BMJ Open

Topical steroid misuse in rural North India: a silent epidemic

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-032829
Article Type:	Research
Date Submitted by the Author:	08-Jul-2019
Complete List of Authors:	Thomas, Molly; Herbertpur Christian Hospital Herbertpur, Dermatology Department, Wong, Celeste; Skin and Cancer Foundation Australia, Dermatology Anderson, Pam; University of Melbourne, Nossal Institute for Global Health Grills, Nathan; The University of Melbourne School of Population and Global Health, Nossal Institute for Global Health
Keywords:	Topical steroid, misuse, Tinea, infective, rural, DERMATOLOGY

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Topical steroid misuse in rural North India: a silent epidemic

Running title: The silent epidemic of topical steroid misuse

Authors: Molly Thomas[1], Celeste Wong[2], Pam Anderson[3], Nathan Grills[4]

1. Dermatology Department, Herbertpur Christian Hospital, Herbertpur P.O, Dehradun, Uttarakhand, India-248142.
2. Dermatology Department, Skin and Cancer Foundation Inc, 1/80 Drummond Street , Carlton Victoria 3053.
3. Nossal Institute for Global Health, School of Population and Global Health, University of Melbourne, Level 5, 333 Exhibition Street, Melbourne 3000, Australia.
4. Associate professor, Nossal Institute for Global Health, School of Population and Global Health, University of Melbourne, Level 5, 333 Exhibition Street, Melbourne 3000, Australia.

Corresponding author: Dr Molly Thomas, Herbertpur Christian Hospital, Herbertpur P.O, Dehradun, Uttarakhand, India-248142

Telephone number- +91 9897532821

Email ID- vijuandmolly@gmail.com

Word Count: 3,133

ABSTRACT

Introduction: Current evidence indicates an alarming increase in topical steroid (TS) misuse in India. Data is deficient regarding the magnitude and characteristics of this problem in rural India where 68% of the population resides, as well as factors which promote this dangerous practice. This study analyses the magnitude, causes, characteristics and consequences of TS misuse in rural India and also examines the association between TS misuse and patients' perception of skin disease.

Methods: A cross sectional observational study was conducted among the attendees of the dermatology outpatient department of a secondary level hospital, in rural North India. Those with a history of TS misuse were analysed for behaviour patterns and outcome.

Results: Out of 723 patients, 211 (29.2%) misused TS. Clobetasol propionate (58.2%) was most commonly misused. 70 different unethical brands were recovered from the patients. Chemists and local healers together contributed to 78% of the sources for steroid misuse. 57.8% perceived their skin conditions to be allergic reactions to food, when in fact 70.1% were tinea, 10% scabies and 9% acne. 80% with tinea had tinea incognito and 97% had extensive lesions. 85% with scabies had atypical lesions and 80% with acne had steroid rosacea or aggravation of acne. The median expenditure incurred in purchasing these unethical creams was Rs1,000 (equivalent to 3 days' wages of a labourer).

Conclusion: Steroid misuse is a grave problem of epidemic proportion causing a huge economic burden in rural India. This practice is changing the profile of many common and infective skin conditions, which portends diagnostic dilemmas and therapeutic challenges for clinicians. Misconception about skin disease drives the public to seek "quick fixes" doled out by un-professionals who enjoy unrestricted access to potent steroids. There is hence a dire

urgency to tighten regulatory controls over the manufacturing and sale of irrational TS combinations.

Keywords: Topical steroid, misuse, Tinea, infective, rural

ARTICLE SUMMARY

Strengths and limitations of this study

- This study is one of the very few cross-sectional studies which focuses on TS misuse in the rural area in Uttarakhand, North India.
- A mixed method of structured questionnaire supplemented with qualitative interviews was used to assess TS misuse.
- The development of research objectives were informed by patients of topical steroid use particularly those who had experienced the side effects from TS use.
- The frequency of misuse may be underestimated due to the difficulty of identifying corticosteroids by respondents.
- Generalisability is limited by the sample being restricted to one outpatient department in one location.

INTRODUCTION

The usefulness of Topical steroids (TS), the most widely used therapeutic agents in dermatology, has become a double edged sword with increasing prevalence of misuse, leading to disastrous consequences.[1, 2] Of grave concern is the unprecedented increase in fungal infections as well as the emergence of resistant dermatophytosis, in India, most likely due to irrational use of Fixed Drug Combination (FDC) creams containing steroid.[2] In addition, children also become inevitable victims of this malpractice. They are more vulnerable to the systemic effects of potent topical corticosteroids as well as to the spread of infections.[2] Non-medical use of TS in fairness creams has led to increasing occurrences of a condition which has been described as topical steroid damaged face (TSDF).[3, 4] Chemists and often qualified medical practitioners readily prescribe and dispense potent topical steroids given that they provide dramatic symptomatic relief. The pharmaceutical industry also contributes to the problem as they manufacture and promote unethical creams containing potent TS in combination with antifungals and antibacterials. This problem is further compounded by the unregulated over- the- counter (OTC) supply and unrestricted sale of TS. Public and professional ignorance, legal ambiguity, and government indifference create a grave problem whereby FDC creams are used as a panacea for all skin problems.[5] The unprecedented increase in sales of these "steroid cocktails", by an alarming 26% in 2014-15, is a reflection of the public appeal of these dangerous combinations.[6] This is especially unfortunate, given these medications are not only ineffective in curing but cause more harm than benefit. In addition, this unnecessary expenditure can cause an economic drain impoverishing many who have scarce or no financial reserve. Though efforts are being made to draw attention to the multiple factors behind this problem in India,[4, 6, 7] it remains largely uncharacterised in rural areas. Earlier studies were conducted in the urban setting of tertiary care hospitals with

emphasis on TS usage on face.[6, 7, 9-12] No data is available to understand the impact of this epidemic in the rural areas where 68.84% of the Indian population dwells.[13]

This study hence analyses the magnitude of topical steroid abuse, its causes, characteristics and consequences, including the economic impact, among a rural population in North India. We also seek to better understand the relation between TS misuse and patients' perception of skin disease.

MATERIALS AND METHODS

A cross sectional study of patients was conducted over a period of 3 months (March 2016 to May 2016) amongst patients attending the dermatology outpatient department of a secondary level hospital, located in rural part of Uttarakhand, North India. Patients of both genders and all ages who fulfilled the following criteria were recruited:

1. Having a skin condition for which topical steroid is absolutely contraindicated i.e. acne, bacterial, viral, fungal or parasitic cutaneous infections such as tinea, furuncle, scabies etc.

2. History of topical steroid usage for that condition.

Topical steroid includes either plain or combination of topical steroids with antibiotics or antifungals. The patients were recruited following a clinical examination by the consultant dermatologist, after obtaining an informed consent. Parents were interviewed for gathering data regarding their children. Using a mixed method of structured questionnaire supplemented with qualitative interviews, patients were assessed for misuse of TS in terms of indication, duration, types of steroid used, source of recommendation, expense incurred and side effects. All patients with tinea were subjected to direct microscopy and those who were negative were

added only after positive response to antifungal therapy. Ethics approval was obtained from the Institutional Ethics Committee of the Emmanuel Hospital Association, New Delhi (Protocol No.129). The patients were also counselled regarding dangers of TS misuse and appropriate treatment was given for side effects, when present.

Patient and Public Involvement

While patients were not involved in the recruitment to and conduct of the present study, the development of research objectives were informed by patients of topical steroid use, particularly those who had experienced the side effects from TS use and expressed the need for more to be done about this problem. The pilot of this study also involved getting feedback from patients in how questions were asked. The results will inform the production of a video and patient information handout to the communities from which the patients came.

Data analysis

Data analysis was done using Stata 14 (StataCorp, Texas, U.S.). Major variables of interest were dermatological conditions for which steroids were misused, types and quantities of steroids used, sources of prescriptions, adverse effects of misusing steroids, expenditure incurred and patients' perception of the disease. Data was presented as percentage with the exceptions of age and expenditure which were expressed in median (Q1-Q3). For multiple-response questions (side-effects, types and sources of topical steroids), we used MRTAB (Ben Jann & Hilde Schaeper, 2004) to generate simple frequencies. To test the associations between major demographic variables and profile of misuse, we performed Chi-squared test with the level of significance set at 0.05.

RESULTS

Demographics

Of the 723 new patients seen in the dermatology OPD, 211 (29.2%, 95% CI: 25.9; 32.6) had a history of topical steroid misuse. The male to female ratio in our sample was 1.43:1. The median age was 30 years. Fifty-five percent of the cases were in the 15-34 years age group. Those having primary education seemed to be most affected topical steroid misuse (Table 1).

Table 1. Demographic details of patients who had a history of topical steroid misuse

	No. of observations	Percentage
Age (yrs)		
up to 14	11	5.2
15-24	56	26.5
25-34	61	28.9
35-44	44	20.9
45 and over	39	18.5
Gender		
Male	124	58.8
Female	87	41.2
Education		
Illiterate	37	17.5
Primary	66	31.3
*High school	50	23.7
College	10	4.7
*Graduate	48	22.8

*Included 1 imputed value based on father's highest level of education
n=211

Profile of steroid misuse

Dermatological conditions mismanaged with steroids:

The most common condition for steroid misuse was tinea (70.1%) followed by scabies (10%) and acne (9%%). A small number had two concomitant diseases such as tinea with scabies, tinea with acne or acne with scabies. Other conditions for which steroid was misused were vulval candidiasis, herpes genitalis, tinea versicolor, furuncle and melasma.

Types of steroid formulations used

FDC containing either a triple or quadruple combination of antifungal, antibacterial and steroid were the commonly used creams. Although most of the participants (66%) used only one class of TS, 32% used two classes and 3% used three classes. The most commonly used topical steroid (Table 2) was clobetasol propionate (58.2% of 287 responses). About 70 different creams (Table 3), produced by a myriad of pharmaceutical companies were recovered from the patients during the study. As shown in table 4, the ten most commonly misused combinations creams have very similar compositions although packaged under different names and appearances. Patients often think they are prescribed a new cream at every visit while in fact they are using one with the same molecule, most often clobetasol propionate (class I potency), thereby perpetuating the side effects. Twenty-five percent of respondents reported use of either oral steroids (OS) or injectables or both in addition to TS. Of this, 39.6% had concomitant use of OS, 37.7% used both oral and injectable steroid and 22.7% used injectables along with TS. These patients reported that the OS were easily procured over the counter. Use of injectable steroid was found to be associated with highest level of education (p=0.04). Users of injectable steroids obtained them from local healers.

Table 2. Types of topical steroid misused

Steroid molecule	No. of observations	Percentage
Clobetasol propionate	167	58.2
Beclomethasone/Betamethasone	91	31.7
Mometasone	11	3.8
Fluocinolone	17	5.9
Clobetasone	1	0.4

Multiple responses were allowed in this question. Percentages were based on total number of responses
Total no. of response=287
Total no. of cases = 211

Table 3 List of 70 different brand creams, many having same composition of steroid, antibiotic and anti-fungal molecules, recovered from patients during the study

Brand name	Steroid	Antibiotic	Antifungal
Panderm+, Terderm+, Orniderm, Nikderm+, Oltef-NF, Laboderm-oc, Terbinaforce+, Terbicad, Fourderm, DermikemOC, Pardum+, Castor-NF, Totalderm+, Terogood, Terogood, Orkid4, Sarvocin-CT, Orkaderm, Soltex, Bifine-plus, Dermek-TC, Turgoderm-oc, Tocoderm+, Onflox-TC,	Clobetasol propionate	Ofloxacin, Ornidazole	Terbinafine Hydrochloride
Dermacin-k5, Amitone-5, Clotebate-GM, Clobezine-CM, Tecderm-KT, Dermiford, Dermifrench-KT, Dermiford-K5	Clobetasol propionate	Iodochlorhydroxyquinoline, Gentamicin	Ketoconazole, tolnaftate
Clostar-GM, Ring-out+, Clobriv-MG, Clobeta GM, Adoderm-MN, Zincodem-GM, Candid 3D, Iobate, Neo Clobenate-GM, Clobenate-GM, Lucobet-GM, Cosvate-GM	Clobetasol, propionate	Neomycin sulphate	Clotrimazole
Medisalic , Clorap-s, Lozivate-MF, Lozivate	Clobetasol Propionate & salicylic acid		
Lobate GM	Clobetasol Propionate	Neomycin sulphate	Miconazole
Unikderm	Clobetasol proprionate	Gentamicin	ketoconazole
EVzole	Beclomethasone dipropionate	Neomycin sulphate	Clotrimazole
Betnovate-C	Betamethasone valerate	Clioquinol	Chlorocresol
Betnovate-N,	Betamethasone valerate	Neomycin sulphate	Chlorocresol
Nuforce-GM, Betamil, Quadriderm RF, Canditas-BG, Lupiderm-GM, Onabet-B, Quadriderm, Surfaz-SN, Zenoderm, CBN,	Beclomethasone dipropionate	Neomycin sulphate	Clotrimazole
Sertamide-B	Beclomethasone dipropionate		Sertaconazole
Candid -B	Beclomethasone		Clotrimazole
Cipro-CF, Ceflox-CF,	Fluocinolone acitonide	Ciprofloxacin Neomycin sulphate	Clotrimazole
Zole-F	Fluocinolone acitonide		Miconazole
Flucort-H	Fluocinolone acitonide		
Sure-KT	Clobetasone	Gentamicin	ketoconazole
Aluderm	Clobetasol proprionate	Ofloxacin	Ornidazole

