF) = 8.208

The Great Indian Epidemic of Superficial Dermatophytosis: An Appraisal

We would like to admit that if we were purists, it would prove to be a difficult task to choose between the terms "epidemic" and "hyperendemic" to describe the current alarming situation of increased incidence as well as the prevalence of superficial dermatophytosis in India. For both terms, it would be essential to have comparative epidemiological data of the past and the present, and sadly, we are lacking in both. There is a dire need for well-designed studies as well as more solid evidence for various issues pertaining to the dermatophytosis scenario in India.[1]

It is an indisputable fact that there is an increase in the prevalence of dermatophytosis over the past 4–5 years across the country. Comparison of studies done on superficial fungal infections in cities such as Kolkata, Ahmedabad, and Chennai during different time frames have revealed an increasing trend of dermatophytosis.[2-7] We, however, need larger epidemiological studies to further bolster our nationwide observation of the alarming increase in its incidence as well as the prevalence.[1] Dermatophytosis has undergone a sea change in its clinical pattern in the past few years. The standard treatment recommendations which we have been following from the Western and Indian literature are no longer valid or even realistic[8-10] [Table 1]. In a country like India, where there is a paucity of original studies of dermatophytosis and its treatment, it is becoming amply clear that experience-based treatment of dermatophytosis is ruling the roost and is proving to be more effective than the standard guidelines provided in current literature that one often considers most valid and evidence based. While environmental factors, erratic use of topical and oral antifungal agents, increased prevalence of *Trichophyton mentagrophytes* infections causing inflammatory lesions and probably a growing resistance to antifungal agents may play an important role, one of the most formidable enemies that we have encountered in the recent times is the irrational fixed drug combination (FDC) creams containing a steroid, antifungal, and antibacterial with three to five molecules in the product.[1,11]

There are many proponents of topical FDCs containing an antifungal and corticosteroid. An important article highlighting the conclusions of an expert panel meeting on topical treatment of superficial dermatophytoses written after reviewing numerous meta-analyses arrived at some conclusions supporting these combination creams. The authors of this seminal article concluded that adding topical corticosteroid to a topical antifungal agent in the beginning of the therapy can mitigate bothersome inflammation, reduce secondary colonisation with bacteria and enhance the efficacy of the antifungal drug. All the five authors practice in European countries where laws controlling the production and sales of drugs are stringent and are implemented. Therefore, this publication though comprehensive and erudite is not entirely relevant in the Indian context. The authors have specifically mentioned that the corticosteroid may be added in the initial part of the treatment and improper use of the combination creams may lead to both failure of treatment and adverse reactions.[12,13] Both points are very relevant for India. Topical corticosteroids used in combination with antifungal agents are very often potent molecules like clobetasol propionate, they are available over the counter and are grossly abused which includes buying over the counter and applying at will for weeks, months and sometimes years.[1,11,14-19] This leads to chronic, treatment resistant dermatophytosis which is causing a havoc in India.

This editorial is aimed at highlighting what seems a significant putative role of these FDCs in the dramatic increase in the number of chronic, recurrent, refractory cases of superficial dermatophytosis that we are encountering for the past 4–5 years. A significant temporal association has also been observed between the free availability of irrational FDCs and the epidemic proportion superficial dermatophytosis has assumed.

We have categorized this editorial into an elaboration on changing clinical patterns of tinea corporis and tinea cruris which are the most frequently encountered, the effect of freely available irrational FDC creams, the current drug control policies of the government, which the errant companies are taking advantage of and finally some recommendations based on our own experiences and those of several key opinion leaders from India.

Changing Clinical Patterns

There is a veritable epidemic of steroid modified tinea in India. Topical antifungals used for this condition are most often in combination with potent topical steroids and antibacterials.[1,11] Such formulations account for about 50% of the sales of all topical steroids. The most common combination in India at present is clobetasol propionate, ornidazole, ofloxacin, and terbinafine.[1,11] This speaks volumes about the inadequate understanding of the drug control authorities of India who grant permissions to companies manufacturing them. They cost

a mere fraction of pure antifungal creams and hence are very popular. They are often bought over the counter, suggested and sold by the pharmacist or prescribed by the general practitioners. Moreover, they are used erratically, often only for symptom control and that too without any instructions or supervision. People often stop using them when the itching and redness are mitigated and begin to apply again when the symptoms reappear.

The cutaneous inflammatory response that the skin mounts to resist and limit the fungal infection is majorly suppressed by topical as well as systemic steroids. However, this effect of topical steroids is said to be more profound than with the other routes. Concomitantly, there is local suppression of T-cell mediated immune response to the dermatophyte. It is this "double trouble" that is most likely responsible for the altered patterns seen increasingly in the past few years. This temporary suppression of the host-induced inflammation leads to ineffective elimination of the dermatophyte, and the process becomes chronic and also widespread. At times, the borders of lesions become unclear resulting in ill-defined and bizarre-shaped lesions. The dermatophyte continues its centrifugal march albeit without adequate central clearing. This phenomenon leads to lesions that insidiously increase in size, adopt unusual shapes including tinea pseudoimbricata, eczematous lesions in the center, etc.

It is a common observation that severity of changes in the clinical pattern correlates with the duration of the abuse of topical steroids. The following are observations regarding the most common patterns occurring in India, namely, tinea cruris and tinea corporis: the classic description of lesion of tinea corporis or tinea cruris being circinate with an active erythematous well-defined border and central clearing is no longer valid [Figure 1]. We are seeing an increasing number of atypical presentations, cases that have been vitiated by topical steroids due to the adverse reactions over the treated and surrounding areas and many patients with chronic, recurrent, widespread lesions, many of whom do not respond to standard protocols of therapy. This trend is evident both in private practice as well as in large teaching hospitals. A tertiary care academic department in North India reported a prevalence of about 5%–10% of all new cases, many presenting with recurrent, chronic dermatophytosis with varied clinical presentations.[14]

We are seeing larger sized and greater number of lesions in individual patients [Figures 2a and b]. It is now more common to see patients with more than one lesion of tinea in more than one anatomical location. Tinea cruris et corporis is getting more common.

We are seeing more women with active tinea corporis, tinea cruris, and tinea corporis et tinea cruris. These women often present secondary to the index case that is most often a male. Fashion trends are changing, and tight fitting clothing such as figure hugging denims, leggings, and jeggings are increasingly preferred by youngsters who do not pay heed to practical aspects like their nonsuitability to our hot and humid climate. This could explain the increased prevalence of tinea cruris and tinea corporis not only in overweight but also in otherwise hygiene conscious, young, slim women with no other risk factors. A large number of women present with a submammary location of the infection that involves the inframammary fold more than the skin of the breasts. This underscores the role of friction and maceration resulting from moisture of perspiration. We are also seeing more children with dermatophytosis [Figure 3]. In the past,

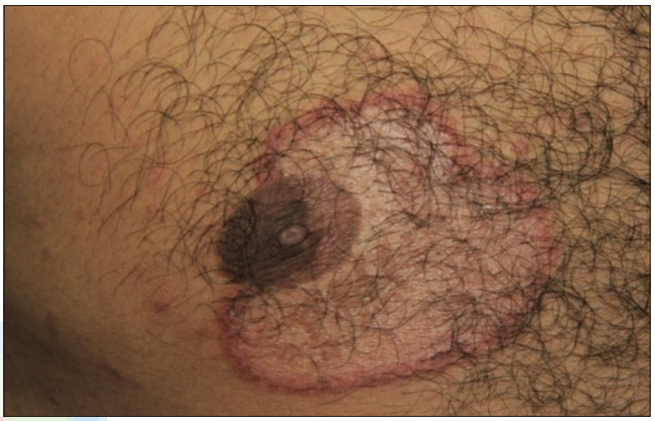

Figure 1: Scaly patch with an erythematous edge

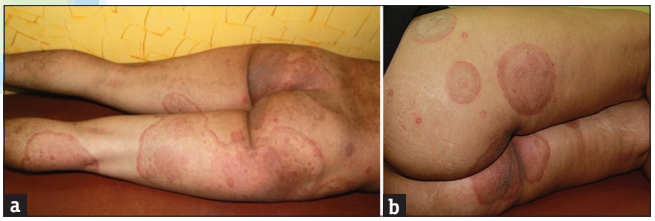

Figure 2: (a and b) Large sized, erythematous patches with active border over the gluteal regions and legs

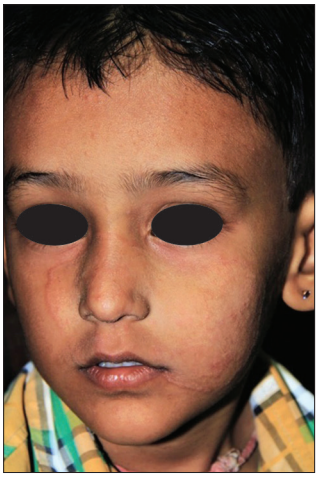

Figure 3: Tinea faciei in a child

tinea capitis was considered to be the most common fungal infection occurring in children.[10] Tinea cruris and few small lesions of tinea corporis were uncommonly seen in infants and toddlers being handled by mothers and grandmothers suffering from tinea corporis with lesions on the trunk. In contrast, it is not uncommon now, to see children present with large-sized lesions and involvement of multiple sites. This can be explained by the increased spore load in the families by virtue of multiple family members being affected or perhaps an increased virulence and infectivity of the organism. It is also an indicator of the easy transmissibility of the dermatophyte. The role of fomites seems to be highlighted in the case of children because sharing of beds, linen, and clothing is all too common in them. In the author's experience, obese children are afflicted more. We are seeing a similarity between superficial dermatophytosis and scabies in that both show a distinct familial tendency. This underscores the importance of eliciting a careful family history during all visits. The importance of an untreated and undocumented affected family member being a constant source of reinfection that is often mistaken for treatment failure is being widely recognized in India. The practice of sharing the prescription of one family member with others for the purpose of symptom relief is common, which can also lead to clinical resistance.

