Original Article

Evaluation of practice patterns of general practitioners and dermatologists in treating naïve and recalcitrant dermatophytosis – an online survey

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Abstract

Dermatophytosis is a common presentation in clinic attendees. Recently there is an emergence of patients with dermatophyte infections which are non-responding to standard treatments. To find solutions to this problem it is important to have a basic understanding of the prevalent fungal species and prescription patterns of dermatologists and General Practitioners (GPs) and clinical response of the patients. With this background this online survey was conducted to evaluate the practice patterns of dermatologists and GPs in naïve and recalcitrant dermatophytosis.

Fifty dermatologists and fifty-four GPs participated in the online survey. Both dermatologists (85.5%) and GPs (80.3%) selected Miconazole as their preferred first line topical application in treating tinea infections in the government hospital. Griseofulvin was the commonly used (54%) oral antifungal by dermatologists in government sector and they seem to be preferring either Itraconazole or Terbinafine (36% each) in private sector. Majority of GPs used Fluconazole as the first line oral medication in both sectors. 60% of GPs admitted that there is a possibility of adding a topical steroid when the diagnosis of Dermatophyte infection was not sure.

88% dermatologists and 53.7% of GPs thought that there is a current trend of low therapeutic response in dermatophytosis. Both groups agreed that education of primary care physicians as a priority in overcoming this problem.

Introduction

Superficial fungal infections affecting skin, hair and nail are a common presentation to dermatological practice. Globally this is estimated to be more than one billion of patients per year[1]. The clinic prevalence of this disease is 10% in Sri Lanka[2]. Out of these dermatophyte infections are the most common superficial fungal infection in skin. This includes members from Trichophyten, Microsporum and Epidermophyton genera[3].

Dermatophyte infections were once thought to be an easily treatable disease by dermatologists. However, this pattern is changing and we see quite a large number of chronic and recalcitrant dermatophyte infections. Worldwide, a lack of therapeutic response to antifungal drugs are experienced by clinicians[4-6]. The causative factors for the therapeutic failure are multifactorial. Decreased host immunity, environmental factors, change of fashion sense, overcrowding are all thought to be contributing[7]. Inadvertent use of topical steroids for dermatophyte infections is thought to be a major contributory factor in the therapeutic failure[8,9]. Resistance to antifungal drugs is also documented[10,11]. Itraconazole and Terbinafine are the drugs thought to be effective against Dermatophyte infections with Fluconazole showing lesser efficacy[12]. However, Azole resistance is on the rise and this hypothesized to be linked with extensive use of these compounds in the agriculture field[11]. Although to a lesser degree, resistance to Terbinafine is also reported making the treatment of Dermatophyte infection really a challenge to dermatologists[13].

Presently there are no proper guidelines in treating dermatophytosis or strategies to overcome the lack of therapeutic response to antifungals. Dermatologists are using various methods on their own discretion as prolonged duration, higher doses and combinations of antifungals[14]. General Practitioners (GPs) make the frontier of managing dermatophyte infections. Their prescription pattern in treating a naïve and a recalcitrant dermatophyte patient is equally important to understand and find solutions to this problem.

Objectives

1. To know the first line topical and oral antifungal drugs and duration of treatment in managing dermatophyte infections by GPs and dermatologists.
2. To assess the extent of steroid usage in dermatophyte infection.
3. To assess the awareness of the emerging problem of low therapeutic response in dermatophytosis and the measures taken in such situations by GPs and dermatologists.

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Methodology

An online questionnaire was developed to cover the above objectives targeting GPs and dermatologists separately. The SurveyMonkey® tool was used to generate the questionnaire, filling the questionnaire and analyzing the results. The questionnaire consisted of 18 questions for each group. There were slight variations in certain questions for the two groups. The questionnaire was sent to the Sri Lanka College of Dermatologists and Sri Lanka College of General Practitioners and thereby distributed among their membership. Reminders were sent through the same survey tool every week for two weeks. People who voluntarily filled the online survey within these two weeks were included in the study.

Results

50 dermatologists and 54 GPs participated in the online survey. Average time taken to fill the questionnaire was 7 minutes and there was a 100% response rate for almost all questions. Only 3 people from GP group and 1 from dermatology group had skipped 1-2 questions.

Participants' experience in dermatology was less than 5 years in 18%, 5-10 years in 40% and more than 10 years in 42%. Out of GPs, 12.9% were of less than 5 years, 22.2% of 5 to 10 years and 64.8% of more than 10 years' experience. 66% of dermatologists and 50% GPs were working both in the government and private sector.