Table 4. Ten most commonly used fixed drug combination creams containing steroid

Brand name	Composition	No. of Responses(%)
Neoclobenate GM	Clobetasol propionate,Miconazole,Neomycin	55 (17.7%)
Castor NF	Clobetasol propionate, Ofloxacin, Ornidazole, Terbinafine hydrochloride	43 (13.8%)
Quadriderm	Beclomethasone dipropionate, Clotrimazole, Neomycin	32 (10.3%)
Betnovate-N	Betamethasone valerate, Neomycin	30 (9.7%)
Dermiford	Ketoconazole, iodoxychlorhydroquinoline, Tolnaftate, Genatamicin and Clobetasol propionate	30 (9.7%)
Betnovate-C	Betamethasone valerate, Clotrimazole	26 (8.4%)
Dermikem OC	Clobetasol propionate, Ofloxacin, Ornidazole, Terbinafine hydrochloride	25 (8.0%)
Lobate GM	Clobetasol propionate,Miconazole nitrate,Neomycin sulphate	25 (8.0%)
CBN	Beclomethasone dipropionate, Clotrimazole, Neomycin sulphate, Chlorocresol	25 (8.0%)
Terbinaforce plus	Clobetasol propionate, Ofloxacin, Ornidazole, Terbinafine hydrochloride	20 (6.4%)

Sources of steroid procurement or prescription and steroid usage patterns

More than half of respondents (65.9%) indicated one single source for procurement of TS, most often being chemists (56.8%). Patients reported that chemists freely dispensed TS for any complaints of itching, provided a quick remedy and avoided cumbersome procedures required in a hospital. There was statistically significant gender difference (χ^2 =7.1; p=0.008) in relation to steroid procurement from non-professional sources, suggesting that females were less likely to approach medical practitioners for treating their skin infections.

Economic burden

There was a wide range in the number of tubes used by the respondents. Twenty-one percent (44) used one tube while about three percent (7) used more than 100 tubes. The majority (63%) used topical steroid combinations for less than 6 months. Approximately 16% of respondents used TS for over a year. The pattern of steroid usage was erratic, varying from using either one

tube intermittently over few months alone or most often in combination with oral and/or injectable steroids, or using more than 100 tubes continuously. Expenditure by patient ranged from 30 rupees (Rs), (equivalent to less than a dollar) to more than 1 lakh rupees. The median expenditure was Rs1,000 (Rs 200 - Rs 4,000), equivalent to 3 days' wages of a daily labourer. These FDC creams are available at very low cost in comparison to plain antifungal creams.

Adverse effects of topical and systemic steroid misuse

A) *Effect on Dermatological conditions* – ninety-seven percent of patients with steroid modified tinea had extension of tinea to non-flexural areas of body i.e. face, ears, wrists, entire trunk, dorsum of hands and genitalia in males. Eighty percent had tinea incognito which presented with atypical clinical signs like lichenification, eczematisation, large geographic patterns, pseudoimbricata, arciform, pustular and polycyclic lesions as well as lesions mimicking other diseases like psoriasis, pityriasis rosea, lichen planus, and seborrheic dermatitis. Three percent of tinea infection had localised exacerbation with pustulations. Fifty-eight percent of patients with acne developed features of either steroid rosacea, pustular or nodulocystic acne. Ninety-five percent of patients with scabies had generalized papules instead of the characteristics areas making it difficult to recognize (scabies incognito).

B) Other effects

i) Striae – six patients (2.5%) had striae and these were very extensive over the groins, inner thighs, lateral sides of abdomen and axillae. Three of these patients concomitantly used oral and/or injectable steroids.

ii) Cushingoid facies – eleven patients (4.6%) showed Cushingoid features mainly characterised by facial puffiness. Seven of them concomitantly used oral and/or injectable steroids.

iv) Hypertension – eight respondents (3.3%) had new onset hypertension. Three of these patients concomitantly used oral and/or injectable steroids.

v) Diabetes – five individuals (2.1%) had new onset diabetes. Four of them concomitantly used oral and/or injectable steroids.

Patients' perception of the disease

The majority (57.8%) considered their itchy skin condition or eruptions to be an allergic response to some food or drink which heats up the body (Fig. 1). About nine percent thought it was infective and approximately six percent related it to dampness. Nineteen percent did not know the cause. Five percent believed that their skin condition was due to impure blood. Some resorted to tonics such as "Koon safi" (blood purifier) and even "blood purification". One respondent regularly withdrew small quantity of his blood, mixed it with triamcinolone and injected the mixture back into his body. Other explanations (3.8%) for their skin conditions were bowel irregularities, heredity, unclean water and few even considered it to be due to evil spirits.

DISCUSSION

TS misuse is a very significant public health issue in rural India. In this study, three out of ten patients who came to the dermatology department were using topical steroids inappropriately. This is much higher in comparison to an urban study done in a similar setting in Delhi (11.8%) [7] as well as the Pan Indian study (15%) conducted among urban population [4]. Our study demonstrated a slight male preponderance. This is in contrast to the Pan Indian study which showed a female preponderance,[4] most likely because the study was restricted to facial steroid usage as a skin whitener. The average age of usage in our study as 32 years old which was similar to findings from the studies in urban areas of India.[4, 7]

Tinea was the most common indication for steroid misuse in our study. This concurs with the findings in other recent studies in India.[6, 7] However, acne was the most common indication for steroid misuse in one urban study from South India.[9] In another study by Dey VK,[12] skin lightening was the main reason for using TS in the absence of any primary dermatosis while in the study by Saraswat A et al, TS were most commonly used for both skin lightening and acne.[4] This difference in usage patterns could be due to infections like tinea being more prevalent in rural areas and skin colour being of more concern in urban areas.

Steroid treatment also makes recognition of skin diseases more difficult and results in misdiagnosis, mistreatment and ultimately increased morbidity.[2] Tinea incognito and extension of lesions were seen in majority of patients with dermatophytosis. For health care providers, topical steroid abuse can make tinea difficult to distinguish from other common diseases like eczema, contact dermatitis and psoriasis. This is because the steroids alter the characteristic "ring or annular" lesion.[2, 10] These cases of tinea incognito could range from vague erythematous plaques to lesions with oozing, prominent scaling, pustulation to large geographic lesions mimicking diseases like psoriasis. Thus, when treated with steroids, it can be difficult for even dermatologists to accurately recognize steroid modified tinea. Our study substantiates the concern that this entity is present in epidemic proportions and is perhaps underdiagnosed due to the unrecognizable varied clinical patterns.[2] We have also observed an increased occurrence in genital tinea, which was once a rare feature, as has been highlighted by Verma SB.[2] There is a need to educate the medical fraternity, especially in training institutions, about the wide variation in clinical presentation of steroid modified tinea so as to enable proper clinical diagnosis.

TS abuse in scabies can cause scaly and widespread lesions that are unrecognizable as scabies. Scabies incognito or steroid modified scabies can be a serious public health problem since it is very contagious and any diagnostic difficulty can lead to an epidemic of scabies. Acne being

the third most prevalent reason for steroid misuse also leads to increased possibilities for Topical Steroid Damaged Face and disfiguring sequelae of acne.

In our study, nearly half of the patients received their TS from chemists. Likewise, in studies from other parts of the sub-continent, chemists were the most common source of inappropriate steroid use.[4, 10, 14] They often function as doctors, especially where the local health services are underdeveloped or unavailable, giving rise to a scenario where medications are misused. Given the rarity of dermatologists, and even MBBS trained doctors, available in rural areas, many people seek treatment for skin diseases from local charlatans and alternative medicine practitioners, belonging to AYUSH. These accounts for 31% of the topical steroid misuse in our study which is of great concern, given that it is illegal for a practitioner of alternative medicine to prescribe drugs of modern medicine (like TS). Despite being illegal there is no legal restriction on marketing of TS by salespersons to AYUSH practitioners.[10] The fact that 21% of these medications were prescribed by MBBS trained doctors is also concerning. Unfortunately, general physicians and even some dermatologists are also responsible for prescribing TS unnecessarily. This highlights the insufficient training of medical/paramedical personnel about the judicious use of topical corticosteroids and their potentially serious side effects. Saraswat's study on facial steroid use found that poor availability of physicians in rural areas was associated with non-physicians being likely to prescribe TS to the public.[4]

Our study found that clobetasol propionate was the most common steroid misused, which is also the most potent topical steroid. Betamethasone valerate was the most widely known and misused steroid in other studies.[4, 7, 9] Our finding is consistent with Saraswat et al who noted in their study that patients from rural areas were more likely to use potent or super potent topical steroids.[4] Use of injectable steroid was found to be associated with highest level of education (p=0.04). This could reflect the misplaced expectation of a cure or fast relief from 'injections' and the desire for quick remedies among working class. Most of those who used both oral and

injectable steroid had either no education or only primary schooling. This could reflect their unwavering trust in the local healers.

In order to understand the reason behind the rampant steroid abuse, this study also delved into the patients' perception of their skin disease. Eighty-six percent of respondents either misunderstood or did not know the cause of their skin disease. All pruritic symptoms or eruptions were considered to be an allergic response, most likely to hot, spicy food or impure blood. This wrong perception can shift the attention from common hygienic measures, necessary to respond to infective conditions like tinea and scabies, towards focussing on unrelated factors like abstinence from certain food, unwarranted blood investigations and usage of unethical products and procedures purported to purify blood. An important reason for patients seeking primary recourse from nonmedical personnel could be due to a lack of proper understanding regarding the cause of their illness. This aspect has often been overlooked while addressing the problem of TS abuse. Hence, unless patients are educated about the actual cause of their skin conditions, they are unlikely to seek appropriate treatment.

Our study is consistent with the observations that factors leading to misuse of TC may occur at various stages during its journey from the factory to the face.[15] The alarming plethora of TS combinations recovered from the patients clearly indicates the ease of purchase and the spurious claims of irrational TS combinations promoted by pharmaceutical companies. In spite of the fact that these drugs can cause serious adverse effects, they are sold without medical prescription or regulations. Although steroids have been included under schedule H drugs, which requires proper prescription, the enforcement of the regulation at the ground level is rare.[2] For chemists and local healers, FDC creams seem to be the answer to all skin conditions, regardless of the aetiology of the disease (whether it is a bacterial or fungal infection or inflammation). Unfortunately, many clinicians and occasionally even dermatologists also promote these multidrug combinations. At the consumer level there is little awareness about

the adverse effects. To address this, stringent regulations on the manufacture and sale of steroid cocktail creams are required.

Limitations

It was difficult for many patients to understand what corticosteroid was until they were shown samples of these drugs. Moreover, flooding of the market with innumerable brands containing corticosteroids made it difficult to show a sample of each and every brand for the patient to recognize. This could have led to under-estimation of the frequency of the malpractice in our study. Also, recollection of duration and quantity of use was difficult for patients who have used topical corticosteroids over a long time period. Generalisability is limited by the sample being restricted to one outpatient department in one location.

CONCLUSIONS

The epidemic of steroid modified dermatoses in rural India due to injudicious use of topical steroids is caused by multifaceted factors. Concerted, multipronged actions are needed to address the professional and public ignorance, political apathy and profit incentives for drug companies and chemists. Continuous education of clinicians to recognize the current altered and 'unrecognizable' steroid modified dermatoses as well as the potentially harmful effects of TS is also required. In addition, drug control agencies should ensure strict regulation of TS sale and prohibit manufacturing of steroid cocktails. The ministry of Health and Welfare could helpfully create awareness through social media and advertisements to warn people about the danger of TS misuse.