We are seeing an increasing number of lesions with multiple concentric circles. It has also been described as "tinea pseudoimbricata" because it is reminiscent of tinea imbricata characterized by multiple concentric rings and has been explained to be occurring due to partial immune response. It has been seen in persons with immune suppression and those applying corticosteroids.[20] This has been described in India too, after associating its appearance with the use of topical corticosteroid combinations.[21] The authors have suggested that this is included as a manifestation of tinea incognito or rather steroid modified tinea induced by erratic use of antifungal and topical steroids combinations. The formation of concentric circles can be explained by the topical corticosteroid induced local immunosuppression and also its anti-inflammatory effect. The centrifugal spread of dermatophytosis is because of the cell-mediated immunity clearing the fungus in the center of the lesion and the dermatophyte moving radially further out at a rate that is faster than the rate of shedding of the outer corneocytes to survive.[22] It is felt that use of TCS, especially intermittently, would lead to suppression of inflammation and therefore promote survival of the dermatophyte which spreads centrifugally but also remains in the center due to inadequate clearance. If this happens repeatedly, it would lead to multiple active borders with intermittent clearing in areas where the organism has been cleared forming circles concentrically leading to "tinea pseudoimbricata." Although one of us (Verma) has used the terms "tinea incognito" and "tinea pseudoimbricata" in previous publications, we find the following two terms easier and more accurate. Looking carefully at lesions of tinea pseudoimbricata, one observes that the lesions do not always have multiple concentric rings, but very commonly two rings and those too are not always complete. Perhaps the term "double-edged tinea" which is an important clinical pointer to the diagnosis of corticosteroid modified tinea is more appropriate and easier to comprehend for primary care physicians [Figures 4a and 4b]. There is also a difference between the terms "tinea incognito" and "steroid modified tinea." We feel the term, "tinea incognito" should be used only in cases where the disease is rendered unrecognizable due to its altered appearance, most commonly due to topical corticosteroids.[23] However, in most cases of superficial dermatophytosis in which topical steroids and their irrational combinations have been used, it is possible to recognize the fungal infection. Therefore, "steroid modified tinea" is a more appropriate term.[23] And finally, it is pointed out that, grammatically the phrase "tinea incognito" is incorrect and should actually be "tinea incognita."[23]

As mentioned earlier, a large number of lesions do not show central clearing. Instead, there are eczematized areas, within the lesions of tinea cruris and tinea corporis [Figure 5]. As explained in the pathogenesis

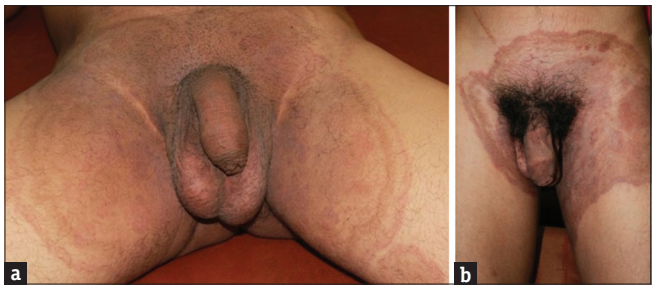

Figure 4: (a and b) Classic "Double edged tinea" in the groins and lower abdomen

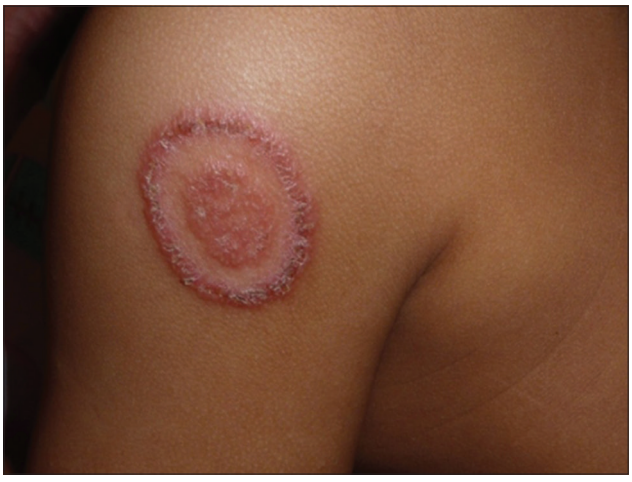

Figure 5: Eczematous patch within a lesion of tinea corporis

of tinea pseudoimbricata, the central eczematization could possibly be due to inadequate clearing of the dermatophytes, owing to topical steroid application, and the inflammatory response that the viable dermatophytes would produce in those areas.

We see arciform lesions, an increasing number of multiple annular lesions of various sizes showing confluence, the dumbbell-shaped tinea formed by the juxtaposition of two large annular lesions with eczematized centers and at times a curious clustering of multiple small annular lesions with active erythematous pustular borders [Figures 6a-c]. Some lesions show pustular borders [Figure 6d]. The latter has been attributed to a probable higher virulence of the organism promoting a stronger inflammatory response.

A distinct variant of dermatophytosis which seems to have been partially obscured and buried under the more visible rubble of tinea cruris is male genital tinea. There have been earlier reports of genital tinea written over two decades ago, in which Indian authors have observed it frequently whereas there have been scattered reports of the entity from West.[24-28] There has been a paucity of recent literature from India on genital dermatophytosis barring one written by the author and Vasani which describes the current increase in male genital tinea against the backdrop of steroid abuse.[15] Genital dermatophytosis is observed to be seen more commonly in males and occurs more commonly on the penis rather than the scrotum. It is almost always accompanied by tinea cruris or tinea cruris et corporis treated by irrational FDCs.[15] When it occurs in women, it usually affects the mons pubis and labia majora. While annular lesions with classic active borders may be seen on the penile shaft, some variants like areas of ill-defined scaly lesions and powdery scaling are also seen [Figures 7a and b]. Often, these patients have lesions on the base of the penis that are hidden by pubic hair as well as on the perineum and scrotum [Figure 7c]. The lateral aspects of the shaft too may be affected [Figure 7d]. This makes it essential to examine the penis by lifting it away from the scrotum which too may be affected uncommonly. The patient should be preferably in a reclining position so that the perineal lesions, often extensions of tinea cruris, do not get missed. Not explaining this to the patient often results in inadequate treatment because of the skipped areas. The untreated genitoperineal lesions become a nidus of a chronic infection unresponsive to conventional treatment.

More number of tinea faciei are being seen. Most of these patients have an infection of other body areas such as tinea corporis or tinea cruris. Many of these cases of tinea faciei are probably true examples of tinea incognita because it is often difficult to appreciate the active borders of these lesions [Figure 8]. However, the pinna of the affected side is often involved as has been reported in tinea capitis in children as "ear sign."[29]

There are said to be more number of cases of adult tinea capitis, and these have been found to be an extension from the face or the neck and is termed as "glabrous type of tinea capitis" which is the most common type of tinea capitis in adults [Figure 9].

We are seeing more numbers of erythrodermic variants of tinea corporis, where there is widespread involvement of body surface with variable erythema with profuse scaling. Most of these patients are immunocompetent.

Many of the presentations enumerated above have accompanying stigmata of topical steroid abuse within the lesions of dermatophytosis as well as in their vicinity. The most frequently seen side effects in steroid modified tinea are striae, hypopigmentation, atrophy, and telangiectasias [Figures 10a-c]. Among these, it is the striae that show the starkest appearance. Never before

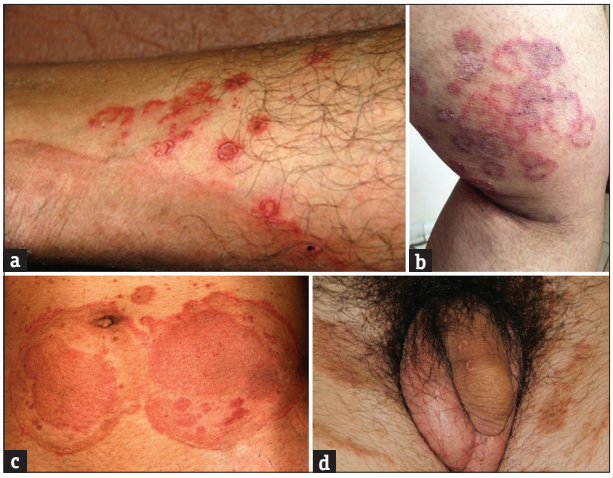

Figure 6: (a) Multiple erythematous annular and arciform lesions with pustules in the periphery, adjacent to a large scaly patch. (b) Multiple annular lesions with erythematous borders showing confluence. (c) "Dumb-bell shaped tinea" formed by confluence of two large lesions. (d) Tinea genitalis lesion with pustular border

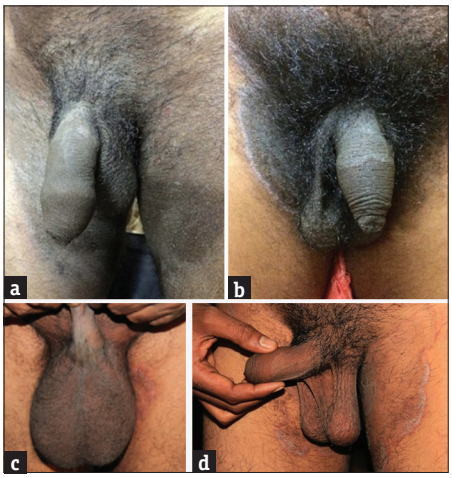

Figure 7: (a and b) Scaly patch over the shaft of penis. (c) The lateral aspects of the shaft too may be affected. (d) Ill-defined patch over the base of the penis

have we seen so many dramatic presentations of striae induced by topical steroids. They sometimes appear as early as 3–4 weeks of application of FDCs containing antifungals, antibacterials, and potent steroid molecules such as clobetasol propionate. Once formed, a minority of them get inflamed, edematous, and even ulcerated with superadded bacterial infections. Moreover, it is frustrating to see patients continuing to apply the same preparations to the striae leading to a vicious cycle. Many patients are seen with superadded irritant contact dermatitis.