Both dermatologists (85.5%) and GPs (80.3%) selected Miconazole as their preferred first line topical application in treating tinea infections in the government hospital. Clotrimazole was the second preferred by both groups in government sector. Miconazole remained the first preference for GPs in the private sector (51.8%). 38% of dermatologists preferred Terbinafine and 30% preferred Miconazole in the private sector. The second most preferred drug for GPs was Ketoconazole (25.9%) whereas this was the third choice by dermatologists (18%) in the private sector. None of the dermatologists preferred Clotrimazole in the private sector.

The preferred first line oral drug was Griseofulvin by dermatologists in the government sector (54%). Dermatologists preferred usage of Itraconazole and Terbinafine in equal proportion of 36% each in the private sector (Figure 1). In contrast, majority of GPs preferred Fluconazole as their first line oral antifungal drug for the treatment of dermatophytosis in both government and private sectors (Figure 2). Majority of GPs who used Fluconazole as the first line used it in 150mg weekly dosage.

38.8% of GPs stated they would give either Itraconazole or Terbinafine for 2 weeks for naïve Tinea and 14. 3% said they will give only for 1 week. When asked about the confidence level of diagnosing and treating dermatophytosis, 37% of GPs stated they are fully confident. However, majority (53.7%) stated, to a certain extent and 9.2% stated not at all. 60% of GPs admitted that there is a possibility of adding a topical steroid when the diagnosis of dermatophyte infection was not sure. In this context, 27.3% each of all GPs preferred 1% Hydrocortisone and Betamethasone while a lower percentage (3.2%) preferred Clobetasol.

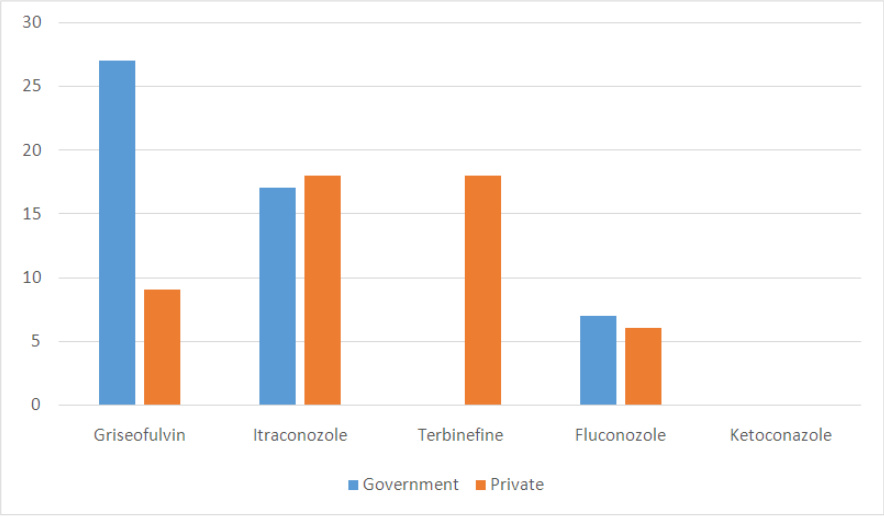

Figure 1. *Preferred first line oral antifungal by dermatologists in government and private sectors.*

Response of the two groups on combination of topical steroid and topical antifungals in clinically confirmed inflammatory tinea, is illustrated in Figure 3.

When dermatologists were asked to recall their last 10 patients with dermatophytosis, 34% stated that 7-10 patients, and 46% stated that 4-6 patients were inadvertently treated with steroids. Duration of treatment with either Itraconazole or Terbinafine for tinea incognito was 2 weeks in the majority (38.7%) of dermatologists (Figure 4).