Funding sources – This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of Interests: None to be declared

Data sharing statement: Data are available upon reasonable request by emailing to corresponding author (Dr Molly Thomas: vijuandmolly@gmail.com). No additional data are available for this study.

Authors' contributions:

Dr Molly Thomas: principal investigator, contributed to the study design and methods, interpreted the data and drafted the manuscript.

Dr Nathan Grills: developed concept of research, interpreted the data, reviewed, edited and approved the final manuscript

Dr Celeste Wong: contributed to the study design and methods, reviewed, edited and approved the final manuscript

Pam Anderson: conducted statistical analysis, summarised and interpreted findings, reviewed, edited and approved the final manuscript

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in BMJ Open and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

References

1 Coondoo A, Phiske M, Verma S, et al. Side-effects of topical steroids: A long overdue revisit. *Indian Dermatol Online J* 2014;5:416-25.

2 Verma S, Madhu R. The great Indian epidemic of superficial dermatophytosis: An appraisal. *Indian J Dermatol* 2017;62:227-36.

3 Kumar S, Goyal A, Gupta YK. Abuse of topical corticosteroids in India: Concerns and the way forward. *J Pharmacol Pharmacother* 2016;7:7-15.

4 Saraswat A, Lahiri K, Chatterjee M, *et al*. Topical corticosteroid abuse on the face: A prospective, multicenter study of dermatology outpatients. *Indian J Dermatol Venereol Leprol* 2011;77:160-6.

5 Verma SB. Topical steroid misuse in India is harmful and out of control. *BMJ* 2015; 351:h6079.

6 Meena S, Gupta LK, Khare AK, *et al*. Topical corticosteroids abuse: A clinical study of cutaneous adverse effects. *Indian J Dermatol* 2017;62:675.

7 Mahar S, Mahajan K, Agarwal S, *et al*. Topical Corticosteroid Misuse: The Scenario in Patients Attending a Tertiary Care Hospital in New Delhi. *J Clin Diagn Res* 2016;10:FC16-FC20.

8 Verma SB. Sales, status, prescriptions and regulatory problems with topical steroids in India. *Indian J Dermatol Venereol Leprol* 2014;80:201-3.

9 Nagesh TS, Akhilesh A. Topical Steroid Awareness and Abuse: A Prospective Study among Dermatology Outpatients. *Indian Journal of Dermatology* 2016;61:618-621.

10 Dutta B, Rasul ES, Boro B. Clinico-epidemiological study of tinea incognito with microbiological correlation. *Indian J Dermatol Venereol Leprol* 2017;83:326-31.

11 Sharma R, Abrol S, Wani M. Misuse of topical corticosteroids on facial skin. A study of 200 patients. *Journal of Dermatological Case Reports* 2017;11:5-8.

12 Dey VK. Misuse of topical corticosteroids: A clinical study of adverse effects. *Indian Dermatol Online J* 2014;5:436–40.

13 Government of India, Census 2011. http://censusindia.gov.in

14 Sinha A, Kar S, Yadav N, Madke B. Prevalence of Topical Steroid Misuse Among Rural Masses. *Indian Journal of Dermatology*. 2016;61:119.

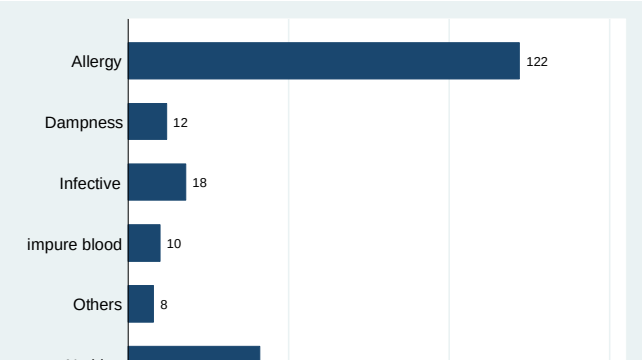
15 Coondoo A. Topical Corticosteroid Misuse: The Indian Scenario. *Indian Journal of Dermatology* 2014;59:451-455.

Figure legend

Fig. 1 Patients' perception of causes of their skin conditions

Total number of cases: 211

Fig 1.



BMJ Open

Magnitude, characteristics and consequences of topical steroid misuse in rural North India - an observational study among dermatology outpatients.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-032829.R1
Article Type:	Research
Date Submitted by the Author:	24-Dec-2019
Complete List of Authors:	Thomas, Molly; Herbertpur Christian Hospital Herbertpur, Dermatology Department, Wong, Celestine; Skin and Cancer Foundation Australia, Dermatology Anderson, Pam; University of Melbourne, Nossal Institute for Global Health Grills, Nathan; The University of Melbourne School of Population and Global Health, Nossal Institute for Global Health
Primary Subject Heading:	Dermatology
Secondary Subject Heading:	Public health
Keywords:	Topical steroid, misuse, Tinea, infective, rural

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Magnitude, characteristics and consequences of topical steroid misuse in rural North India - an observational study among dermatology outpatients.

Running title: Topical steroid misuse in rural North India

Authors: Molly Thomas[1], Celestine Wong[2], Pam Anderson[3], Nathan Grills[4]

1. Dermatology Department, Herbertpur Christian Hospital, Herbertpur P.O, Dehradun, Uttarakhand, India-248142.
2. Dermatology Department, Skin and Cancer Foundation Inc, 1/80 Drummond Street , Carlton Victoria 3053.
3. Nossal Institute for Global Health, School of Population and Global Health, University of Melbourne, Level 5, 333 Exhibition Street, Melbourne 3000, Australia.
4. Associate professor, Nossal Institute for Global Health, School of Population and Global Health, University of Melbourne, Level 5, 333 Exhibition Street, Melbourne 3000, Australia.

Corresponding author: Dr Molly Thomas, Herbertpur Christian Hospital, Herbertpur P.O, Dehradun, Uttarakhand, India-248142

Telephone number- +91 9897532821

Email ID- vijuandmolly@gmail.com

Word Count: 3,528

ABSTRACT

Introduction: Current evidence indicates an alarming increase in topical steroid (TS) misuse in India. Data regarding the magnitude and characteristics of this problem in rural India, where 68% of the population resides, are insufficient. This study analyses the magnitude, causes, characteristics and consequences of TS misuse in rural India. It also examines the association between TS misuse and patients' perception of skin disease.

Methods: A mixed method observational study was conducted among the attendees of the dermatology outpatient department in a rural North Indian hospital. Those with a history of TS misuse were analysed for behaviour patterns and outcome.

Results: Out of 723 patients, 213 (29.2%) misused TS. Clobetasol propionate (58.2%) was most commonly misused. Seventy brands of inappropriate fixed drug combination steroid creams were recovered from the patients. Pharmacists and local healers together contributed to 78% of the sources for steroid misuse. Almost 58% of participants perceived their skin conditions to be allergic reactions to food, when in fact 70.1% were tinea, 10% scabies and 9% acne. Eighty percent of respondents having tinea had tinea incognito and 97% had extensive lesions. Eighty-five percent of participants with scabies had atypical lesions and 80% with acne had steroid rosacea or aggravation of acne. The median expenditure incurred in purchasing these potentially harmful steroid creams was Rs1,000 (US$14.1, equivalent to 3 days' wages of a labourer).

Conclusion: Steroid misuse is a problem of epidemic proportion in rural India. This practice is changing the profile of many common and infective skin conditions, which portends diagnostic dilemmas and therapeutic challenges for clinicians. Misconceptions about skin

disease drives the public to seek "quick fixes" from non-allopathic providers who have unrestricted access to potent steroids. There is an urgent need to tighten regulatory controls over the manufacturing, sale and prescription of irrational TS combinations.

Keywords: Topical steroid, misuse, Tinea, infective, rural

ARTICLE SUMMARY

Strengths and limitations of this study

- This mixed methods study is one of the few studies which focuses on TS misuse in rural India.
- A mixed method of structured questionnaire supplemented with qualitative interviews was used to assess TS misuse.
- The development of research objectives was informed by patients who had used topical steroids particularly those who had experienced side effects.
- The frequency of misuse may be underestimated due to the difficulty in identifying corticosteroids by respondents.
- Generalisability is limited by the sample being restricted to one outpatient department in one location.

INTRODUCTION

The usefulness of Topical steroids (TS), the most widely used therapeutic agents in dermatology, has become a double edged sword with increasing prevalence of misuse, leading to disastrous consequences.[1, 2] Of concern is the unprecedented increase in fungal infections as well as the emergence of resistant dermatophytosis in India, most likely due to unnecessary use of Fixed Drug Combination (FDC) creams containing steroid.[2] Children are often victims of topical steroid misuse as they are more vulnerable to the systemic effects of potent topical corticosteroids as well as to the spread of infections.[2] Non-medical use of TS in fairness creams has led to increasing occurrences of a condition which has been described as topical steroid damaged face (TSDF).[3-5] Pharmacists and often qualified medical practitioners readily prescribe and dispense potent topical steroids given that they provide dramatic symptomatic relief. The pharmaceutical industry also contributes to the problem as they manufacture and promote inappropriate FDC containing potent TS in combination with antifungals and antibacterials. This problem is further compounded by the unregulated over-the- counter (OTC) supply and unrestricted sale of TS. Public and professional ignorance, legal ambiguity, and government inaction create a serious problem whereby FDC creams are used as a panacea for all skin problems.[6] In India, the unprecedented increase in sales of these "steroid cocktails" by an alarming 26% in 2014-15 is a reflection of the public appeal of these dangerous combinations.[5,7] This is especially unfortunate, given these medications are not only ineffective in curing but cause more harm than good. In addition, this unnecessary expenditure can cause an economic drain impoverishing many who have scarce or no financial reserve. Though efforts are being made to draw attention to the multiple factors behind this problem in India,[4,5,7,8] it remains largely under researched in rural areas. Earlier studies were conducted in the urban setting of tertiary care hospitals with emphasis on TS usage on

face.[7-12] However, no data is available to understand the impact of this epidemic in the rural areas where 68.84% of the Indian population dwells.[13]

This study analyses the magnitude, causes, characteristics, consequences, and economic impact of topical steroid misuse in a rural hospital in North India. We also seek to better understand the relation between TS misuse and patients' perception of skin disease.

MATERIALS AND METHODS

A mixed-methods observational study of patients was conducted over a period of 3 months (March 2016 to May 2016) amongst all new patients attending the dermatology outpatient department of a secondary level hospital, located in a rural part of Uttarakhand, North India.

Our data at Herbertpur Christian Hospital shows an estimated figure of 16% for steroid abuse in ring worm (Tinea) infections. Using this as an estimated prevalence of topical steroid misuse and a margin of error of 5% and a 95% confidence interval, the sample size required was approximately 160.

We undertook the study over a long enough time period (a quarter) in order to account for week-on-week variation and to smooth out any effects of unique events such as festivals, strikes and elections. Male and female patients of all ages who fulfilled the following criteria were recruited:

1. Having a skin condition for which topical steroid is contraindicated i.e. acne, bacterial, viral, fungal or parasitic cutaneous infections such as tinea, furuncle, scabies etc.
2. History of topical steroid usage for that condition.

Topical steroids include either single ingredient steroid products or a combination of topical steroid molecule with antibiotics or antifungals. The patients were recruited following a clinical examination by the consultant dermatologist, after obtaining an informed written consent. Parents were interviewed for the purpose of gathering data regarding their children. Using a mixed method of structured questionnaire supplemented with qualitative interviews, patients were assessed for misuse of TS. Taking this information into account, a trained clinician researcher then made a decision as what constituted misuse based on inappropriate indication, prolonged duration, unnecessary use of potent steroids, expense incurred and side effects. All patients with tinea were subjected to direct microscopy and those who were tested negative were added only after positive response to antifungal therapy. Ethics approval was obtained from the Institutional Ethics Committee of the Emmanuel Hospital Association, New Delhi (Protocol No.129). The patients were also counselled regarding dangers of TS misuse and appropriate treatment was given for side effects, when present.

To minimise bias in reporting steroid use, we required patients to provide the actual tubes where available. Survey answers were also verified by a combination of clinical examination, interview and structured questionnaire.