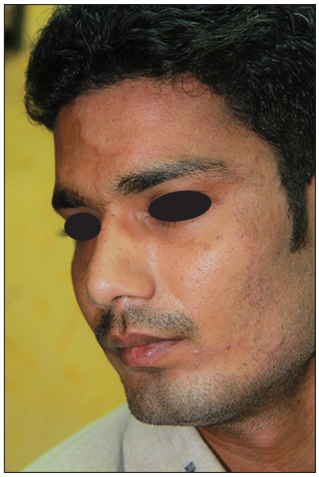

Figure 8: Tinea incognita – tinea faciei

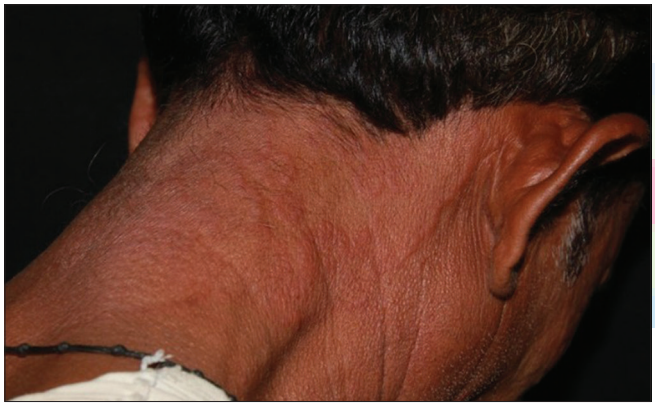

Figure 9: Glabrous type of tinea capitis in an adult

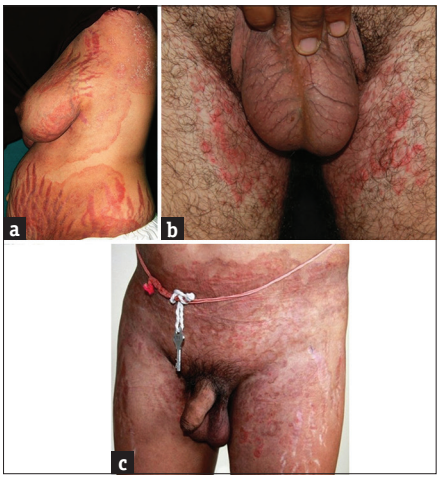

Figure 10: (a) Extensive striae against a backdrop of active tinea. (b) Thinning of the scrotal skin with telangiectasia resulting from steroid application over the crural areas seen. Hypopigmentation over both the thighs also seen. (c) Skin atrophy and striae seen along with active, erythematous tinea corporis and tinea cruris due to the topical steroid abuse

An under-discussed fact is the financial burden that superficial dermatophytosis imposes on the patient and family. Often there are multiple family members affected, and for effective treatment, every member has to visit a dermatologist and buy drugs out of their own pocket. This is often a deterrent to many people for financial reasons who buy drugs only for one member and experiment with them for other members by taking self-treatment for short durations which further compounds the problem.

Changing Scenario of Dermatophytes

In the recent years, there seems to be an epidemiological transformation of dermatophytes in India. Although many studies done across India have found *Trichophyton rubrum*, to be the most common organism, the prevalence is much less compared to the past. In all these studies, *Trichophyton mentagrophytes* has emerged as the co-dominant pathogen with an increased prevalence in comparison to what was seen in the past.[2,30-38] A decline in the occurrence of the downy form of T rubrum has also been observed.[39] Recent mycological studies undertaken across the country have demonstrated Trichophyton mentagrophytes to be the predominant causative organism.[33,35,40-46] This organism has been found to exhibit a rapid growth in the primary culture within 5–7 days.[39] This change may be responsible for the widespread and inflammatory lesions that *T. mentagrophytes* is associated with. This change also affects the way we view the role of fomites in transmission of tinea. In an interesting study, *T. rubrum* survived for <12 weeks on a towel while *T. mentagrophytes* survived for >25 weeks on towels.[47] This fact highlights the importance of disinfection of clothes which could be best done by washing in hot water at 60°C and drying in sunlight, as sunlight is considered to be the most effective disinfectant for dermatophytes.[48]

Many consider antifungal resistance to be the most important cause for the treatment failure of dermatophytosis. To understand the reality, it is essential for us to consider few facts about antifungal resistance, the occurrence of which has to be considered independently for each antifungal class and for each fungal genus. Antifungal resistance is broadly classified into microbiological resistance and clinical resistance. Microbiological resistance refers to nonsusceptibility of a fungus to an antifungal agent as determined by *in vitro* susceptibility testing, in which the minimum inhibitory concentration (MIC) exceeds the susceptibility

breakpoint for that organism. Microbiological resistance can be primary or secondary resistance. Primary or the intrinsic resistance occurs naturally among certain fungi without prior exposure to the drug as is the resistance of *Candida krusei* to fluconazole and *Cryptococcus neoformans* to echinocandins. Secondary or the acquired resistance which develops among previously susceptible strains after exposure to the antifungal agent is usually dependent on altered gene expression. This is illustrated by fluconazole resistance among *Candida albicans* and *C. neoformans* species. Clinical resistance is the failure to eliminate a fungal infection despite the administration of an antifungal agent which may or may not demonstrate MIC's in the resistance range for that organism. Clinical resistance may be due to a combination of factors related to the host, the pathogen or the antifungal agent. There have been few isolated reports of resistance of dermatophytes to griseofulvin and terbinafine.[49]

Standard antifungal susceptibility tests (AST) for the molds are generally cumbersome to perform than the antibacterial susceptibility tests. Hence, they are best performed by reference laboratories. At present, standard guidelines have been proposed by the Clinical Laboratory Standards Institute (CLSI), United States and European Committee on Antibiotic Susceptibility Testing (EUCAST) for *in vitro* antifungal susceptibility testing of dermatophytes. Broth microdilution method of AST recommended by CLSI and EUCAST is presently accepted as the standard method of testing. MIC is defined as the lowest concentration of an antifungal agent that will inhibit the visible growth of microorganism. Although antifungal resistance is usually correlated with increased MIC, MIC values do not always correlate with clinical response to antifungal drugs. The discordance between the *in vivo* and *in vitro* resistance in candidiasis has been illustrated by the "90–60 rule," which states that that infections due to susceptible strains respond to appropriate therapy in 90% of cases, whereas infections due to resistant strains respond in approximately 60% of patients. Breakpoints also termed as interpretive criteria are used to denote susceptibility and resistance to antifungal agents, as the outcome of AST. They are categorized as susceptible, intermediate, and resistant. However, till now, the breakpoints have not been defined for the dermatophytes due to lack of data on the clinical correlation, pharmacokinetic/pharmacodynamic studies, or epidemiological cutoff MIC values.[49, 50] Hence, experts opine that it is logical to not to use the term, "resistant" in the absence of these definitive criteria for dermatophytes.[39] With this background, increase in the MIC values of isolates to terbinafine, fluconazole, and griseofulvin observed in various studies does not imply that there is an absolute resistance, instead this only warrants the use of adequate or higher dosage of these drugs or a longer duration of treatment to get the clinical response. Current scenario calls for standardized antifungal susceptibility studies across the country to know the pattern and any increase in MIC of the antidermatophyte drugs, pending recognition of definitive interpretive breakpoints for dermatophytes by the CLSI. The above reiterates the observations and exhortations made in the recent editorial in the IJDVL regarding the dire need for more studies and a stronger evidence base' for the epidemiology, mycology and treatment recommendations of the current epidemic of superficial dermatophytosis in India.[51]

The Indiscriminate Use of Topical Corticosteroid Combinations and Lax Government Policies

Topical steroids of all strengths, alone or in combination with other molecules, have always, for all practical purposes, been sold over the counter because of nebulous laws open to different interpretations.[1] The Drug Controller General of India (DCGI) finally paid heed to the constant exhortations and recommendations of Indian Association of Dermatologists, Venereologists and Leprologists (IADVL) in August 2016 and included most major topical steroid molecules as Schedule H drugs meaning they legally cannot be sold over the counter and without a valid prescription of a medical practitioner. However, the Gazette notification to this effect issued in the third quarter of 2016 has still not been implemented and all topical steroids continue to be sold freely in the market. The DCGI, in another welcoming step also banned many major irrational and easily available topical FDCs containing an antifungal, steroid, and antibacterial molecule.[52,53] Unfortunately, the pharmaceutical industries have succeeded in bringing a stay order in a high court of India and they continue to be manufactured and sold with impunity. It is worth noting that no major developing nation, let alone developed nations, has been able to obtain licenses to manufacture so many irrational FDCs. A fine example of this category of topical drugs is the highest selling FDC containing clobetasol, ofloxacin, ornidazole and terbinafine.[11] Numerous other combinations which are essentially permutations and combinations of a topical antifungal, an antibacterial, and a steroid molecule, are freely available in the market and have become the bane of Indian dermatologists. The DCGI and state licensing authorities have also issued permissions to manufacture scientifically irrational products with a high potential to induce antifungal resistance such as itraconazole powder, itraconazole cream, topical amphotericin B, and oral FDCs containing terbinafine and itraconazole. These permissions stand out as especially irrational and potentially a public health threat considering the fact that the World Health Organization (WHO) is making concerted efforts to combat antimicrobial resistance (AMR). We would like to

quote two relevant key facts from the fact sheet updated by WHO as recently as September 2016. (1) "AMR is an increasingly serious threat to global public health that requires action across all government sectors and society." (2) "The cost of health care for patients with resistant infections is higher than care for patients with nonresistant infections due to longer duration of illness, additional tests, and use of more expensive drugs."[54] All new drugs and their combinations are required by law to furnish their safety and efficacy data to the DCGI. One wonders if data pertaining to such dubious FDCs have been presented at all and if so, on what grounds and with what understanding of dermatology has the Central Drug Standards Control Organization (CDSCO) approved them. It is common knowledge that quite often state licensing authorities issue permissions without the knowledge or consent of the DCGI, a reflection of pervasive bad governance and corruption in a system that deals directly with the health of the people.