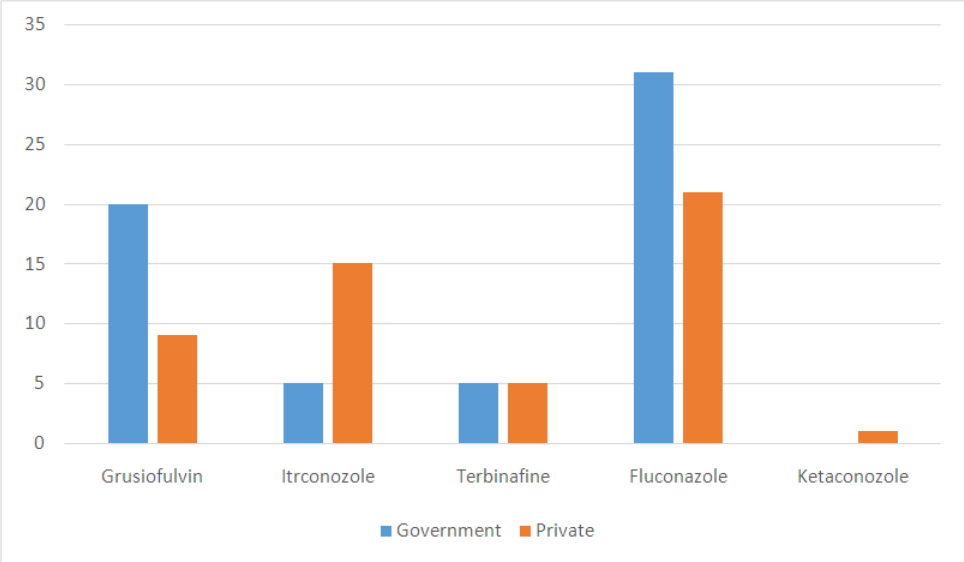

Figure 2. *Preferred first line oral antifungal by general practitioners in government and private sectors.*

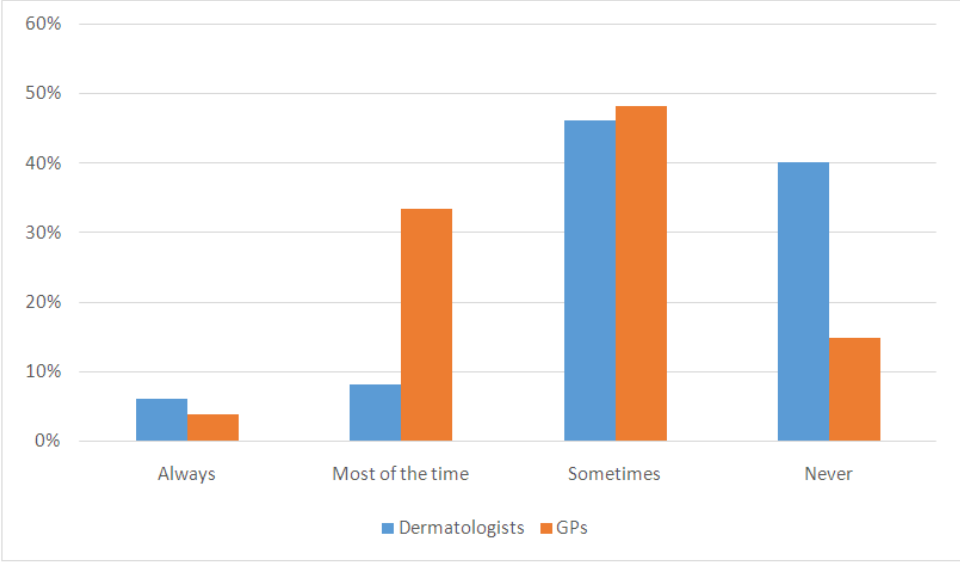

Figure 3. *Chance of adding a topical steroid in an inflammatory tinea infection by dermatologists and GPs.*