Patient and Public Involvement

The results of the study informed the production of a video and patient information handout to the communities from which the patients came. While patients were not involved in the recruitment to and the conduct of the present study, the development of research objectives was informed by patients using topical steroid, particularly those who had experienced side effects. The study was piloted to get feedback from patients on the formation of the questions .

Data analysis

Data analysis was done using Stata 14 (StataCorp, Texas, U.S.). Major variables of interest were dermatological conditions for which steroids were misused, types and quantities of steroids used, sources of prescriptions, adverse effects of misusing steroids, expenditure incurred and patients' perception of the disease. All the original variables were categorical, except number of tubes, duration of TS misuse and expenditure on TS, which were converted from numeric to categorical data for analysis. Data were presented as percentage with the exceptions of age and expenditure which were expressed in median (Q1-Q3). For multiple-response questions (side-effects, types and sources of topical steroids), we used MRTAB (Ben Jann & Hilde Schaeper, 2004) to generate simple frequencies. To test the associations between major demographic variables and profile of misuse, we performed Chi-squared test with the level of significance set at 0.05.

RESULTS

Demographics

Of the 723 new patients seen in the dermatology OPD, 213 (29.5%, 95% CI: 26; 32.6) had a history of topical steroid misuse and were eligible for the study (Fig.1). Two did not give written consent to be involved leaving 211 patients. Nearly 60% were male and the median age was 30 years. Fifty-five percent of the cases were in the 15-34 years age group. Those having only primary education seemed to be most affected by topical steroid misuse (Table 1).

Table 1. Demographic details of patients who had a history of topical steroid misuse

	No. of observations	Percentage
Age (yrs)		
up to 14	11	5.2
15-24	56	26.5
25-34	61	28.9
35-44	44	20.9
45 and over	39	18.5
Gender		
Male	124	58.8
Female	87	41.2
Education		
Illiterate	37	17.5
Primary	66	31.3
*High school	50	23.7
College	10	4.7
*Graduate	48	22.8

*Included 1 imputed value based on father's highest level of education
n=211

Profile of steroid misuse

Dermatological conditions mismanaged with steroids:

The most common condition for which steroids were misused was tinea (70.1%), followed by scabies (10%) and acne (9%). A small number had two concomitant diseases such as tinea with scabies, tinea with acne or acne with scabies. Other conditions for which steroid was misused were vulval candidiasis, herpes genitalis, tinea versicolor, furuncle and melasma. In the case of melasma, for which MILD potency steroids admix with hydroquinone and retinoids are used, patient misuses consisted of inappropriate combinations of potent steroids with antifungal and antibacterial creams extended use.

Types of steroid formulations used

Fixed dose combinations containing either a triple or quadruple combination of antifungal, antibacterial and steroid were the commonly used creams. Quadruple combinations are steroid creams which contain 4 ingredients i.e. 2 antibiotics 'ofloxacin and ornidazole' or

others with 4 different ingredients. Such combinations have no clinical justification. Although most of the participants (66%) used only one class of TS, 32% used two classes and 3% used three classes. The most misused topical steroid (Table 2) was clobetasol propionate (58.2% of 287 responses). About 70 different creams (Table 3), produced by a myriad of pharmaceutical companies were recovered from the patients during the study. As shown in table 4, the ten most misused combinations creams have very similar compositions although packaged under different names and appearances. Patients often think they are prescribed a new cream at every visit while in fact they are using one with the same molecule, most often clobetasol propionate (class I potency), thereby perpetuating the side effects.

Twenty-five percent of respondents reported concomitant use of either oral steroids (OS) or injectable steroids or both along with the TS. Of this, 39.6% had concomitant use of oral steroids, 37.7% used both oral and injectable steroid and 22.7% used injectables along with TS. These patients reported that the OS were easily procured over the counter. Use of injectable steroid was found to be associated with highest level of education (p=0.04) and were obtained from local healers.

Table 2. Types of topical steroid misused

Steroid molecule	No. of observations	Percentage
Clobetasol propionate	167	58.2
Beclomethasone/Betamethasone	91	31.7
Fluocinolone	17	5.9
Mometasone	11	3.8
Clobetasone	1	0.4

Multiple responses were allowed in this question. Percentages were based on total number of responses

Total no. of response=287

Total no. of cases = 211

Table 3 List of 70 different brand creams, many having same composition of steroid, antibiotic and anti-fungal molecules, recovered from patients during the study

Brand name	Steroid	Antibiotic	Antifungal
Panderm+, Terderm+, Orniderm, Nikderm+, Oltef-NF, Laboderm-oc, Terbinaforce+, Terbicad, Fourderm, DermikemOC, Pardum+, Castor-NF, Totalderm+, Terogood, Terogood, Orkid4, Sarvocin-CT, Orkaderm, Soltex, Bifine-plus, Dermek-TC, Turgoderm-oc, Tocoderm+, Onflox-TC,	Clobetasol propionate	Ofloxacin, Ornidazole	Terbinafine Hydrochloride
Dermacin-k5, Amitone-5, Clotebate-GM, Clobezine-CM, Tecderm-KT, Dermiford, Dermifrench-KT, Dermiford-K5	Clobetasol propionate	Iodochlorhydroxyquinoline, Gentamicin	Ketoconazole, tolnaftate
Clostar-GM, Ring-out+, Clobriv-MG, Clobeta GM, Adoderm-MN, Zincodem-GM, Candid 3D, Iobate, Neo Clobenate-GM, Clobenate-GM, Lucobet-GM, Cosvate-GM	Clobetasol, propionate	Neomycin sulphate	Clotrimazole
Medisalic , Clorap-s, Lozivate-MF, Lozivate	Clobetasol Propionate & salicylic acid		
Lobate GM	Clobetasol Propionate	Neomycin sulphate	Miconazole
Unikderm	Clobetasol proprionate	Gentamicin	ketoconazole
EVzole	Beclomethasone dipropionate	Neomycin sulphate	Clotrimazole
Betnovate-C	Betamethasone valerate	Clioquinol	Chlorocresol
Betnovate-N,	Betamethasone valerate	Neomycin sulphate	Chlorocresol
Nuforce-GM, Betamil, Quadriderm RF, Canditas-BG, Lupiderm-GM, Onabet-B, Quadriderm, Surfaz-SN, Zenoderm, CBN,	Beclomethasone dipropionate	Neomycin sulphate	Clotrimazole
Sertamide-B	Beclomethasone dipropionate		Sertaconazole
Candid -B	Beclomethasone		Clotrimazole
Cipro-CF, Ceflox-CF,	Fluocinolone acitonide	Ciprofloxacin, Neomycin sulphate	Clotrimazole
Zole-F	Fluocinolone acitonide		Miconazole
Flucort-H	Fluocinolone acitonide		
Sure-KT	Clobetasone	Gentamicin	ketoconazole
Aluderm	Clobetasol proprionate	Ofloxacin	Ornidazole

Table 4. Ten most commonly used fixed drug combination creams containing steroid

Brand name	Composition	No. of Responses(%)
Neoclobenate GM	Clobetasol propionate,Miconazole,Neomycin	55 (17.7%)
Castor NF	Clobetasol propionate, Ofloxacin, Ornidazole, Terbinafine hydrochloride	43 (13.8%)
Quadriderm	Beclomethasone dipropionate, Clotrimazole, Neomycin	32 (10.3%)
Betnovate-N	Betamethasone valerate, Neomycin	30 (9.7%)
Dermiford	Ketoconazole, iodoxychlorhydroquinoline, Tolnaftate, Genatamicin and Clobetasol propionate	30 (9.7%)
Betnovate-C	Betamethasone valerate, Clotrimazole	26 (8.4%)
Dermikem OC	Clobetasol propionate, Ofloxacin, Ornidazole, Terbinafine hydrochloride	25 (8.0%)
Lobate GM	Clobetasol propionate,Miconazole nitrate,Neomycin sulphate	25 (8.0%)
CBN	Beclomethasone dipropionate, Clotrimazole, Neomycin sulphate, Chlorocresol	25 (8.0%)
Terbinaforce plus	Clobetasol propionate, Ofloxacin, Ornidazole, Terbinafine hydrochloride	20 (6.4%)

Sources of steroid procurement or prescription and steroid usage patterns

More than half of respondents (65.9%) indicated one single source for procurement of TS, most often being pharmacists (56.8%). Patients reported that pharmacists freely dispensed TS for any complaints of itching, provided a quick remedy and avoided cumbersome procedures required in a hospital. There was statistically significant gender difference (χ^2 =7.1; p=0.008) in relation to steroid procurement from non-allopathic providers, suggesting that females were less likely to approach medical practitioners for treating their skin infections.

Extent of use and cost of usage

There was a wide range in the number of tubes (mostly 15g, a few are 20g and some 25g) used by the respondents. Twenty-one percent (44) used one tube while about three percent

(7) used more than 100 tubes. The majority (63%) used topical steroid combinations for less than 6 months. Approximately 16% of respondents used TS for over a year. The pattern of steroid usage was erratic, varying from using either one tube intermittently over a few months or most often in combination with oral and/or injectable steroids, or using more than 100 tubes continuously.

Expenditure on TS ranged from US$0.5 to more than US$2,500. The median expenditure was US$20 (Q1:US$4; Q3:US$80), equivalent to 3 days' wages of a daily labourer. These FDC creams are available at lower cost than single ingredient antifungal creams. The plain antifungal creams (available as 30gm tubes) are 3 times more costly than the FDC creams containing potent steroid and antifungal combinations available in smaller sizes. Due to the low cost, the pharmacists stock the FDC creams as they have quick turn over while plain antifungal tubes are not stocked and are hence hard to procure. It would benefit the community significantly if the government could supply plain antifungal creams at economic prices.

Adverse effects of topical and systemic steroid misuse

Table 5 shows the adverse effects reported by 204 respondents.

A) *Effect on Dermatological conditions* – ninety-seven percent of patients with steroid modified tinea had extension of tinea to non-flexural areas of body i.e. face, ears, wrists, entire trunk, dorsum of hands and genitalia in males. Eighty percent had tinea incognito, a term used when appearance of tinea is varied or modified from the normal as a result of steroid misuse. This presented with atypical clinical signs like lichenification, eczematisation, large geographic patterns, pseudoimbricata, arciform, pustular and polycyclic lesions as well as lesions mimicking other diseases like psoriasis, pityriasis

rosea, lichen planus, and seborrheic dermatitis. Three percent of tinea infection had localised exacerbation with pustulations. Fifty-eight percent of patients with acne developed features of either steroid rosacea, pustular or nodulocystic acne. Ninety-five percent of patients with scabies had generalized papules instead of the characteristics areas making it difficult to recognize (scabies incognito).

B) Other effects

i) Striae – six patients (2.5%) had striae and these were very extensive over the groins, inner thighs, lateral sides of abdomen and axillae. Three of these patients concomitantly used oral and/or injectable steroids.

ii) Cushingoid facies – eleven patients (4.6%) showed Cushingoid features mainly characterised by facial puffiness. Seven of them concomitantly used oral and/or injectable steroids.

iv) Hypertension – eight respondents (3.3%) had new onset hypertension. Three of these patients concomitantly used oral and/or injectable steroids.

v) Diabetes – five individuals (2.1%) had new onset diabetes. Four of them concomitantly used oral and/or injectable steroids.

Table 5. Adverse effects reported by participants

	Frequency	Percent of responses	Percent of cases
Tinea extension	145	60.17	71.08
Tinea exacerbation	5	2.07	2.45
Scabies extension	20	8.30	9.8
Scabies exacerbation	1	0.41	0.49
Acne extension (steroid rosacea)	11	4.56	5.39
Acne exacerbation	9	3.73	4.41
Cushingoid*	11	4.56	5.39

Hypertension*	8	3.32	3.92
Striae*	6	2.49	2.94
Weight gain*	6	2.49	2.94
Diabetes*	5	2.07	2.45
Other exacerbation	5	2.07	2.45
Other complications	9	3.73	4.41

*Patients used systematic steroids in addition to topical steroids.
Multiple responses were allowed in this question. Percentages were based on total number of responses
Total no. of response=241
Total no. of cases = 204

Patients' perception of the disease

The majority (57.8%) considered their itchy skin condition or eruptions to be an allergic response to some food or drink which heats up the body (Fig.2). About nine percent thought it was infective and approximately six percent related it to dampness. Nineteen percent did not know the cause. Five percent believed that their skin condition was due to impure blood. Some resorted to tonics such as "Koon safi" (blood purifier) and even "blood purification". One respondent regularly withdrew a small quantity of his blood, mixed it with triamcinolone and injected the mixture back into his body. Other explanations (3.8%) for their skin conditions were bowel irregularities, heredity, unclean water and few even considered it to be due to evil spirits.