Commonly Employed Treatment Measures

We are seeing a sea change in the prescription patterns of dermatologists in private practice as well as in academic departments. The accepted guidelines of western books do not hold true anymore. We are using higher doses of oral antifungals for a longer time and these tend to benefit the patients more. Similarly, we have observed that even topical antifungal creams need to be applied for a longer duration. Stopping the oral or topical therapy before 3 weeks is often associated with a reappearance of preexisting lesions or even new lesions in other areas. Hundreds of brands of oral as well as topical antifungal drugs are available in India. We have observed that many cheaper brands made by relatively obscure companies often do not have satisfactory efficacy when compared to well-known brands of reputed companies. It would be worthwhile doing a study of bioavailability of various brands. It is also frightening to see how drug companies manage to obtain permission to introduce newer antifungal formulations such as fluconazole powder, itraconazole powder as well as cream and amphotericin B gel. Weight-based dosing of terbinafine and occasionally of itraconazole instead of a blanket recommendation of terbinafine 250 mg for 15 days and itraconazole 100 mg for 15 days or 200 mg for 7 days is found to be more beneficial[8-10] [Table 1]. Even the older antifungal agents such as Griseofulvin given in a dosage of 500 mg twice a day for 6 weeks or fluconazole in a dose of 150 mg thrice weekly for 8 weeks seem to lead to a good clinical outcome in patients with recalcitrant dermatophytosis. However, it is important to perform baseline liver and renal function tests and a periodic monitoring whenever one contemplates the use of systemic antifungals in a higher dosage, always remembering the drug-drug interactions, especially in patients who are on multiple drugs. The recommendations given by three of the most popularly read textbooks of dermatology in India given in Table 1 do not seem relevant in today's scenario. We need treatment guidelines based on Indian experiences that are backed up by our own studies. A large number of dermatologists vouch for the inadequacy of 100 mg of itraconazole for 2-4 weeks and are administering 200 mg of the drug for 3-4 weeks or more and have observed good clinical response.

Newer topical antifungals such as eberconazole and sertaconazole are found to be more efficacious compared to the older azoles like clotrimazole probably because they exert better anti-inflammatory effect.[55,56] The uncomfortable truth is that all these changes in pattern of prescriptions are happening, even if to the benefit of the patient, without a simple potassium hydroxide (KOH) examination in most patients especially in the case of private practitioners who form the majority of caregivers. Although it is thought to be essential in many countries, it is not practical because it is time consuming and most often the doctors do not have trained assistants to do this. While the initial diagnosis of dermatophytosis does not warrant KOH examination unless in doubt, there is a need for performing the test before extending the treatment with the newer oral antifungals beyond 1 month, in case of partial resolution.

The following are measures found to be beneficial by most:

- Strict avoidance of any antifungal preparation, wherein a steroid is added. Strong counseling highlighting the obvious perils of these FDCs is mandatory

Table 1: Treatment schedule of tinea corporis

Drug	Dose/day and duration of treatment					
	Rook's 2016		Fitzpatrick 2012		IADVL 2015	
	Dose/day	Weeks	Dose/day	Weeks	Dose/day	Weeks
Griseofulvin	1 G	4	500 mg	2–4	500 mg od	4-8
Fluconazole	-	-	150–300/week	4–6	150-300 mg/1 dose/week	4-6
Itraconazole	100 mg	2-4	100 mg	1	200-400 mg	1
Terbinafine	250 mg	2-3	250 mg	2–4	250 mg	2

IADVL: Indian Association of Dermatologists, Venereologists and Leprologists

- Stressing on the importance of regularity of medication and adherence to the advice of the physician. The topical antifungals should be applied 2 cm beyond the margin of the lesion for at least 2 weeks beyond clinical resolution. We call this recommendation of applying topical antifungals 2 cm beyond the margin, twice a day for 2 weeks beyond clinical resolution "The rule of Two"
- Advice against wearing tight garments such as jeans, leggings, and jeggings
- Wearing loose, cotton garments
- Discouraging sharing of bed linen if feasible, towels and clothes. Regular washing of towels and bed linen
- Taking regular showers. Wearing clothes only after thoroughly drying the body
- Washing clothes and bed linen in hot water and then sunning them. Sunlight is known to destroy dermatophytes. In the absence of sunlight, ironing the clothes would be beneficial too
- Drying of clothes inside out. Wearing well dried inner garments after about 3–4 days of washing if ironing is not possible
- Washing infected clothes separately
- Instructing patients with tinea cruris to wear "boxer shorts" instead of the tight fitting ones that hug the groin and cut into it
- Removing waistband, wristband, etc.
- Preferring nonocclusive footwear
- Dusting, wet mopping or vacuuming the house followed by cleaning with detergent so as to reduce the spore load in the immediate environment
- Explaining all this is time-consuming, however, it is vital to ensure the compliance and to enhance the awareness levels of the patient. We could issue pamphlets or use posters to ensure the strict adherence to all these measures.

The Future and the Challenges

We need to recognize and appreciate the fact that there is a lack of documentation and evidence in almost every problematic aspect that we have witnessed regarding this frightening epidemic of superficial dermatophytosis in India. The way forward are large-scale systematic studies proving the association of topical steroids, especially the combinations and chronic widespread dermatophytosis, which is indeed a daunting task for operational reasons. We are just beginning to explore the resistance patterns, if any, by antifungal susceptibility testing. We need to delve into more genetic aspects and immunological aspects that are known to lead to chronic widespread dermatophytosis (CWD). However, while doing so, it is abundantly clear that the menace of topical steroids has to be minimized. The easy availability of TCS and combinations containing TCS and antifungals has to be controlled stringently. Topical steroids and their combinations need to be sold as "prescription only" aka "Schedule H" drugs. The government will most likely face resistance from pharmaceutical companies, but the rule has to be strictly implemented with punitive measures for defaulters. Only then, shall we see a decline in steroid modified tinea and many cases of chronic widespread dermatophytosis. The CDSCO in New Delhi and all state licensing authorities need to actively take the wise counsel of an expert panel of dermatologists before issuing licenses to new FDCs. They need to summarily revoke the licenses given so far. IADVL has initiated concerted efforts to educate public, chemists and medical practitioners about this issue. The association has also made several representations to the DCGI and other senior bureaucrats in the Ministry of Health and Family Welfare. Irrational FDCs and formulations are also exported to many developing countries. It is highly unfortunate that the pharmaceutical industry, one of the major players globally in manufacturing as well as exports is responsible for this chaotic situation which could have been easily avoided.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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ORIGINAL ARTICLE

Prevalence and clinical characteristics of itch in epidemic-like scenario of dermatophytoses in India: a cross-sectional study

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Abstract

Background Itch is an integral part of clinical picture of superficial dermatophytoses which constitute a common and growing problem in India.

Objectives The study aimed to evaluate the prevalence, intensity and clinical characteristics of itch in superficial dermatophytosis.

Methods The data concerning disease history and clinical type of dermatophytosis were obtained. The presence and various characteristics of itch were documented. Numerical Rating Scale (NRS) was utilized to assess the worst intensity of itch during the last 3 days and during the course of the disease. 4-Item Itch Questionnaire was utilized to assess itch extent, intensity, frequency and associated sleep impairment, while quality of life (QoL) impairment was assessed via Dermatology Life Quality Index.

Results Ninety-nine patients with direct microscopic confirmation of dermatophytosis were included in the study. In 46.5% of subjects, the coexistence of tinea corporis and tinea cruris was noted, followed by tinea cruris (25.2%) and tinea corporis (13.1%). The majority of patients reported itch in the last 3 days (99%) and complained of itch limited to skin lesions (89.9%). According to NRS, the mean intensity of worst itch in the last 3 days was 6.8 $\pm$ 1.8 points. Severe and very severe itch was reported by 74.7% of patients. Itch was an isolated sensation in 34.3% of subjects, while 46.9% reported associated burning sensation. Itch was frequently exacerbated by sweating, hot temperature and wearing tight clothes. Difficulties in falling asleep and sleep awakenings were reported by 34.3% and 54.6% of subjects, respectively. Itch negatively influenced the well-being of patients and its intensity correlated with QoL impairment.

Conclusions Itch is an important symptom in superficial dermatophytoses and is associated with negative impact on sleep and carries a significant psychosocial burden. Acknowledging its presence is necessary in a holistic approach to these patients.

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Conflicts of interest

The authors declare no conflicts of interest regarding this manuscript.

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Introduction

Superficial dermatophytoses are currently the most common skin infections in India. The observed epidemic situation is strongly associated with irrational, uncontrolled usage of topical corticosteroid preparations widely available over-the-counter, etiological shift from *Trichophyton rubrum* to *Trichophyton mentagrophytes* and increased resistance to antifungal drugs.[1–4] The infections are often chronic and recurrent.[1,3,4]

Itch is defined as a subjective unpleasant sensation leading to scratching.[5] It is an important, almost constant element of clinical manifestation of superficial dermatophytoses.[6] Its occurrence in the course of superficial dermatophytoses may be associated with the inflammatory response of the host.[7] To the best of our knowledge, there is no study available addressing the clinical characteristics of itch in this spectrum of skin diseases. This is probably due to the fact that dermatophytoses in the Western

World are not long-lasting and in the vast majority of cases easy to cure within a few weeks. The special situation in India coupled with the chronicity of the disease led us to conduct the current study to evaluate the prevalence, intensity and clinical characteristics of itch in superficial dermatophytoses.