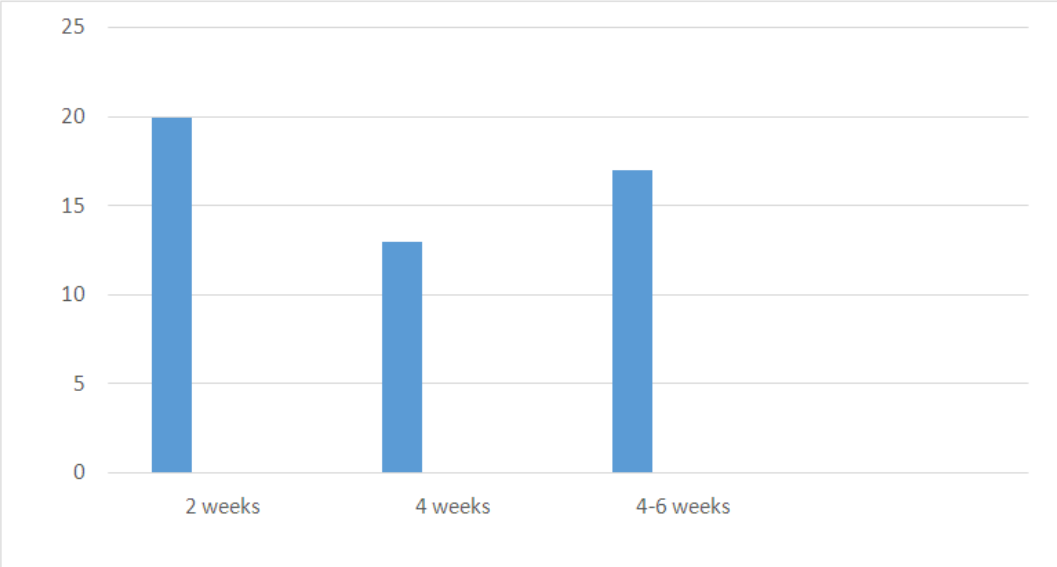

Figure 4. *Duration of treatment with Itraconazole or Terbinafine for Tinea Incognito by dermatologists.*

When asked if they think there is a lack of therapeutic response in dermatophytosis 88% dermatologists stated "yes", and the rest (12%) said they were "not sure". For the same question 53.7% of GPs marked "yes", 5.6% marked "No" and 40.7% marked "Not sure".

In the management of recurrent or recalcitrant tinea infections, 54% of dermatologists stated they would give the same antifungals for prolonged durations and 76% stated they would switch to another class of drugs (Table 1).

In the same setting 64.1% of GPs would refer to a dermatologist while 26.2% would switch to a different class of drugs. Prolonged duration of the same drug (11.3%) and higher dosages of the same drug (3.7%) were stated in lower proportions by GPs when compared to dermatologists.

Table 1. Management options by the two groups in recalcitrant dermatophytosis (Allowed to tick more than one option)

Choice	*Percentage of Dermatologists*	*Percentage of GPs*
Switch to another class of antifungal agent	76%	26.3%
Increase the duration of treatment of the same drug	54%	11.3%
Increase the dosage strength of the same drug	20%	3.7%
Give a combination of different classes of oral drugs	24%	11.3%
Use keratolytic agents	18%	
Improve skin barrier properties	10%	
Refer to a dermatologist		64.1%

When inquired about investigations in recalcitrant cases, 63.7% of dermatologists had stated they would "occasionally" do skin scrapings for microscopy and 42.3% would "occasionally" do fungal culture. 20.4% stated they would "mostly" do microscopy and only 12.4% had stated they would "mostly" do fungal cultures.

The final question for both groups was, "what should be done to minimize the emerging therapeutic failure in dermatophytosis?". Both groups thought education of primary care physicians as a key point in overcoming this problem (Table 2).

Discussion

Low therapeutic response in dermatophytosis is widely reported from various countries[4-6]. Sri Lanka too seem to be following this trend. In this setting it is very important to have an insight into the practice patterns of GPs and dermatologists in managing dermatophytosis. This online survey was undertaken with this intention in mind.

From the survey it is seen that there is a wide variation in prescribing the topical antifungals among these two groups. Currently there is no clear guidelines for the usage of topicals and this is widely based on the availability and personnel experience of the prescribers.

Griseofulvin is the widely used oral drug by both groups in the government sector. Although it is a time tested drug, owing to its fungistatic properties and longer duration of treatment it is not a widely recommended option in the current scenario. Resistance/ recurrence after Griseofulvin therapy in patients with *T. rubrum* and *T. tonsurans* has been known since 1960's[14]. Both Itraconazole and Terbinafine has been recommended as the first line drug in treating dermatophytosis in the recently published expert consensus of management of dermatophytosis in India[15].

Fact that the dermatologists are using more of Terbinafine and Itraconazole in the private sector shows that they are limited to the available drugs in the government sector but picking the better options in the private sector. Fluconazole shows as a popular option among GPs. The efficacy of Fluconazole is very limited for dermatophytosis. Several in vitro antifungal susceptibility tests have shown higher Minimal Inhibitory Concentrations (MIC) values in several dermatophyte species for Fluconazole[12,16]. Furthermore, there are only very few studies that show its clinical efficacy in dermatophytosis and that is with a daily dose of 50 mg for 4 weeks[17]. Fluconazole is a drug which should be preserved for the use of Candida infections, and weekly dosage of Fluconazole can give rise to resistance[18]. Thus the use of Fluconazole in treating dermatophytosis among GPs should be strongly discouraged.