DISCUSSION

Our study found that nearly 1/3 of new dermatology outpatients had misused TS and clobetasol propionate was the most common steroid misused. Tinea incognito and extension of lesions

were seen in majority of patients with dermatophytosis. Most of the TS misusers in our study did not know the real cause of their skin disease. Nearly 80% of the patients received their TS from pharmacists or local healers.

This study demonstrates that TS misuse is a significant public health issue in rural India, with three out of ten new dermatology outpatients using topical steroids inappropriately. This result is much higher than those found in urban studies in India where prevalence of misuse was 11.8% in Delhi [8] and 15% in a Pan Indian urban study.[4] Our study demonstrated a male preponderance in contrast to the Pan Indian study which showed a female preponderance.[4] This is likely because the study was restricted to facial steroid usage. The average age of usage in our study was 32 years old which was similar to findings from the studies in urban areas of India.[4, 8]

Tinea was by far the most common indication for steroid misuse in our study followed by acne and scabies. This concurs with some recent studies [7, 8] but other studies in India showed greatest TS use for acne [9] and skin lightening.[12] In another study by Saraswat A et al, TS were most commonly used for both skin lightening and acne.[4] This difference in usage patterns could be due to infections like tinea being more prevalent in rural areas and skin colour being of more concern in urban areas.[14] This disparity could also be due to the recent spurt in dermatophytosis in India as a whole with its burden being felt in rural India as well.[15] The florid signs and symptoms caused by Trichophyton mentagrophyes, an inflammatory zoophilic species, which has emerged as a major causative organism for this epidemic, could be a reason for the rural poor to seek quick relief with cheap and easily accessible options like FDC containing TS.[16]

For health care providers, topical steroid abuse can make tinea difficult to distinguish from other common diseases like eczema, contact dermatitis and psoriasis and therefore increases

misdiagnosis, mistreatment and even increased morbidity.[2] Tinea incognito and extension of lesions were seen in majority of patients with dermatophytosis because steroids tend to alter the characteristic "ring or annular" lesion.[2, 10] These cases can range from vague erythematous plaques to lesions with oozing, prominent scaling, pustulation to large geographic lesions mimicking diseases like psoriasis. As seen in our study, it can be difficult for even dermatologists to accurately recognize steroid modified tinea. We also observed an increased occurrence in genital tinea, which was once rare. There is a need to educate the medical professionals about the wide variation in clinical presentation of steroid modified tinea to enable proper diagnosis.

TS abuse in scabies, second after tinea in our study, can cause scaly and widespread lesions that are unrecognizable as scabies. Scabies incognito or steroid modified scabies can be a serious public health problem since it is very contagious and diagnostic difficulty can increase the prevalence of scabies. Acne, the third most prevalent reason for steroid misuse, also leads to increased possibilities for Topical Steroid Damaged Face and disfiguring sequelae of acne.

In our study, nearly half of the patients received their TS from pharmacists who had variable training. Likewise, in studies from other parts of the sub-continent, pharmacists were the most common source of inappropriate steroid use.[4, 10, 17] They often function as doctors, especially where the local health services are underdeveloped or unavailable. Many people also seek treatment from charlatans and AYUSH (Ayurvedic, Yoga and Naturopathy, Unani, Siddha and Homeopathy) practitioners, given the rarity of dermatologists and MBBS trained doctors in rural areas. AYUSH account for 31% of the topical steroid misuse in our study. This is of great concern since it is illegal for a practitioner of alternative medicine to prescribe modern medicines like TS. Nevertheless, salespersons are still able to market TS to AYUSH practitioners.[10] Unfortunately, general physicians and even some dermatologists are also responsible for prescribing TS unnecessarily. This indicates the need for training of

medical/paramedical personnel about the judicious use of topical corticosteroids and their potentially serious side effects. Saraswat's study on facial steroid use found that poor availability of physicians in rural areas was associated with non-physicians being likely to prescribe TS.[4]

Our study found that clobetasol propionate - the most potent topical steroid - was the most common steroid misused. Betamethasone valerate was the most widely misused steroid in urban studies.[4, 8, 9] This is consistent with Saraswat et al who noted that patients from rural areas tended to use potent topical steroids.[4] Use of injectable steroids in our study was found to be associated with the highest education level ($p=0.04$). Most of those who used oral and injectable steroids concomitantly with TS had either no education or only primary schooling. This could reflect their unwavering trust in the local healers.

This study also explored patient perception of their skin disease. Eighty-six percent of respondents either misunderstood or did not know the cause of their skin disease. All pruritic symptoms or eruptions were perceived as allergic responses to hot, spicy food or impure blood. This wrong perception shifts the attention from common hygienic measures necessary to respond to infective conditions like tinea and scabies, to unrelated factors like abstinence from certain food, unwarranted blood investigations and blood purification. An important reason for patients seeking primary recourse from nonmedical personnel could be lack of proper understanding regarding aetiology of their illness and lack of access to quality allopathy.[18]

Our study is consistent with the observations that factors leading to misuse of TS may occur at various stages during its journey from the factory to the skin.[19] The plethora of TS combinations recovered from the patients clearly indicates the ease of purchase and the unsubstantiated claims of TS combinations promoted by pharmaceutical companies. Despite the serious adverse effects, these drugs are manufactured and sold without appropriate

regulatory control in India. Existing regulations pertinent to the prescriptions of these drugs are far from comprehensive. Although steroids have been included under Schedule H drugs, which requires proper prescription, inappropriate FDCs containing potent TS in combinations with antifungals and antibacterials are not on the same list.[20] Furthermore, the enforcement of the regulation regarding prescriptions of steroids at the ground level is rare.[2] For pharmacists and local healers, FDC creams are prescribed as one stop answer to all skin conditions, regardless of the aetiology of the disease (whether it is a bacterial or fungal infection or inflammation). Unfortunately, many clinicians and occasionally even dermatologists also promote these multidrug combinations. At the consumer level, we found little awareness about the adverse effects. To address this, stringent regulations on the manufacture, sale and marketing of steroid cocktail creams are urgently required.

Limitations

It was difficult for many patients to understand what TS were until they were shown samples. However, flooding of the market with innumerable brands containing topical steroids made it difficult to show a sample of all brands. This could have led to under-estimation of the frequency of the malpractice in our study.

Recollection of duration and quantity of use was difficult for patients who have used topical steroids over a long period. This may also have led to under or over estimation of the total expenditure on topical steroids. However, since the majority of participants used TS for less than 6 months, such potential inaccuracies were likely to be minimal.

Generalisability of our study is limited by the sample being restricted to one outpatient department in one location. To capture the true magnitude of the multifaceted problem of topical steroid misuse in rural areas, a multicentric community study across the country is recommended.

CONCLUSIONS

The epidemic of steroid modified dermatoses in rural India due to injudicious use of topical steroids is caused by multifaceted factors. Concerted, multipronged actions are needed to address professional and public ignorance, political apathy and profit incentives for drug companies and pharmacists. Continuous education of clinicians and traditional practitioners to recognize the current altered and 'unrecognizable' steroid modified dermatoses as well as the potentially harmful effects of TS is also required. Furthermore, there is a pressing need to increase the availability of family physicians, or equivalent, in rural areas where people go to whoever is local and affordable. In addition, drug control agencies should ensure strict regulation of TS sale and prohibit manufacturing of steroid cocktails. The ministry of Health and Welfare could helpfully create awareness through social media and advertisements to warn people about the danger of TS misuse.

Funding sources – This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of Interests: None to be declared

Data sharing statement: Data are available upon reasonable request by emailing to corresponding author (Dr Molly Thomas: vijuandmolly@gmail.com). No additional data are available for this study.

Authors' contributions:

Dr Molly Thomas: principal investigator, contributed to the study design and methods, interpreted the data and drafted the manuscript.

Dr Nathan Grills: developed concept of research, interpreted the data, reviewed, edited and approved the final manuscript

Dr Celestine Wong: contributed to the study design and methods, reviewed, edited and approved the final manuscript

Pam Anderson: conducted statistical analysis, summarised and interpreted findings, reviewed, edited and approved the final manuscript

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in BMJ Open and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

References

1 Coondoo A, Phiske M, Verma S, *et al*. Side-effects of topical steroids: A long overdue revisit. *Indian Dermatol Online J* 2014;5:416-25.

2 Verma S, Madhu R. The great Indian epidemic of superficial dermatophytosis: An appraisal. *Indian J Dermatol* 2017;62:227-36.

3 Kumar S, Goyal A, Gupta YK. Abuse of topical corticosteroids in India: Concerns and the way forward. *J Pharmacol Pharmacother* 2016;7:7-15.

4 Saraswat A, Lahiri K, Chatterjee M, *et al*. Topical corticosteroid abuse on the face: A prospective, multicenter study of dermatology outpatients. *Indian J Dermatol Venereol Leprol* 2011;77:160-6.

5 Jha AK, Sinha R, Prasad S. Misuse of topical corticosteroids on the face: A cross-sectional study among dermatology outpatients. *Indian Dermatol Online J* 2016;7:259-63.

6 Verma SB. Topical steroid misuse in India is harmful and out of control. *BMJ* 2015; 351:h6079.

7 Meena S, Gupta LK, Khare AK, *et al*. Topical corticosteroids abuse: A clinical study of cutaneous adverse effects. *Indian J Dermatol* 2017;62:675.

8 Mahar S, Mahajan K, Agarwal S, *et al*. Topical Corticosteroid Misuse: The Scenario in Patients Attending a Tertiary Care Hospital in New Delhi. *J Clin Diagn Res* 2016;10:FC16-FC20.

9 Nagesh TS, Akhilesh A. Topical Steroid Awareness and Abuse: A Prospective Study among Dermatology Outpatients. *Indian J Dermatol* 2016;61:618-621.

10 Dutta B, Rasul ES, Boro B. Clinico-epidemiological study of tinea incognito with microbiological correlation. *Indian J Dermatol Venereol Leprol* 2017;83:326-31.

11 Sharma R, Abrol S, Wani M. Misuse of topical corticosteroids on facial skin. A study of 200 patients. *J Dermatol Case Rep* 2017;11:5-8.

12 Dey VK. Misuse of topical corticosteroids: A clinical study of adverse effects. *Indian Dermatol Online J* 2014;5:436-40.

13 Government of India, Census 2011. http://censusindia.gov.in

14 Wong C, Wong S, Tang H, *et al*. Use of skin-lightening products among outpatient attendees in a North Indian Hospital. *Indian J Public Health* 2017;61:137-40.

15 Panda S, Verma S. The menace of dermatophytosis in India: The evidence that we need. *Indian J Dermatol Venereol Leprol* 2017;83:281-4.

16 Nenoff P, Verma SB, Vasani R, *et al*. The current Indian epidemic of superficial dermatophytosis due to Trichophyton mentagrophytes—A molecular study. *Mycoses* 2019;00:1–21.

17 Sinha A, Kar S, Yadav N, Madke B. Prevalence of Topical Steroid Misuse Among Rural Masses. *Indian J Dermatol* 2016;61:119.

18 Balaji A, Velavan J, Raji B, *et al.* A Multicentric Cross-sectional Study to Characterise the Scale and Impact of Polypharmacy in Rural Indian Communities, Conducted as Part of Health Workers Training. *J Family Med Prim Care* 2019;8:2234-2241

19 Coondoo A. Topical Corticosteroid Misuse: The Indian Scenario. *Indian J Dermatol* 2014;59:451-455.

20 Verma SB. Sales, status, prescriptions and regulatory problems with topical steroids in India. *Indian J Dermatol Venereol Leprol* 2014;80:201-3.