Material and methods

Patients

Ninety-nine consecutive patients with dermatophytosis from two centres in India (Vadodara and Mumbai) were included into the study. Among them, 50 were males and 49 were female subjects. The age of patients ranged from 16 to 74 years, with the mean 32.2 ± 14.4 years. The mean duration of the disease was assessed as 6.3 ± 18.0 months (range: 0.1–144 months). All patients with any itchy skin diseases and systemic disorders that may contribute to itch sensation were excluded from the study. The study was approved by local Ethics Committee.

Methods

Demographic data and detailed disease history were collected from all the patients. Physical dermatological examination was performed, and different clinical types of superficial dermatophytosis were noted. The diagnosis of tinea was based on characteristic clinical manifestation, subsequently confirmed with direct microscopic examination (10% KOH).

The presence of itch was documented, along with the location of the symptom (lesional and non-lesional skin). The worst intensity of itch during the last 3 days and during the disease course was assessed with Numerical Rating Scale (NRS).[8] Severity cut-off points for NRS were taken as follows: mild itch (0–<3 points), moderate itch (≥3–7 points), severe itch (≥7–9 points) and very severe itch (≥9 points). Moreover, 4-Item Itch Questionnaire (4IIQ), previously successfully used by our group in different types of itch,[9–13] was employed. The instrument estimates the extent (1–3 points), intensity (1–5 points), frequency (1–5 points) and sleep disturbances (0–6 points) caused by itch during the 3 days prior to the examination. Ratings range from 3 (mild pruritus) to 19 points (very severe itch). Moreover, all patients reported their NRS score for the worst intensity of itch due to mosquito bite that they have ever experienced. This served as a reference for the intensity of itch. Additionally, data on the description of cutaneous sensations associated with itch, emotional burden, sleep impairment, alteration of itch intensity due to various factors, and impact of itch on patients' psyche were documented. All patients filled in Dermatology Life Quality Index (DLQI) questionnaire.[14]

Statistical analysis

The sample size of the study cohort was determined by sample size calculation using the principle of the anticipated response distribution of 50%, with 95% confidence interval (CI) and 10% precision. All data were assessed for parametric or non-parametric distribution. Differences between groups were determined using the Mann–Whitney *U*-test as analysed variables were of abnormal distribution. Correlations were determined by Spearman's correlation analysis. The resulting *P*-values were considered nominally significant at $P < 0.05$ level; the Holm–Bonferroni correction for multiple comparisons was used. Statistical analyses were performed using Statistica 12 software (StatSoft, Tulsa, OK, USA).

Results

Patients suffered from various clinical types of dermatophytosis (Table 1). In 60 (60.6%) subjects, lesions in at least two different locations (different types of tineas) were diagnosed. The biggest group comprised patients with simultaneous occurrence of tinea corporis and tinea cruris (46 patients – 46.5%), followed by those with tinea cruris (25 patients – 25.2%) and tinea corporis (13 subjects – 13.1%). Onychomycosis was diagnosed only in two patients and in both of them nail involvement was associated with other clinical types of tinea (Table 1).

Table 1 Itch severity in patients with different clinical manifestations of dermatophytoses

Type of tinea	Number of patients	% of patients	NRS during last 3 days (points)	NRS during whole disease course (points)	4-Item Itch Questionnaire (points)
Tinea corporis	13	13.1	7.1 ± 1.2	6.7 ± 1.2	7.2 ± 2.5
Tinea cruris	25	25.2	6.9 ± 1.9	6.7 ± 1.7	7.1 ± 3.0
Tinea faciei	1	1	8	8	12
Tinea corporis + Tinea cruris (one patient additionally with onychomycosis)	46	46.5	6.6 ± 2.1	6.5 ± 1.8	7.2 ± 3.5
Tinea corporis + Tinea faciei	6	6.1	6.3 ± 2.2	6.8 ± 0.5	7.0 ± 2.8
Tinea cruris + Tinea faciei	2	2	8.0 ± 0	3.5 ± 3.5	8.5 ± 3.5
Tinea corporis + Tinea cruris + Tinea faciei (one patient additionally with onychomycosis)	6	6.1	7.3 ± 0.5	6.8 ± 0.4	10.2 ± 2.8
Total	**99**	**100**	**6.8 ± 1.8**	**6.6 ± 1.7**	**7.4 ± 3.2**

NRS, Numerical Rating Scale.

The presence of itch during the last 3 days was reported by 98 patients (99%). In the vast majority of them (89 subjects – 89.9%), itch was limited to the skin lesions, while in the remaining nine patients (9.1%), the itch sensation involved both lesional and non-lesional skin. The mean intensity of worst itch during the last 3 days, assessed by NRS, was 6.8 ± 1.8 points, indicating moderate itch severity. There was almost no difference between itch intensity assessed during the last 3 days and during the whole duration of skin infection (6.6 ± 1.7 points). However, the itch intensity due to dermatophytoses appeared significantly more severe ($P < 0.001$) than its intensity reported after mosquito bite (3.6 ± 1.2 points). According to the 4IIQ, the mean intensity of itch was assessed as 7.4 ± 3.2 points. The intensity of itch in different clinical types of dermatophytoses, based on our cohort of patients, is given in Table 1. There was no significant difference ($P > 0.05$) in itch intensity between patients with various clinical types of dermatophytoses.

Based on the cut-off values for NRS (itch intensity during the last 3 days), 74.7% patients reported severe and very severe itch, followed by those with moderate pruritus (20.2%; Fig. 1). The majority of patients (62 subjects – 62.6%) suffered from the most severe itch during late afternoons and evenings. Patients who were previously treated with topical agents containing corticosteroids reported no significant change in itch intensity ($P > 0.05$) with such regimen (detailed data not shown).

Thirty-four patients (34.3%) reported isolated itch sensation, whereas in 46 subjects (46.9%) associated burning sensation, in 10 (10.1%) stinging, in 7 (7.1%) biting and in 1 (1%) crawling were noted. As the vast majority of our patients suffered from long-lasting dermatophytosis, we were able to assess the influence of various factors on itch intensity. Sweating, hot temperature and wearing tight clothes appeared the most important factors exacerbating itch. In contrast, cold temperature and cold water were considered the factors markedly reducing itch intensity (Table 2).

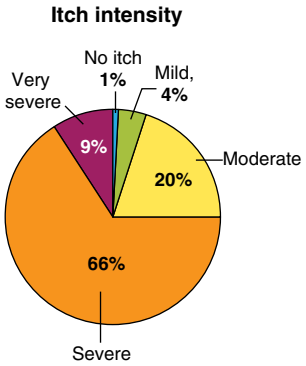

Figure 1 Itch severity in dermatophytoses (worst itch during the last 3 days assessed by Numerical Rating Scale).

Table 2 Factors influencing itch intensity in dermatophytoses

Factor	Increase (%)	Decrease (%)	No effect (%)	Missing data (%)
Stress	41 (41.8)	1 (1)	51 (52)	5 (5.1)
Physical activity	30 (30.6)	8 (8.2)	55 (56.1)	5 (5.1)
Sweating	85 (86.7)	0 (0)	10 (10.2)	3 (3.1)
Tiredness	16 (16.3)	1 (1)	77 (78.6)	4 (4.1)
Dry air	4 (4.1)	43 (43.9)	45 (45.9)	6 (6.1)
Hot temperature	75 (76.5)	0 (0)	18 (18.4)	5 (5.1)
Cold temperature	2 (2)	61 (62.2)	29 (29.6)	6 (6.1)
Hot water	34 (34.7)	13 (13.3)	45 (45.9)	6 (6.1)

Common difficulties in falling asleep were reported by 34 patients (34.3%), 54 subjects (54.6%) complained of sleep awakenings during the night. The vast majority of them (81.5%) suffered from short awakenings lasting 1–10 min, the remaining 18.5% experienced longer (more than 10 min) awakenings. Eight pruritic patients (8.1%) used soporifics to control their sleep disturbance due to itching.

Itch markedly influenced patients' well-being. Forty patients (40.4%) felt depressed, 22 (22.2%) reported decreased mood and 10 subjects (10.1%) complained of anger. The DLQI data were available from 76 patients. There was a significant correlation between itch intensity and quality of life impairment ($r = 0.37$, $P < 0.002$ for the worst NRS itch assessment during the last 3 days; $r = 0.38$, $P < 0.002$ for the worst NRS itch assessment during the whole disease course; and $r = 0.35$, $P < 0.002$ for 4IIQ, respectively).