The survey reveals that 60% of GPs have admitted the possibility of using a topical steroid when the diagnosis of dermatophytosis is not sure in the treatment of dermatophytosis. Use of steroids will reduce the cell mediated immunity which is important in fungal elimination[8]. Therefore, this will give rise to chronic persistent dermatophyte infections which need prolonged courses of oral antifungals for effective clearance. Steroid misuse has been identified as major contributory factor in this emerging low therapeutic response in dermatophytosis[5].

Table 2. Opinions of both groups in overcoming the lack of therapeutic response in dermatophytosis in Sri Lanka (Allowed to tick more than one option)

Opinion	*Percentage of Dermatologists*	*Percentage of GPs*
Educating the primary care physicians on proper diagnosis to minimize steroid misuse	96%	83%
Continuing antifungal treatments for the proper duration	80%	56.6%
Introduction of newer antifungal agents	33%	9.4%
Establish an early referral system to Dermatologists	66%	47.1%

Combination of a topical steroid may attenuate the inflammatory component and increase patient compliance in inflammatory tinea infection[19]. It was noted that 60% of dermatologists and 85.2% GPs stated they may use a topical steroid in the treatment of inflammatory tinea. However, the current recommendation is to avoid a topical steroid even in the context of inflammatory tinea due to reasons discussed earlier[15].

14. 3% of GPs would give either Itraconazole or Terbinafine for one week in naïve tinea and 38.7% dermatologists would give oral antifungals for 2 weeks for tinea incognito. Current recommendation is for to use either Itraconazole or Terbinafine for a minimum of 2 to 4 weeks in naïve infections and 4-6 weeks in tinea incognito[15]. As inadequate treatment duration is one of the major causes for lack of therapeutic response and drug resistance this practice pattern has to be corrected early.

88% of dermatologists and 53.7% of GPs thought that there is a current trend of having low therapeutic response in dermatophytosis. This shows that Sri Lanka too is following the recent trend of poorly responding dermatophyte infections in South East Asia. There was varied response from both groups of their management strategies in recalcitrant dermatophyte infections. Switching to different class of antifungals, higher dosages and prolonged treatments are all being described in the literature[4,6,14]. However, there is no proper consensus on this management problem at present. This would vary largely on the locally prevalent dermatophyte species and its susceptibility for different antifungals.

It was observed that even in recalcitrant dermatophytosis, dermatologists are rarely performing fungal microscopy and culture. 20% stated that they would mostly do microscopy and only 14.3% stated they would mostly do fungal culture. Low availability of these facilities, high cost and long wait for reports may be the reasons for dermatologists' non enthusiastic response for laboratory investigations. Furthermore, it is known that clinical unsuccessful treatment does not always correlate with the MIC value of antifungals *(in-vitro)*. The discordance between the *in-vivo* and *in-vitro* resistance in fungi has been illustrated by the "90-60 rule", which states 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[20].

It is encouraging to see that both groups have identified the lack of therapeutic response in dermatophytosis as an emerging health issue. As both groups agree on proper education of primary care physicians on management of dermatophytosis, this should be the starting point in overcoming an epidemic of recalcitrant dermatophytosis in Sri Lanka.

Recommendations

Dermatophytosis has to be taken as a public health issue and a multidisciplinary team involving dermatologists, primary care physicians, mycologists, health care policy makers should work together, to overcome the problem of low therapeutic response. A continuous supply of different groups of oral anti-fungal drugs should be available at all times. This will enable dermatologists to use the current evidence based, best practiced treatments even in the government sector. Usage of weekly dose of Fluconazole as first line treatment for dermatophytosis should be strongly discouraged. Proper education of primary care physicians on management of dermatophytosis has to be taken up as a priority. This will invariably lead to reduction of steroid misuse in tinea infections. Both GPs and Dermatologists should be aware of the adequate duration of treatment of antifungals, both in naïve tinea infections and tinea incognito. Local guidelines on managing naïve and recalcitrant dermatophytosis should be developed which will streamline the practice patterns of clinicians. Scientific studies to identify the locally prevalent dermatophyte species, their clinical response to various groups of antifungals, and antifungal susceptibility testing should guide these local management strategies.