Figure legend

Fig. 1 Patient recruitment flow chart

Fig. 2 Patients' perception of causes of their skin conditions

Total number of cases: 211

Fig. 1

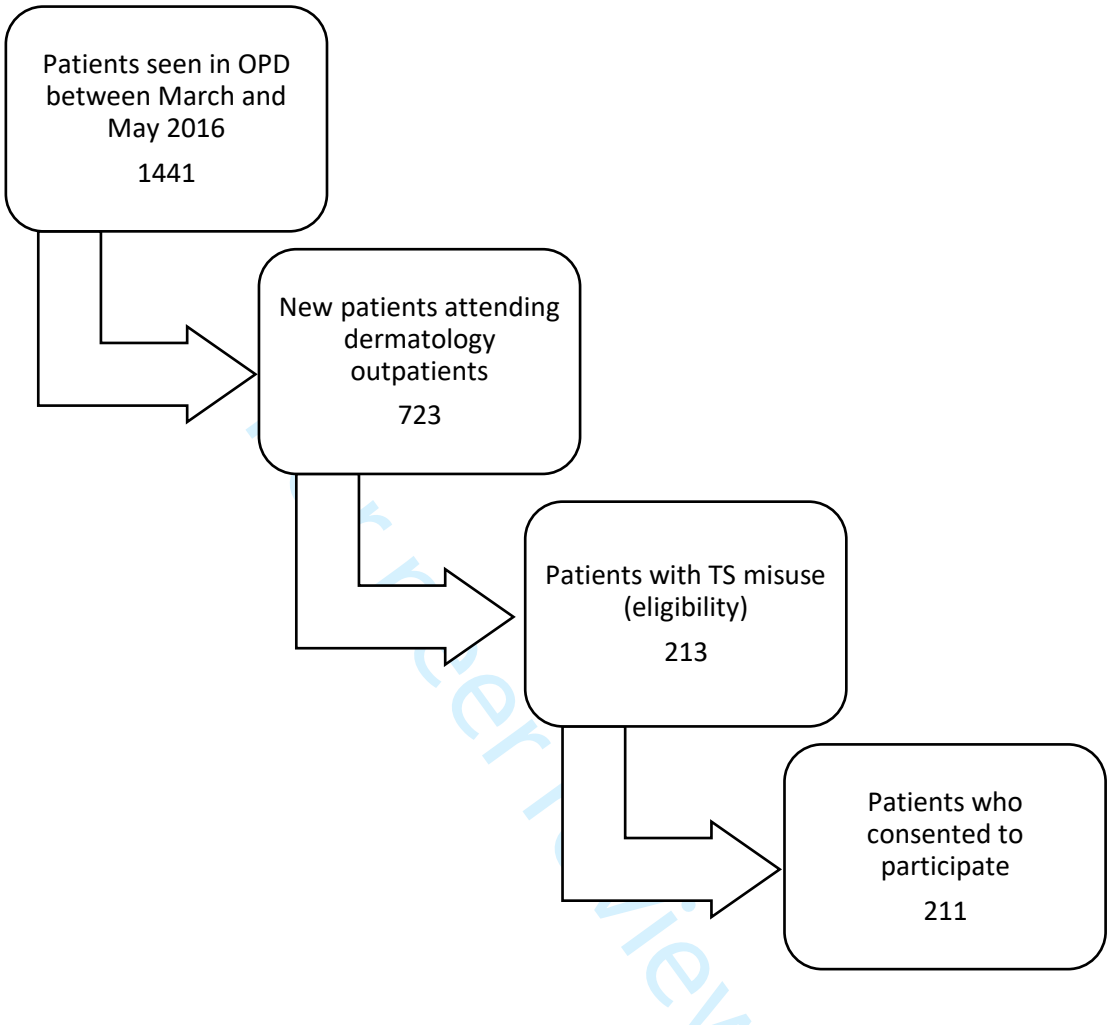
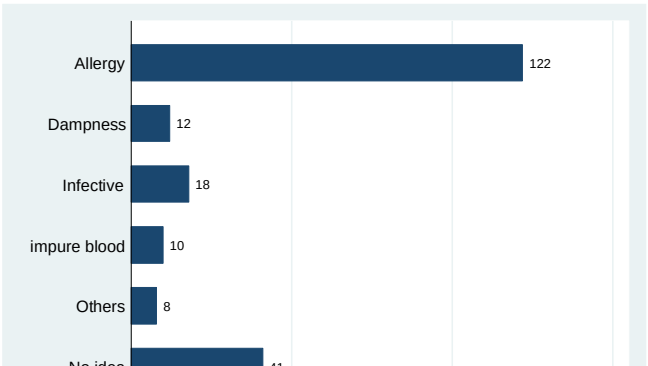


Fig 2.



STROBE Statement

Manuscript title: Magnitude, characteristics and consequences of topical steroid misuse in rural North India - an observational study among dermatology outpatients.
Authors: Molly Thomas, Celestine Wong, Pam Anderson, Nathan Grills

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page, lines 1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	p. 2, line 1 – p.3, line 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction, p.4, line 3- p.5, line 2
Objectives	3	State specific objectives, including any prespecified hypotheses	p.5, lines 3-5 (*this is an observational study)
Methods			
Study design	4	Present key elements of study design early in the paper	p.5, lines 8-21 (Materials and Methods)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p.5,line 8 – p.6, line 13 (Materials and Methods)
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	p5, lines 17-21;
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	p.7, lines 2-12 (Materials and Methods-Data analysis)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Variables of interests (see Data analysis, p.7, lines 2-10)
Bias	9	Describe any efforts to address potential sources of bias	p.6 Lines 14 -16
Study size	10	Explain how the study size was arrived at	p.5, lines 11-14.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	p.7, lines 2-12 (Materials & methods- Data analysis)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	p.7, lines 2-12 (Materials & methods- Data analysis)
		(*b*) Describe any methods used to examine	NA

		subgroups and interactions	
		(*c*) Explain how missing data were addressed	No missing data
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	p. 7 (Fig. 1 Patient recruitment flow chart)
		(b) Give reasons for non-participation at each stage	See fig. 1 (flow chart) on p.7
		(c) Consider use of a flow diagram	Yes, see fig. 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P.8 (Table 1)
		(b) Indicate number of participants with missing data for each variable of interest	No missing data.
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p.7 line 16 (95% CI) (this study mainly presented descriptive statistics)
		(*b*) Report category boundaries when continuous variables were categorized	p.11, line 14 – p.12, line 6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	p.14, line 20- p.15, line 3 (Discussion)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p.18, lines 13-24 (Limitations, with recommendations for future studies)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p. 15, line 4 – p.17, line 21
Generalisability	21	Discuss the generalisability (external validity) of the study results	We recognised this as our limitation (p.18, lines 21-24)

Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p.20, lines 1-2 (Declaration of no funding sources)

BMJ Open

Magnitude, characteristics and consequences of topical steroid misuse in rural North India - an observational study among dermatology outpatients.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-032829.R2
Article Type:	Research
Date Submitted by the Author:	24-Jan-2020
Complete List of Authors:	Thomas, Molly; Herbertpur Christian Hospital Herbertpur, Dermatology Department, Wong, Celestine; Skin and Cancer Foundation Australia, Dermatology Anderson, Pam; University of Melbourne, Nossal Institute for Global Health Grills, Nathan; The University of Melbourne School of Population and Global Health, Nossal Institute for Global Health
Primary Subject Heading:	Dermatology
Secondary Subject Heading:	Public health
Keywords:	Topical steroid, misuse, Tinea, infective, rural

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

Magnitude, characteristics and consequences of topical steroid misuse in rural North India - an observational study among dermatology outpatients.

Running title: topical steroid misuse in rural North India

Authors: Molly Thomas[1], Celestine Wong[2], Pam Anderson[3], Nathan Grills[4]

1. Dermatology Department, Herbertpur Christian Hospital, Herbertpur P.O, Dehradun, Uttarakhand, India-248142.
2. Dermatology Department, Skin and Cancer Foundation Inc, 1/80 Drummond Street , Carlton Victoria 3053.
3. Nossal Institute for Global Health, School of Population and Global Health, University of Melbourne, Level 5, 333 Exhibition Street, Melbourne 3000, Australia.
4. Associate professor, Nossal Institute for Global Health, School of Population and Global Health, University of Melbourne, Level 5, 333 Exhibition Street, Melbourne 3000, Australia.

Corresponding author: Dr Molly Thomas, Herbertpur Christian Hospital, Herbertpur P.O, Dehradun, Uttarakhand, India-248142

Telephone number- +91 9897532821

Email ID- vijuandmolly@gmail.com

Word Count: 3,528

ABSTRACT

Introduction: Current evidence indicates an alarming increase in topical steroid (TS) misuse in India. Data regarding the magnitude and characteristics of this problem in rural India, where 68% of the population resides, are insufficient. This study analyses the magnitude, causes, characteristics and consequences of TS misuse in rural India. It also examines the association between TS misuse and patients' perception of skin disease.

Methods: A mixed method observational study was conducted among the attendees of the dermatology outpatient department in a rural North Indian hospital. Those with a history of TS misuse were analysed for behaviour patterns and outcome.

Results: Out of 723 patients, 213 (29.2%) misused TS. Clobetasol propionate (58.2%) was most commonly misused. Seventy brands of inappropriate fixed drug combination steroid creams were recovered from the patients. Pharmacists and local healers together contributed to 78% of the sources for steroid misuse. Almost 58% of participants perceived their skin conditions to be allergic reactions to food, when in fact 70.1% were tinea, 10% scabies and 9% acne. Eighty percent of respondents having tinea had tinea incognito and 97% had extensive lesions. Eighty-five percent of participants with scabies had atypical lesions and 80% with acne had steroid rosacea or aggravation of acne. The median expenditure incurred in purchasing these potentially harmful steroid creams was Rs1,000 (US$14.1, equivalent to 3 days' wages of a labourer).

Conclusion: Steroid misuse is a problem of epidemic proportion in rural India. This practice is changing the profile of many common and infective skin conditions, which portends diagnostic dilemmas and therapeutic challenges for clinicians. Misconceptions about skin

disease drives the public to seek "quick fixes" from non-allopathic providers who have unrestricted access to potent steroids. There is an urgent need to tighten regulatory controls over the manufacturing, sale and prescription of irrational TS combinations.

Keywords: Topical steroid, misuse, Tinea, infective, rural

ARTICLE SUMMARY

Strengths and limitations of this study

- This mixed methods study is one of the few studies which focuses on TS misuse in rural India.
- A mixed method of structured questionnaire supplemented with qualitative interviews was used to assess TS misuse.
- The development of research objectives was informed by patients who had used topical steroids particularly those who had experienced side effects.
- The frequency of misuse may be underestimated due to the difficulty in identifying corticosteroids by respondents.
- Generalisability is limited by the sample being restricted to one outpatient department in one location.

INTRODUCTION

The usefulness of Topical steroids (TS), the most widely used therapeutic agents in dermatology, has become a double edged sword with increasing prevalence of misuse, leading to disastrous consequences.[1, 2] Of concern is the unprecedented increase in fungal infections as well as the emergence of resistant dermatophytosis in India, most likely due to unnecessary use of Fixed Drug Combination (FDC) creams containing steroid.[2] Children are often victims of topical steroid misuse as they are more vulnerable to the systemic effects of potent topical corticosteroids as well as to the spread of infections.[2] Non-medical use of TS in fairness creams has led to increasing occurrences of a condition which has been described as topical steroid damaged face (TSDF).[3-5] Pharmacists and often qualified medical practitioners readily prescribe and dispense potent topical steroids given that they provide dramatic symptomatic relief. The pharmaceutical industry also contributes to the problem as they manufacture and promote inappropriate FDC containing potent TS in combination with antifungals and antibacterials. This problem is further compounded by the unregulated over-the- counter (OTC) supply and unrestricted sale of TS. Public and professional ignorance, legal ambiguity, and government inaction create a serious problem whereby FDC creams are used as a panacea for all skin problems.[6] In India, the unprecedented increase in sales of these "steroid cocktails" by an alarming 26% in 2014-15 is a reflection of the public appeal of these dangerous combinations.[5,7] This is especially unfortunate, given these medications are not only ineffective in curing but cause more harm than good. In addition, this unnecessary expenditure can cause an economic drain impoverishing many who have scarce or no financial reserve. Though efforts are being made to draw attention to the multiple factors behind this problem in India,[4,5,7,8] it remains largely under researched in rural areas. Earlier studies were conducted in the urban setting of tertiary care hospitals with emphasis on TS usage on

face.[7-12] However, no data is available to understand the impact of this epidemic in the rural areas where 68.84% of the Indian population dwells.[13]

This study analyses the magnitude, causes, characteristics, consequences, and economic impact of topical steroid misuse in a rural hospital in North India. We also seek to better understand the relation between TS misuse and patients' perception of skin disease.