Discussion

To the best of our knowledge this is the first paper specifically designed to evaluate itch in superficial dermatophytoses. The mean NRS itch intensity in our patients was 6.8 ± 1.8 points, which is similar to lichen planus (LP; 6.9 ± 2.8 points)[15] and higher than in psoriasis (5.5 ± 2.2 to 5.7 ± 2.3 points),[16,17] in patients with polycythaemia vera suffering from aquagenic itch (5.2 ± 2.4 points)[12] or uraemic itch (4.1 ± 2.0 points).[18] However, patients suffering from atopic dermatitis (AD) and chronic urticaria experienced more severe itch (7.9 ± 2.6 and 7.5 ± 1.8 points respectively).[19,20] In a study involving limited number of subjects ($n = 21$) which evaluated antipruritic effect of topical sertaconazole in tinea pedis, the mean baseline VAS score for itch was 6.86 points,[21] similarly to our recent observations. The vast majority of our patients reported severe itch, and its intensity was significantly related to impaired patients' well-being, underlying its importance in dermatophytosis. Similarly, in other cutaneous and systemic conditions, for example psoriasis, AD, polycythaemia vera or uraemic patients, itch had an important negative influence on patients' psyche.[9,18,22–24]

As expected, in the majority of patients in present study, itch was limited to the skin lesions and only in 9.1% both lesional and non-lesional skin was involved. Comparing to other dermatoses,

generalized itch was reported by approximately 17% of psoriatic patients[16] and 19% of LP subjects.[15] Clinical characteristics of itch in patients with dermatophytosis did not differ markedly from itch in other chronic skin disorders. Burning was the most common associated sensation among patients with dermatophytosis (46.8%), similarly to observations in psoriasis and especially AD and LP (37%, 46% and 47%, respectively).[15,17,19] As in patients with psoriasis, AD and LP, the most severe itch was documented during evenings within our study group. Commonly and similarly to previously mentioned dermatoses, itch was responsible for sleep disturbances, mainly causing difficulties in falling asleep and awakenings. Interestingly, few of our patients took soporifics, in contrast to psoriasis, AD and LP patients (16.5%, 31% and 17%, respectively).[15,17,19] This was most probably due to different etiological nature of disorders. We were not able to disclose important differences in factors aggravating and relieving itch between dermatophytosis and other itchy conditions.[12,15,16,19]

Acknowledging pruritus in the course of superficial dermatophytosis is beneficial for the affected individuals. It is important to emphasize that successful management of the underlying dermatophyte infection leads to alleviation of pruritus, subsequently reducing scratching behaviour and preventing secondary bacterial infections, for example with *Staphylococcus aureus*. These observations are especially relevant in the context of paediatric patients suffering from AD.[25]

We are aware of limitations of this study. The number of patients involved is not a huge one, and the patients were recruited only from two centres. The studied population clearly reflects the current scenario of superficial dermatophytosis in India (chronic, long-lasting infection, predominance of tinea cruris and corporis with no single case of tinea pedis in our cohort of subjects, clinical picture modified by previous topical corticosteroid treatment). Therefore, the presented results should be treated with caution and cannot be directly extrapolated to Western World population.

In conclusion, two-thirds of superficial dermatophytosis patients reported severe or very severe itch. The clinical characteristics of itch in dermatophytosis did not differ markedly from itch in other dermatological conditions. Similarly to other chronic itchy conditions, itch in our cohort negatively influenced patients' sleep and significantly contributed to psychosocial burden. This should be taken into consideration in a holistic therapeutic approach, especially in patients suffering from chronic dermatophytoses.

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Original paper

The influence of superficial dermatophytoses epidemic in India on patients' quality of life

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Abstract

Introduction: Superficial dermatophytoses constitute a common and growing problem in India. However, the associated impact on the affected individuals' quality of life (QoL) has rarely been investigated.
Aim: To assess the quality of life of patients with different dermatophytoses.
Material and methods: Among 100 consecutive Indian patients with dermatophytosis, 76% agreed to participate. The diagnosis was established upon the typical clinical manifestation and direct microscopic mycological examination (10% KOH). Dermatology Life Quality Index (DLQI) was utilized to assess QoL impairment. Participants evaluated the presence and intensity of itch during the last 3 days using Numeral Rating Scale (NRS).
Results: A combination of tinea corporis and tinea cruris was diagnosed most commonly (52.6%), followed by tinea cruris alone (21%) and tinea corporis alone (13.2%). The mean duration of the disease was assessed as 6.3 ±18.0 months. The mean DLQI score was 8.2 ±5.1 points. A very large and extremely large effect on the DLQI was reported by 26.3% of patients, moderate by 40.8%, whereas small by 29%, with females being more heavily affected than males (9.3 ±5.2 and 7.1 ±4.7 points, respectively) (p = 0.038). Patients with a combination of tinea corporis, tinea cruris and tinea faciei demonstrated the lowest QoL (11.0 ±4.5 points). Additionally, a significant correlation between impairment of QoL and itch intensity (mean NRS score: 6.8 ±1.8 points) (r = 0.37; p < 0.002) was documented. Moreover, there was a trend towards lower QoL in patients who have been previously treated with topical agents containing corticosteroids.
Conclusions: Superficial dermatophytoses are associated with a moderate impact on QoL of the affected subjects.

Key words: dermatophytosis, quality of life, Dermatology Life Quality Index.

Introduction

Superficial dermatophytoses are common fungal infections all over the world [1, 2]. Alarming data from India suggest that there is a dramatic increase in the prevalence of dermatophyte infections over the last 5 to 6 years. This may be considered as an epidemic or even hyperendemic situation [3]. Many patients treat themselves or undergo treatment by general practitioners or charlatans with dubious qualifications, usually with topical steroid combination preparations widely available without medical prescription [4]. This has a strong influence on the clinical manifestation of dermatophytoses in India, resulting in so-called steroid modified tinea or *tinea incognita* and widespread disease involving different anatomical regions which is often chronic and recalcitrant [5].

The data on the well-being of patients suffering from dermatophytoses are very limited in the literature.

Aim

The aim of this study was to assess the quality of life (QoL) in Indian patients with dermatophytosis seeking medical treatment and advice from dermatologists.

Material and methods

One hundred consecutive patients with dermatophytosis from two centres in India (Vadodara and Mumbai) were invited to participate in the study. Seventy-six of them agreed to be involved (76% response rate). Among

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them, 38 were females and 38 were male subjects. The age of patients ranged from 16 to 74 years, mean 32.2 ±14.4 years. The mean duration of the disease was assessed as 6.3 ±18.0 months (range: 0.1–144 months). Superficial dermatophytosis was diagnosed based on the typical clinical manifestation and the clinical suspicion was confirmed with a direct microscopic mycological examination (10% KOH). The study was approved by the local Ethical Committee.

The assessment of QoL impairment was performed based on the Dermatology Life Quality Index (DLQI) [6]. DLQI is widely used a dermatology-specific QoL questionnaire which comprises 10 questions relating to symptoms, feelings, daily activities, leisure, work, school, personal relationships and treatment. The total score ranges from 0 to 30 points; the higher the score, the lower the QoL. The cut-off points for DLQI have been proposed as follows: an index of 0–1 point indicates no effect at all on the patient's life; 2–5 points a small effect; 6–10 points a moderate effect; 11–20 points a very large effect; and 21–30 points an extremely large effect [7]. Moreover, patients were asked to assess the presence and intensity of itch during the last 3 days using Numeral Rating Scale (NRS) [8].

Statistical analysis

Statistical analyses were performed using Statistica 12 software (StatSoft, Tulsa, USA). All data were assessed for parametric or nonparametric distribution. Pearson's χ^2 test was applied to sets of categorical data. Differences between groups were determined using the Mann-Whitney *U*-test as analyzed variables were of abnormal distribution. Correlations were determined by Spearman correlation analysis. The resulting *p*-values were considered nominally significant at $p < 0.05$ level.

Results

Among 76 patients with superficial dermatophytoses, the majority of them – 40 (52.6%) subjects – suffered from a combination of tinea corporis and tinea cruris, 16 (21.0%) from tinea cruris alone, 10 (13.2%) from tinea corporis alone. Five (6.6%) subjects were diagnosed with a combination of tinea corporis, tinea cruris and tinea faciei, 4 (5.3%) with tinea corporis and tinea faciei simultaneously, whereas 1 (1.3%) patient presented concurrent lesions of tinea cruris and tinea faciei (Table 1).

The mean DLQI score for the whole group of dermatophytosis patients was 8.2 ±5.1 points, indicating a moderate influence of patients' QoL. A very large and extremely large effect was reported by 20 (26.3%) patients, moderate by 31 (40.8%), small by 22 (29%) subjects, while only in 3 (3.9%) patients the QoL was not influenced (Figure 1). Females were more heavily affected than males (9.3 ±5.2 and 7.1 ±4.7 points, respectively) ($p = 0.038$). Patients with a combination of tinea corporis, tinea cruris and tinea faciei demonstrated the lowest QoL (11.0 ±4.5 points), followed by those with tinea corporis and tinea cruris (9.0 ±5.4 points), tinea corporis (7.8 ±5.7 points) and tinea cruris (6.7 ±3.8 points) (Table 1).

Moreover, a significant correlation between the impairment of QoL and the intensity of itch (mean NRS score: 6.8 ±1.8 points) ($r = 0.37$; $p < 0.002$) was documented (Figure 2). Additionally, there was a clear trend ($p = 0.11$) towards lower QoL in patients who have been previously treated with topical agents containing corticosteroids ($n = 32$; 9.5 ±5.9 points vs. $n = 44$; 6.7 ±4.2 points). No relationships between the QoL impairment and patients' age, socioeconomic status, profession as well as duration of dermatophyte infection were found (data not shown).

Discussion

Dermatophyte infections are common skin diseases worldwide, affecting skin as well as its appendages, such as hairs and nails. In general, instituting an appropriate antifungal therapy leads to a successful treatment outcome. However, certain clinical types of dermatophyte infections (e.g. onychomycosis) frequently constitute a long-lasting clinical problem [9, 10]. Additionally, ster-

Table 1. Types of dermatophytoses and the quality of life according to the Dermatology Life Quality Index (DLQI)

Type of tinea	Number of cases	Percentage (%)	DLQI, mean ± SD [points]	Effect on patients
Tinea corporis	10	13.2	7.8 ±5.7	Moderate
Tinea cruris	16	21.0	6.7 ±3.8	Moderate
Tinea corporis + tinea cruris	40	52.6	9.0 ±5.4	Moderate
Tinea corporis + tinea faciei	4	5.3	4.0 ±2.6	Small
Tinea cruris + tinea faciei	1	1.3	4.0	Small
Tinea corporis + tinea cruris + tinea faciei	5	6.6	11.0 ±4.5	Very large
All	76	100	8.2 ±5.1	Moderate

QoL – quality of life.