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References

1. Bongomin F, Gago S, Oladele RO, Denning DW. Global and Multi-National Prevalence of Fungal Diseases-Estimate Precision. *J Fungi* (Basel) 2017; **3**(4).
2. Kumarasinghe SPW. Prevalance of common skin diseases among dermatology clinic attandees. *Ceylon Journal of Medical Science* 1992; 34-36.
3. Virgili A, Zampino MR, La Malfa V, Strumia R, Bedani PL. Prevalence of superficial dermatomycoses in 73 renal transplant recipients. *Dermatology* 1999; **199**(1): 31-4.
4. Tigga RA, Das S, Bhattacharya SN, *et al*. Burden of Chronic Dermatophytosis in a Tertiary Care Hospital: Interaction of Fungal Virulence and Host Immunity. *Mycopathologia* 2018; **183**(6): 951-9.
5. Verma SB. Emergence of recalcitrant dermatophytosis in India. *Lancet Infect Dis.* 2018; **18**(7): 718-9.
6. Manzano-Gayosso P, Méndez-Tovar LJ, Hernández-

Hernández F, López-Martínez R. Antifungal resistance: an emerging problem in Mexico. *Gac Med Mex*. 2008; **144**(1): 23-6.

7. Sardana K, Kaur R, Arora P, Goyal R, Ghunawat S. Is Antifungal Resistance a Cause for Treatment Failure in Dermatophytosis: A Study Focused on Tinea Corporis and Cruris from a Tertiary Centre? *Indian Dermatol Online J.* 2018; **9**(2): 90-5.
8. Solomon BA, Glass AT, Rabbin PE. Tinea incognito and "over-the-counter" potent topical steroids. *Cutis.* 1996; **58**(4): 295-6.
9. Bishnoi A, Vinay K, Dogra S. Emergence of recalcitrant dermatophytosis in India. *Lancet Infet Dis.* 2018; **18**(3): 250-1.
10. Martinez-Rossi NM, Bitencourt TA, Peres NTA, *et al*. Dermatophyte Resistance to Antifungal Drugs: Mechanisms and Prospectus. *Front Microbiol*. 2018; **9**: 1108.
11. Azevedo MM, Faria-Ramos I, Cruz LC, Pina-Vaz C, Rodrigues AG. Genesis of Azole Antifungal Resistance from Agriculture to Clinical Settings. *J Agric Food Chem*. 2015; **63**(34): 7463-8.
12. Adimi P, Hashemi SJ, Mahmoudi M, *et al*. In-vitro Activity of 10 Antifungal Agents against 320 Dermatophyte Strains Using Microdilution Method in Tehran. *Iran J Pharm Res*. 2013; **12**(3): 537-45.
13. Yamada T, Maeda M, Alshahni MM, *et al*. Terbinafine Resistance of Trichophyton Clinical Isolates Caused by Specific Point Mutations in the Squalene Epoxidase Gene. *Antimicrob Agents Chemother* 2017; **61**(7).
14. Sardana K, Gupta A. Rational for Drug Dosimetry and Duration of Terbinafine in the Context of Recalcitrant Dermatophytosis: Is 500 mg Better than 250 mg OD or BD? *Indian J Dermatol.* 2017; **62**(6): 665-7.
16. Berry CZ. Recurrence of Trichophyton rubrum infection during treatment with griseofulvin. *Arch Dermatol*. 1960; **81**: 982.
15. Rajagopalan M, Inamadar A, Mittal A, Miskeen AK, Srinivas CR, Sardana K, *et al*. Expert Consensus on The Management of Dermatophytosis in India (ECTODERM India). *BMC Dermatol.* 2018; **18**(1): 6.
16. Salehi Z, Fatahi N, Taran M, *et al*. Comparison of in vitro antifungal activity of novel triazoles with available antifungal agents against dermatophyte species caused tinea pedis. *J Mycol Med*. 2020.
17. Sultana T, Saha SK, Hossain M, et al. Current Trends of Using Systemic Antifungal Drugs and their Comparative Efficacy in Tinea Corporis and Tinea Cruris in Outpatient Department of Dermatology in a Tertiary Level Hospital. *Mymensingh Med J.* 2018; **27**(1): 52-6.
18. Rasmus H J. Resistance in Human Pathogenic Yeasts and Filamentous Fungi: Prevalence, Underlying Molecular Mechanisms and Link to the Use of Antifungals in Humans and the Environment. *Dan Med J.* 2016; **63**(10).
19. Schaller M, Friedrich, Papini M, Pujol R M, Verald S. Topical Antifungal-Corticosteroid Combination Therapy for the Treatment of Superficial Mycoses: Conclusions of an Expert Panel Meeting. *Mycoses*. 2016; **59**(6), 365-73.
20. Dogra S, Shaw D, Shivaprakash MR. Antifungal Drug Susceptibility Testing of Dermatophytes: Laboratory Findings to Clinical Implications. *Indian Dermatol Online J.* 2019; **10**(3): 225-33.