MATERIALS AND METHODS

A mixed-methods observational study of patients was conducted over a period of 3 months (March 2016 to May 2016) amongst all new patients attending the dermatology outpatient department of a secondary level hospital, located in a rural part of Uttarakhand, North India.

Our data at Herbertpur Christian Hospital shows an estimated figure of 16% for steroid abuse in ring worm (Tinea) infections. Using this as an estimated prevalence of topical steroid misuse and a margin of error of 5% and a 95% confidence interval, the sample size required was approximately 160.

We undertook the study over a long enough time period (a quarter) in order to account for week-on-week variation and to smooth out any effects of unique events such as festivals, strikes and elections. Male and female patients of all ages who fulfilled the following criteria were recruited:

1. Having a skin condition for which topical steroid is contraindicated i.e. acne, bacterial, viral, fungal or parasitic cutaneous infections such as tinea, furuncle, scabies etc.
2. History of topical steroid usage for that condition.

Topical steroids include either single ingredient steroid products or a combination of topical steroid molecule with antibiotics or antifungals. The patients were recruited following a clinical examination by the consultant dermatologist, after obtaining an informed written consent. Parents were interviewed for the purpose of gathering data regarding their children. Using a mixed method of structured questionnaire supplemented with qualitative interviews, patients were assessed for misuse of TS. Taking this information into account, a trained clinician researcher then made a decision as what constituted misuse based on inappropriate indication, prolonged duration, unnecessary use of potent steroids, expense incurred and side effects. All patients with tinea were subjected to direct microscopy and those who were tested negative were added only after positive response to antifungal therapy. Ethics approval was obtained from the Institutional Ethics Committee of the Emmanuel Hospital Association, New Delhi (Protocol No.129). The patients were also counselled regarding dangers of TS misuse and appropriate treatment was given for side effects, when present.

To minimise bias in reporting steroid use, we required patients to provide the actual tubes where available. Survey answers were also verified by a combination of clinical examination, interview and structured questionnaire.

Patient and Public Involvement

The results of the study informed the production of a video and patient information handout to the communities from which the patients came. While patients were not involved in the recruitment to and the conduct of the present study, the development of research objectives was informed by patients using topical steroid, particularly those who had experienced side effects. The study was piloted to get feedback from patients on the formation of the questions .

Data analysis

Data analysis was done using Stata 14 (StataCorp, Texas, U.S.). Major variables of interest were dermatological conditions for which steroids were misused, types and quantities of steroids used, sources of prescriptions, adverse effects of misusing steroids, expenditure incurred and patients' perception of the disease. All the original variables were categorical, except number of tubes, duration of TS misuse and expenditure on TS, which were converted from numeric to categorical data for analysis. Data were presented as percentage with the exceptions of age and expenditure which were expressed in median (Q1-Q3). For multiple-response questions (side-effects, types and sources of topical steroids), we used MRTAB (Ben Jann & Hilde Schaeper, 2004) to generate simple frequencies. To test the associations between major demographic variables and profile of misuse, we performed Chi-squared test with the level of significance set at 0.05.

RESULTS

Demographics

Of the 723 new patients seen in the dermatology OPD, 213 (29.5%, 95% CI: 26; 32.6) had a history of topical steroid misuse and were eligible for the study (Fig.1). Two did not give written consent to be involved leaving 211 patients. Nearly 60% were male and the median age was 30 years. Fifty-five percent of the cases were in the 15-34 years age group. Those having only primary education seemed to be most affected by topical steroid misuse (Table 1).

Table 1. Demographic details of patients who had a history of topical steroid misuse

	No. of observations	Percentage
Age (yrs)		
up to 14	11	5.2
15-24	56	26.5
25-34	61	28.9
35-44	44	20.9
45 and over	39	18.5
Gender		
Male	124	58.8
Female	87	41.2
Education		
Illiterate	37	17.5
Primary	66	31.3
*High school	50	23.7
College	10	4.7
*Graduate	48	22.8

*Included 1 imputed value based on father's highest level of education
n=211

Profile of steroid misuse

Dermatological conditions mismanaged with steroids:

The most common condition for which steroids were misused was tinea (70.1%), followed by scabies (10%) and acne (9%). A small number had two concomitant diseases such as tinea with scabies, tinea with acne or acne with scabies. Other conditions for which steroid was misused were vulval candidiasis, herpes genitalis, tinea versicolor, furuncle and melasma. In the case of melasma, for which MILD potency steroids admix with hydroquinone and retinoids are used, patient misuses consisted of inappropriate combinations of potent steroids with antifungal and antibacterial creams extended use.

Types of steroid formulations used

Fixed dose combinations containing either a triple or quadruple combination of antifungal, antibacterial and steroid were the commonly used creams. Quadruple combinations are steroid creams which contain 4 ingredients i.e. 2 antibiotics 'ofloxacin and ornidazole' or

others with 4 different ingredients. Such combinations have no clinical justification. Although most of the participants (66%) used only one class of TS, 32% used two classes and 3% used three classes. The most misused topical steroid (Table 2) was clobetasol propionate (58.2% of 287 responses). About 70 different creams (Table 3), produced by a myriad of pharmaceutical companies were recovered from the patients during the study. As shown in table 4, the ten most misused combinations creams have very similar compositions although packaged under different names and appearances. Patients often think they are prescribed a new cream at every visit while in fact they are using one with the same molecule, most often clobetasol propionate (class I potency), thereby perpetuating the side effects.

Twenty-five percent of respondents reported concomitant use of either oral steroids (OS) or injectable steroids, or both along with TS. Of this, 39.6% had concomitant use of oral steroids, 37.7% used both oral and injectable steroid and 22.7% used injectables along with TS. These patients reported that the OS were easily procured over the counter. Use of injectable steroid was found to be associated with highest level of education (p=0.04) and were obtained from local healers.

Table 2. Types of topical steroid misused

Steroid molecule	No. of observations	Percentage
Clobetasol propionate	167	58.2
Beclomethasone/Betamethasone	91	31.7
Fluocinolone	17	5.9
Mometasone	11	3.8
Clobetasone	1	0.4

Multiple responses were allowed in this question. Percentages were based on total number of responses

Total no. of response=287

Total no. of cases = 211

Table 3 List of 70 different brand creams, many having same composition of steroid, antibiotic and anti-fungal molecules, recovered from patients during the study

Brand name	Steroid	Antibiotic	Antifungal
Panderm+, Terderm+, Orniderm, Nikderm+, Oltef-NF, Laboderm-oc, Terbinaforce+, Terbicad, Fourderm, DermikemOC, Pardum+, Castor-NF, Totalderm+, Terogood, Terogood, Orkid4, Sarvocin-CT, Orkaderm, Soltex, Bifine-plus, Dermek-TC, Turgoderm-oc, Tocoderm+, Onflox-TC,	Clobetasol propionate	Ofloxacin, Ornidazole	Terbinafine Hydrochloride
Dermacin-k5, Amitone-5, Clotebate-GM, Clobezine-CM, Tecderm-KT, Dermiford, Dermifrench-KT, Dermiford-K5	Clobetasol propionate	Iodochlorhydroxyquinoline, Gentamicin	Ketoconazole, tolnaftate
Clostar-GM, Ring-out+, Clobriv-MG, Clobeta GM, Adoderm-MN, Zincodem-GM, Candid 3D, Iobate, Neo Clobenate-GM, Clobenate-GM, Lucobet-GM, Cosvate-GM	Clobetasol, propionate	Neomycin sulphate	Clotrimazole
Medisalic , Clorap-s, Lozivate-MF, Lozivate	Clobetasol Propionate & salicylic acid		
Lobate GM	Clobetasol Propionate	Neomycin sulphate	Miconazole
Unikderm	Clobetasol proprionate	Gentamicin	ketoconazole
EVzole	Beclomethasone dipropionate	Neomycin sulphate	Clotrimazole
Betnovate-C	Betamethasone valerate	Clioquinol	Chlorocresol
Betnovate-N,	Betamethasone valerate	Neomycin sulphate	Chlorocresol
Nuforce-GM, Betamil, Quadriderm RF, Canditas-BG, Lupiderm-GM, Onabet-B, Quadriderm, Surfaz-SN, Zenoderm, CBN,	Beclomethasone dipropionate	Neomycin sulphate	Clotrimazole
Sertamide-B	Beclomethasone dipropionate		Sertaconazole
Candid -B	Beclomethasone		Clotrimazole
Cipro-CF, Ceflox-CF,	Fluocinolone acitonide	Ciprofloxacin, Neomycin sulphate	Clotrimazole
Zole-F	Fluocinolone acitonide		Miconazole
Flucort-H	Fluocinolone acitonide		
Sure-KT	Clobetasone	Gentamicin	ketoconazole
Aluderm	Clobetasol proprionate	Ofloxacin	Ornidazole

Table 4. Ten most commonly used fixed drug combination creams containing steroid

Brand name	Composition	No. of Responses(%)
Neoclobenate GM	Clobetasol propionate,Miconazole,Neomycin	55 (17.7%)
Castor NF	Clobetasol propionate, Ofloxacin, Ornidazole, Terbinafine hydrochloride	43 (13.8%)
Quadriderm	Beclomethasone dipropionate, Clotrimazole, Neomycin	32 (10.3%)
Betnovate-N	Betamethasone valerate, Neomycin	30 (9.7%)
Dermiford	Ketoconazole, iodoxychlorhydroquinoline, Tolnaftate, Genatamicin and Clobetasol propionate	30 (9.7%)
Betnovate-C	Betamethasone valerate, Clotrimazole	26 (8.4%)
Dermikem OC	Clobetasol propionate, Ofloxacin, Ornidazole, Terbinafine hydrochloride	25 (8.0%)
Lobate GM	Clobetasol propionate,Miconazole nitrate,Neomycin sulphate	25 (8.0%)
CBN	Beclomethasone dipropionate, Clotrimazole, Neomycin sulphate, Chlorocresol	25 (8.0%)
Terbinaforce plus	Clobetasol propionate, Ofloxacin, Ornidazole, Terbinafine hydrochloride	20 (6.4%)

Sources of steroid procurement or prescription and steroid usage patterns

More than half of respondents (65.9%) indicated one single source for procurement of TS, most often being pharmacists (56.8%). Patients reported that pharmacists freely dispensed TS for any complaints of itching, provided a quick remedy and avoided cumbersome procedures required in a hospital. There was statistically significant gender difference (χ^2 =7.1; p=0.008) in relation to steroid procurement from non-allopathic providers, suggesting that females were less likely to approach medical practitioners for treating their skin infections.

Extent of use and cost of usage

There was a wide range in the number of tubes (mostly 15g, a few are 20g and some 25g) used by the respondents. Twenty-one percent (44) used one tube while about three percent

(7) used more than 100 tubes. The majority (63%) used topical steroid combinations for less than 6 months. Approximately 16% of respondents used TS for over a year. The pattern of steroid usage was erratic, varying from using either one tube intermittently over a few months or most often in combination with oral and/or injectable steroids, or using more than 100 tubes continuously.

The total amount of money spent to date on TS ranged from US$0.5 to more than US$2,500. The median expenditure was US$20 (Q1:US$4; Q3:US$80), equivalent to 3 days' wages of a daily labourer. These FDC creams are available at lower cost than single ingredient antifungal creams. The plain antifungal creams (available as 30gm tubes) are 3 times more costly than the FDC creams containing potent steroid and antifungal combinations available in smaller sizes. Due to the low cost, the pharmacists stock the FDC creams as they have quick turn over while plain antifungal tubes are not stocked and are hence hard to procure. It would benefit the community significantly if the government could supply plain antifungal creams at economic prices.

Adverse effects of topical and systemic steroid misuse

Table 5 shows the adverse effects reported by 204 respondents.

A) *Effect on Dermatological conditions* – ninety-seven percent of patients with steroid modified tinea had extension of tinea to non-flexural areas of body i.e. face, ears, wrists, entire trunk, dorsum of hands and genitalia in males. Eighty percent had tinea incognito, a term used when appearance of tinea is varied or modified from the normal as a result of steroid misuse. This presented with atypical clinical signs like lichenification, eczematisation, large geographic patterns, pseudoimbricata, arciform, pustular and polycyclic lesions as well as lesions mimicking other diseases like psoriasis, pityriasis

rosea, lichen planus, and seborrheic dermatitis. Three percent of tinea infection had localised exacerbation with pustulations. Fifty-eight percent of patients with acne developed features of either steroid rosacea, pustular or nodulocystic acne. Ninety-five percent of patients with scabies had generalized papules instead of the characteristics areas making it difficult to recognize (scabies incognito).