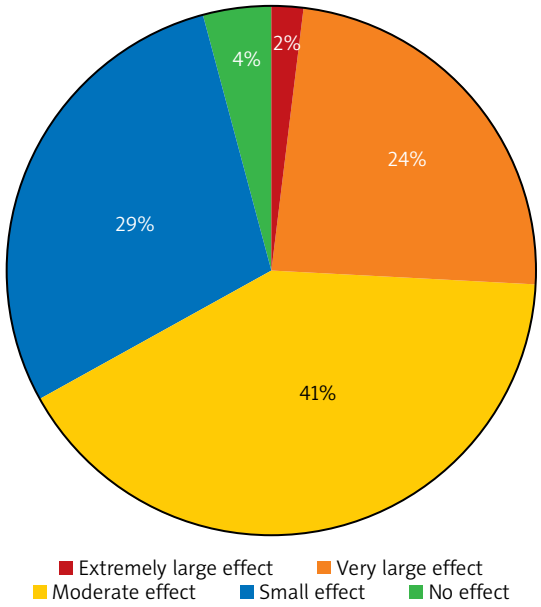

Figure 1. The impact of the superficial dermatophytosis on the sufferers' quality of life as expressed by the Global Question indexing

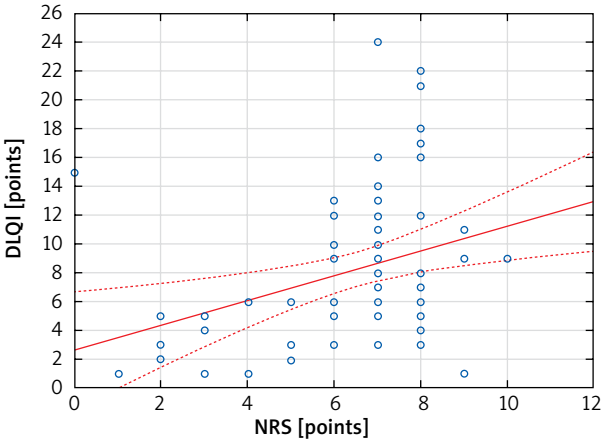

Figure 2. Correlation between the Dermatology Life Quality Index (DLQI) and the intensity of itch according to the Numeral Rating Scale (NRS)

oid modified tinea can cause diagnostic difficulties and may lead to chronicity and recalcitrance [1, 3]. The psychosocial burden of dermatophyte infections has been reported very rarely up till now. The literature data are scant and the available studies mainly concentrated on the influence of onychomycosis on patients' well-being, presumably by its chronicity [9, 10]. The review of DLQI usage during the first 10 years of its availability showed that the instrument was used in one study involving only 10 patients with tinea [11]. The authors demonstrated that the mean DLQI value in those subjects was 5.5 points, which can be considered as a small effect on patients' life. The next review of the DLQI usage published in 2008 did not disclose any new findings in this area [12]. However, a recently published study by Patro *et al.* [13] assessed the DLQI scores among 294 patients with superficial dermatophyte infections. The overall effect on the QoL was moderate among males, subjects with shorter duration of lesions (no more than 6 months), patients with less extensive disease (less than 10% of the Body Surface Area involved) and patients of low to medium socio-economic status. In contrast, a very large effect on the DLQI concerned females, patients with longer duration of lesions, more extensive area of skin involvement, high socio-economic status and those with medium to high education. Moreover, the disability domain of the 5D-pruritus scale was correlated with the DLQI disability score ($r = 0.8$, $p < 0.0001$).

The current epidemic situation in India has led our group to conduct the clinical study on the superficial dermatophytoses and the QoL. To the best of our knowledge, this is the second largest series of patients with tineas in which QoL has been assessed. We have clearly documented that superficial dermatophytoses may be responsible for moderately decreased QoL. The difference between our results and the initial study might be due to the limited number of patients with lower disease severity included by Jobanputra and Bachmann [14] and possibly due to the fact that during the recent decades there has been a shift in the aetiology of dermatophytoses (from the predominant *Trichophyton rubrum* to *Trichophyton mentagrophytes* – a species that can lead to more inflammatory and widespread lesions) [15]. Moreover, similarly to the recent Indian study [13], we have documented that the QoL impairment may be related to the number of skin areas involved and also the intensity of itch. Patients suffering from coexistence of tinea corporis, tinea cruris and tinea faciei reported a very large impact of the skin condition on their life. This is in concordance with other studies on different dermatoses as well, in which correlations between impaired QoL and disease severity, and additionally the intensity of itch, were reported [16–18]. Interestingly, our results indicate that previous treatment of dermatophytosis with topical agents containing corticosteroids may be associated with a trend towards lower QoL. This could be due to the fact that topical corticosteroid therapy may contribute to the prolonged course of the disease and more widespread infection [1, 3, 15].

There are several limitations of our study. Firstly, there was a relatively small number of the participants. Secondly, the findings in this cohort may not necessarily reflect the situation in the general population. Lastly, the confirmation of the diagnosis of dermatophytoses was based upon the clinical picture and direct KOH examination, whereas neither fungal culture nor polymerase chain reaction were performed in our patients. The lack of fungal culture made the definite identification of certain species of fungi impossible. Additionally, as different kinds of dermatophytes are associated with more or less

marked inflammatory cutaneous lesions, we speculate that this issue may possibly influence the quality of life to a different extent. As a result, the impact of different species of dermatophytes on the quality of life remains to be explored in the future. However, fungal culture does not always yield positive results, especially if there is a difficulty in maintaining the wash-out period between the last application of topical medications and the procedure of obtaining the specimen. Currently, the diagnosis of dermatophytoses in India still relies mainly on the clinical picture and direct KOH examination. Unfortunately, due to economic issues, performing culture and subsequently identifying the causative organisms is problematic in most situations. This issue may be obviously regarded as a problem not only in India, but possibly in several other countries in which healthcare is underfinanced. Despite the value of fungal culture as the gold standard in the diagnosis of dermatophytosis, the Expert Consensus on The Management of Dermatophytosis in India (ECTODERM India) does not recommend its routine use in clinical practice [19]. This method should be considered in cases which are recalcitrant or involving multiple areas.

Conclusions

Our study emphasizes the influence of superficial dermatophytoses on the QoL. The alarming increase in the incidence of tinea in India, majorly due to the unsupervised usage of combination creams containing corticosteroids, leads to altered clinical manifestations, widespread disease and prolonged duration of superficial dermatophytoses. As a result, the well-being of the affected subjects is impaired. The responsible authorities should take these facts seriously into consideration in order to develop strategies to combat this problem.

Conflict of interest

The authors declare no conflict of interest.

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CURRICULUM VITAE

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Educational Qualifications

1985- MBBS (Bachelor of Medicine and Bachelor of Surgery including the mandatory one year Internship following it) – - Baroda Medical College, M.S. University of Baroda, India

1987- One year assignment in urban slums of Vadodara in USAID (United States Aid for International Development) sponsored project.

1988 (June to November) - Clinical and research Fellowship in the Department of Dermatology, Venereology and Leprology of SMS Medical College and Hospital in Jaipur, India.

1989- 1990 (Four terms of Six months each) - Diploma in Dermatology and Venereology (D.V.&D)- (First position) in the postgraduate qualification from the Armed Forces Medical College, first rank in Pune University, India)

2012- Conferred Fellowship of Royal College of Physicians, London. (FRCP, LONDON)

Current Occupation

Involved in Private practice in Dermatology, Venereology and Leprology since 1992. Practising from two offices striking a balance between private practice, lecturing for the past 27 years at the most prestigious national and international forums, universities, publishing in well known journals and working for various international and national dermatology organisations in an executive capacity or adviser/organiser.

Awards and Honors

- Recipient of the 'Exchange of the Coin' ceremony at the **Walter Reed Memorial hospital and Uniformed Services University at Bethesda, Maryland, USA** for having delivered three lectures including a Grand Rounds lecture to multifaculty audience.
- Elected International Board member of the **European Academy of Dermatology and Venereology**- (2019-2022)
- DERMAPRACTICE Award from Indian Association of Dermatologists,Venereologists and Leprologists (IADVL) for the **Best Practitioner of West Zone** of India- 2018
- Delivered the **West Zone IADVL Oration**- November 2017
- Recipient of the **plaque of appreciation from International Society of Dermatology** at the International Congress of Dermatology in Buenos Aires, Argentina, 2017.
- Recipient of the **Sentamil Selvi Award** for the best published paper in the area of **mycology** from India, 2017
- **Recipient of American Academy of Dermatology** (AAD) President's 'Members making a difference' Award, Washington DC, USA-2016
- Recipient of the **TC Saikia Oration** from North Eastern branches of IADVL 2016
- Recipient of the **IDOJ Team appreciation Award** for rendering meritorious service to the Indian Dermatology Online Journal, 2016
- **Recipient of the 'Best Case report of the year'** of the Indian Journal of Dermatology, Venereology and Leprology (IJDVL) – 2015

- Recipient of the 'Best Case report of the year' of **Indian Journal of Dermatology**-2014
- Recipient of the **Dr. P.B. Haribhakti Oration of Gujarat state** for 'Practising Privately and Publishing Publicly' 2014
- Recipient of the **Plaque of Appreciation by International Society of Dermatology**-2013
- Recipient of the prestigious **Fulford Oration of Indian Association of Dermatology, Venereology and Leprology, 2008**.

Titles of Associate/Assistant Professor: International Appointments

Probably the only dermatologist in India who has been appointed as a Clinical Faculty member in three prestigious departments of dermatology of USA.

- Adjunct Associate Professor of Dermatology at University of Pennsylvania, Philadelphia, USA- Now reappointed until 2020.
- Clinical Associate Professor of Dermatology at University of Virginia, Charlottesville, USA.- 1998 to April 2014.
- Clinical Assistant Professor of Dermatology at SUNY, Stony Brook, NY, USA

Conferred Honorary Membership of National Societies

- Honorary Life Member of Polish Dermatology Society-2016
- Honorary Life Member of Romanian Society of Dermatology-2012
- Honorary Life Fellow of Palestinian Dermatology Society-2011
- Honorary Life Fellow of Jordanian Dermatology Society-2006

Editorships and Editorial Board

- **Founder Editor in Chief,** ***Indian Dermatology Online Journal (IDOJ)***, official Online Journal of Indian Association of Dermatologists, Venereologists and Leprologists - 2010-2015
- Member, Editorial Board, Journal of American Academy of Dermatology Case reports since May 2015- May 2018

- Member, Editorial Board, **Dermatología Cosmética, Médica y Quirúrgica,** Mexico, 2013
- Member, International Editorial Board- ***Dermatology Online Journal*** - since 2012
- Member, International Editorial Board-***International Journal of Dermatology*** from 2007-2014
- Member, Journal Advisory Board, ***Acta-Dermatovenereologica*** - since 2011
- Member, Journal Advisory Board, Indian ***Journal of Dermatology, Venereology and Leprology*** - since 2011
- Member, Journal Advisory Board***, Indian Journal of Dermatology*** since 2011
- Former Associate Editor and Current Member Advisory Board, ***Journal of Cosmetic Dermatology***, Wiley Blackwell
- Member, International Editorial Board, ***Brazilian Annals of Dermatology***, 2008
- Member, Editorial Board, ***International Journal of Trichology*** - 2009
- Former Editorial Board Member, ***Indian Journal of Dermatologists, Venereologists and Leprologists***. (***IJDVL***)
- Member, International Editorial Board- ***Electronic Textbook of Dermatology*****.**
- Member, International Editorial Board**-** ***Iranian Journal of Dermatology***
- Member, Editorial Board , ***Journal of Association of Cutaneous Surgeons of India***.

Shyam B Verma

Publications in peer reviewed journals

1. **Verma SB**. Tinea confined to tattoo sites - An example of Ruocco's immunocompromised district. *Indian Dermatol Online J* 2019;10:739-40
2. **Verma SB**. Adding 'SKINTED' to the list of immunocompromised districts. *Clin Exp Dermatol*. 2019; doi: 10.1111/ced.14082. [Epub ahead of print]
3. **Verma SB**. What's in a name? Surgical incision sites are potential immunocompromised districts. *Int J Dermatol*. 2019 Sep 4. doi: 10.1111/ijd.14621. [Epub ahead of print]
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5. **Verma SB**. Complex Cost Issues in Treating Dermatophytoses in India-"It All Builds Up". *Indian Dermatol Online J*. 2019; 10:441-443.
6. **Verma S**, Joshi R, Shah R. Acne fulminans in a young man with granulomatosis with polyangiitis (Wegener's granulomatosis): A chance association or marker of serious systemic disease? *Indian J Dermatol Venereol Leprol*. 2019; doi: 10.4103/ijdvl.IJDVL_155_18. [Epub ahead of print]
7. Süß A, Uhrlaß S, Ludes A, **Verma SB**, Monod M, Krüger C, Nenoff P. Extensive tinea corporis due to a terbinafine-resistant Trichophyton mentagrophytes isolate of the Indian genotype in a young infant from Bahrain in Germany].[Article in German] *Hautarzt*. 2019; doi: 10.1007/s00105-019-4431-7. [Epub ahead of print]
8. Nenoff P, **Verma SB**, Vasani R, Burmester A, Hipler UC, Wittig F, Krüger C, Nenoff K, Wiegand C, Saraswat A, Madhu R, Panda S, Das A, Kura M, Jain A, Koch D, Gräser Y, Uhrlaß S.The current Indian epidemic of superficial dermatophytosis due to Trichophyton mentagrophytes - a molecular study. *Mycoses.* 2019;62:336-356.

9. Nenoff P, **Verma SB**. Silke Uhrlaß Anke Burmester Yvonne Gräser. A clarion call for preventing taxonomical errors of dermatophytes using the example of the novel Trichophyton mentagrophytes genotype VIII uniformly isolated in the Indian epidemic of superficial dermatophytosis. *Mycoses* 2018 https://doi.org/10.1111/myc.12848
10. **Verma SB**. Emergence of recalcitrant dermatophytosis in India. *Lancet Infectious disease.* 2018;18:718-719.
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12. **Verma SB**, Vasani RJ, Chandrashekar L, Thomas M. Seborrheic melanosis: An entity worthy of mention in dermatological literature. Indian *J Dermatol Venereol Leprol* 2017;83:285-9.
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14. **Verma SB**. A closer look at the term "tinea incognito:" A factual as well as grammatical inaccuracy. *Indian J Dermatol* 2017;62:219-20.
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65. **Verma SB**. Multiple apocrine hidrocystomas: a confusing clinical diagnosis. *An Bras Dermatol*. 2010;85:260-3
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Book Chapters

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CO-AUTHOR DECLARATION

I, R Madhu, hereby agree that below mentioned scientific paper I have co-authored may be incorporated into a series of publications on which the doctoral thesis of the main author, Shyam B. Verma, will be based.

Shyam Verma, R Madhu
The great Indian epidemic of superficial dermatophytosis: an appraisal.
Indian J. Dermatol. 2017; 62: 227-236

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1. Shyam Verma, Resham Vasani, Radomir Reszke, Łukasz Matusiak, Jacek C Szepietowski
Prevalence and clinical characteristics of itch in epidemic-like scenario of dermatophytoses in India: a cross-sectional study.
J Eur. Acad. Dermatol. Venereol. 2020; doi: 10.1111/jdv.15877

2. Shyam Verma, Resham Vasani, Radomir Reszke, Łukasz Matusiak, Jacek C Szepietowski
The influence of superficial dermatophytoses epidemic in India on patients' quality of life.
Adv. Dermatol. Allergol. 2020; doi: https://doi.org/10.5114/ada.2019.90088

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1. Shyam Verma, Resham Vasani, Radomir Reszke, Łukasz Matusiak, Jacek C Szepietowski
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I, Radomir Reszke, hereby agree that below mentioned scientific papers I have co-authored may be incorporated into a series of publications on which the doctoral thesis of the main author, Shyam B. Verma, will be based.

1. Shyam Verma, Resham Vasani, Radomir Reszke, Łukasz Matusiak, Jacek C Szepietowski
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KOMISJA BIOETYCZNA
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OPINIA KOMISJI BIOETYCZNEJ Nr KB – 556 /2018

Komisja Bioetyczna przy Uniwersytecie Medycznym we Wrocławiu, powołana zarządzeniem Rektora Uniwersytetu Medycznego we Wrocławiu nr 133/XV R/2017 z dnia 21 grudnia 2017 r. oraz działająca w trybie przewidzianym rozporządzeniem Ministra Zdrowia i Opieki Społecznej z dnia 11 maja 1999 r. (Dz.U. nr 47, poz. 480) na podstawie ustawy o zawodzie lekarza z dnia 5 grudnia 1996 r. (Dz.U. nr 28 z 1997 r. poz. 152 z późniejszymi zmianami) w składzie:

dr hab. Jacek Daroszewski (endokrynologia, diabetologia)
prof. dr hab. Krzysztof Grabowski (chirurgia)
dr Henryk Kaczkowski (chirurgia szczękowa, chirurgia stomatologiczna)
mgr Irena Knabel-Krzyszowska (farmacja)
prof. dr hab. Jerzy Liebhart (choroby wewnętrzne, alergologia)
ks. dr hab. Piotr Mrzygłód (duchowny)
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dr hab. Andrzej Wojnar (histopatologia, dermatologia) przedstawiciel Dolnośląskiej Izby Lekarskiej)
dr hab. Jacek Zieliński (filozofia)

pod przewodnictwem
prof. dr hab. Jana Kornafela (ginekologia i położnictwo, onkologia)

Przestrzegając w działalności zasad Good Clinical Practice oraz zasad Deklaracji Helsińskiej, po zapoznaniu się z projektem badawczym pt.:

„Obecna sytuacja zakażeń grzybiczych skóry w Indiach i jej możliwe szersze znaczenie"
„Current scenario of dermatophytosis in India and its possible global impact"

zgłoszonym przez **lek. med. Shyam B Verma** zatrudnionego w Prywatnej Klinice Chorób Skóry „Nirvan" Vadodra w Indiach oraz złożonymi wraz z wnioskiem dokumentami, w tajnym głosowaniu postanowiła **wyrazić zgodę** na przeprowadzenie badania w Katedrze i Klinice Dermatologii, Wenerologii i Alergologii Uniwersytetu Medycznego we Wrocławiu oraz Prywatnej Klinice Chorób Skóry „Nirvan" Vadodra w Indiach pod nadzorem prof. dr hab. Jacka Szepietowskiego **pod warunkiem zachowania anonimowości uzyskanych danych**.

Pouczenie: W ciągu 14 dni od otrzymania decyzji wnioskodawcy przysługuje prawo odwołania do Komisji Odwoławczej za pośrednictwem Komisji Bioetycznej UM we Wrocławiu.

Opinia powyższa dotyczy projektu badawczego będącego podstawą rozprawy doktorskiej.

Wrocław, dnia 28 września 2018 r.

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za zgodność z oryginałem

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