B) Other effects

i) Striae – six patients (2.5%) had striae and these were very extensive over the groins, inner thighs, lateral sides of abdomen and axillae. Three of these patients concomitantly used oral and/or injectable steroids.

ii) Cushingoid facies – eleven patients (4.6%) showed Cushingoid features mainly characterised by facial puffiness. Seven of them concomitantly used oral and/or injectable steroids.

iv) Hypertension – eight respondents (3.3%) had new onset hypertension. Three of these patients concomitantly used oral and/or injectable steroids.

v) Diabetes – five individuals (2.1%) had new onset diabetes. Four of them concomitantly used oral and/or injectable steroids.

Table 5. Adverse effects reported by participants

	Frequency	Percent of responses	Percent of cases
Tinea extension	145	60.17	71.08
Tinea exacerbation	5	2.07	2.45
Scabies extension	20	8.30	9.8
Scabies exacerbation	1	0.41	0.49
Acne extension (steroid rosacea)	11	4.56	5.39
Acne exacerbation	9	3.73	4.41
Cushingoid*	11	4.56	5.39

Hypertension*	8	3.32	3.92
Striae*	6	2.49	2.94
Weight gain*	6	2.49	2.94
Diabetes*	5	2.07	2.45
Other exacerbation	5	2.07	2.45
Other complications	9	3.73	4.41

*Patients used systematic steroids in addition to topical steroids.
Multiple responses were allowed in this question. Percentages were based on total number of responses
Total no. of response=241
Total no. of cases = 204

Patients' perception of the disease

The majority (57.8%) considered their itchy skin condition or eruptions to be an allergic response to some food or drink which heats up the body (Fig.2). About nine percent thought it was infective and approximately six percent related it to dampness. Nineteen percent did not know the cause. Five percent believed that their skin condition was due to impure blood. Some resorted to tonics such as "Koon safi" (blood purifier) and even "blood purification". One respondent regularly withdrew a small quantity of his blood, mixed it with triamcinolone and injected the mixture back into his body. Other explanations (3.8%) for their skin conditions were bowel irregularities, heredity, unclean water and few even considered it to be due to evil spirits.

DISCUSSION

Our study found that nearly 1/3 of new dermatology outpatients had misused TS and clobetasol propionate was the most common steroid misused. Tinea incognito and extension of lesions

were seen in majority of patients with dermatophytosis. Most of the TS misusers in our study did not know the real cause of their skin disease. Nearly 80% of the patients received their TS from pharmacists or local healers.

This study demonstrates that TS misuse is a significant public health issue in rural India, with three out of ten new dermatology outpatients using topical steroids inappropriately. This result is much higher than those found in urban studies in India where prevalence of misuse was 11.8% in Delhi [8] and 15% in a Pan Indian urban study.[4] Our study demonstrated a male preponderance in contrast to the Pan Indian study which showed a female preponderance.[4] This is likely because the study was restricted to facial steroid usage. The average age of usage in our study was 32 years old which was similar to findings from the studies in urban areas of India.[4, 8]

Tinea was by far the most common indication for steroid misuse in our study followed by acne and scabies. This concurs with some recent studies [7, 8] but other studies in India showed greatest TS use for acne [9] and skin lightening.[12] In another study by Saraswat A et al, TS were most commonly used for both skin lightening and acne.[4] This difference in usage patterns could be due to infections like tinea being more prevalent in rural areas and skin colour being of more concern in urban areas.[14] This disparity could also be due to the recent spurt in dermatophytosis in India as a whole with its burden being felt in rural India as well.[15] The florid signs and symptoms caused by Trichophyton mentagrophyes, an inflammatory zoophilic species, which has emerged as a major causative organism for this epidemic, could be a reason for the rural poor to seek quick relief with cheap and easily accessible options like FDC containing TS.[16]

For health care providers, topical steroid abuse can make tinea difficult to distinguish from other common diseases like eczema, contact dermatitis and psoriasis and therefore increases

misdiagnosis, mistreatment and even increased morbidity.[2] Tinea incognito and extension of lesions were seen in majority of patients with dermatophytosis because steroids tend to alter the characteristic "ring or annular" lesion.[2, 10] These cases can range from vague erythematous plaques to lesions with oozing, prominent scaling, pustulation to large geographic lesions mimicking diseases like psoriasis. As seen in our study, it can be difficult for even dermatologists to accurately recognize steroid modified tinea. We also observed an increased occurrence in genital tinea, which was once rare. There is a need to educate the medical professionals about the wide variation in clinical presentation of steroid modified tinea to enable proper diagnosis.

TS abuse in scabies, second after tinea in our study, can cause scaly and widespread lesions that are unrecognizable as scabies. Scabies incognito or steroid modified scabies can be a serious public health problem since it is very contagious and diagnostic difficulty can increase the prevalence of scabies. Acne, the third most prevalent reason for steroid misuse, also leads to increased possibilities for Topical Steroid Damaged Face and disfiguring sequelae of acne.

In our study, nearly half of the patients received their TS from pharmacists who had variable training. Likewise, in studies from other parts of the sub-continent, pharmacists were the most common source of inappropriate steroid use.[4, 10, 17] They often function as doctors, especially where the local health services are underdeveloped or unavailable. Many people also seek treatment from charlatans and AYUSH (Ayurvedic, Yoga and Naturopathy, Unani, Siddha and Homeopathy) practitioners, given the rarity of dermatologists and MBBS trained doctors in rural areas. AYUSH account for 31% of the topical steroid misuse in our study. This is of great concern since it is illegal for a practitioner of alternative medicine to prescribe modern medicines like TS. Nevertheless, salespersons are still able to market TS to AYUSH practitioners.[10] Unfortunately, general physicians and even some dermatologists are also responsible for prescribing TS unnecessarily. This indicates the need for training of

medical/paramedical personnel about the judicious use of topical corticosteroids and their potentially serious side effects. Saraswat's study on facial steroid use found that poor availability of physicians in rural areas was associated with non-physicians being likely to prescribe TS.[4]

Our study found that clobetasol propionate - the most potent topical steroid - was the most common steroid misused. Betamethasone valerate was the most widely misused steroid in urban studies.[4, 8, 9] This is consistent with Saraswat et al who noted that patients from rural areas tended to use potent topical steroids.[4] Use of injectable steroids in our study was found to be associated with the highest education level ($p=0.04$). Most of those who used oral and injectable steroids concomitantly with TS had either no education or only primary schooling. This could reflect their unwavering trust in the local healers.

This study also explored patient perception of their skin disease. Eighty-six percent of respondents either misunderstood or did not know the cause of their skin disease. All pruritic symptoms or eruptions were perceived as allergic responses to hot, spicy food or impure blood. This wrong perception shifts the attention from common hygienic measures necessary to respond to infective conditions like tinea and scabies, to unrelated factors like abstinence from certain food, unwarranted blood investigations and blood purification. An important reason for patients seeking primary recourse from nonmedical personnel could be lack of proper understanding regarding aetiology of their illness and lack of access to quality allopathy.[18]

Our study is consistent with the observations that factors leading to misuse of TS may occur at various stages during its journey from the factory to the skin.[19] The plethora of TS combinations recovered from the patients clearly indicates the ease of purchase and the unsubstantiated claims of TS combinations promoted by pharmaceutical companies. Despite the serious adverse effects, these drugs are manufactured and sold without appropriate

regulatory control in India. Existing regulations pertinent to the prescriptions of these drugs are far from comprehensive. Although steroids have been included under Schedule H drugs, which requires proper prescription, inappropriate FDCs containing potent TS in combinations with antifungals and antibacterials are not on the same list.[20] Furthermore, the enforcement of the regulation regarding prescriptions of steroids at the ground level is rare.[2] For pharmacists and local healers, FDC creams are prescribed as one stop answer to all skin conditions, regardless of the aetiology of the disease (whether it is a bacterial or fungal infection or inflammation). Unfortunately, many clinicians and occasionally even dermatologists also promote these multidrug combinations. At the consumer level, we found little awareness about the adverse effects. To address this, stringent regulations on the manufacture, sale and marketing of steroid cocktail creams are urgently required.

Limitations

It was difficult for many patients to understand what TS were until they were shown samples. However, flooding of the market with innumerable brands containing topical steroids made it difficult to show a sample of all brands. This could have led to under-estimation of the frequency of the malpractice in our study.

Recollection of duration and quantity of use was difficult for patients who have used topical steroids over a long period. This may also have led to under or over estimation of the total expenditure on topical steroids. However, since the majority of participants used TS for less than 6 months, such potential inaccuracies were likely to be minimal.

Generalisability of our study is limited by the sample being restricted to one outpatient department in one location. To capture the true magnitude of the multifaceted problem of topical steroid misuse in rural areas, a multicentric community study across the country is recommended.

CONCLUSIONS

The epidemic of steroid modified dermatoses in rural India due to injudicious use of topical steroids is caused by multifaceted factors. Concerted, multipronged actions are needed to address professional and public ignorance, political apathy and profit incentives for drug companies and pharmacists. Continuous education of clinicians and traditional practitioners to recognize the current altered and 'unrecognizable' steroid modified dermatoses as well as the potentially harmful effects of TS is also required. Furthermore, there is a pressing need to increase the availability of family physicians, or equivalent, in rural areas where people go to whoever is local and affordable. In addition, drug control agencies should ensure strict regulation of TS sale and prohibit manufacturing of steroid cocktails. The Ministry of Health and Welfare could helpfully create awareness through social media and advertisements to warn people about the danger of TS misuse.

Funding sources – This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Conflict of Interests: None to be declared

Data sharing statement: Data are available upon reasonable request by emailing to corresponding author (Dr Molly Thomas: vijuandmolly@gmail.com). No additional data are available for this study.

Authors' contributions:

Dr Molly Thomas: principal investigator, contributed to the study design and methods, interpreted the data and drafted the manuscript.

Dr Nathan Grills: developed concept of research, interpreted the data, reviewed, edited and approved the final manuscript

Dr Celestine Wong: contributed to the study design and methods, reviewed, edited and approved the final manuscript

Pam Anderson: conducted statistical analysis, summarised and interpreted findings, reviewed, edited and approved the final manuscript

I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in BMJ Open and any other BMJ products and to exploit all rights, as set out in our licence.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which Creative Commons licence will apply to this Work are set out in our licence referred to above.

References

1 Coondoo A, Phiske M, Verma S, *et al*. Side-effects of topical steroids: A long overdue revisit. *Indian Dermatol Online J* 2014;5:416-25.

2 Verma S, Madhu R. The great Indian epidemic of superficial dermatophytosis: An appraisal. *Indian J Dermatol* 2017;62:227-36.

3 Kumar S, Goyal A, Gupta YK. Abuse of topical corticosteroids in India: Concerns and the way forward. *J Pharmacol Pharmacother* 2016;7:7-15.

4 Saraswat A, Lahiri K, Chatterjee M, *et al*. Topical corticosteroid abuse on the face: A prospective, multicenter study of dermatology outpatients. *Indian J Dermatol Venereol Leprol* 2011;77:160-6.

5 Jha AK, Sinha R, Prasad S. Misuse of topical corticosteroids on the face: A cross-sectional study among dermatology outpatients. *Indian Dermatol Online J* 2016;7:259-63.

6 Verma SB. Topical steroid misuse in India is harmful and out of control. *BMJ* 2015; 351:h6079.

7 Meena S, Gupta LK, Khare AK, *et al*. Topical corticosteroids abuse: A clinical study of cutaneous adverse effects. *Indian J Dermatol* 2017;62:675.

8 Mahar S, Mahajan K, Agarwal S, *et al*. Topical Corticosteroid Misuse: The Scenario in Patients Attending a Tertiary Care Hospital in New Delhi. *J Clin Diagn Res* 2016;10:FC16-FC20.

9 Nagesh TS, Akhilesh A. Topical Steroid Awareness and Abuse: A Prospective Study among Dermatology Outpatients. *Indian J Dermatol* 2016;61:618-621.

10 Dutta B, Rasul ES, Boro B. Clinico-epidemiological study of tinea incognito with microbiological correlation. *Indian J Dermatol Venereol Leprol* 2017;83:326-31.

11 Sharma R, Abrol S, Wani M. Misuse of topical corticosteroids on facial skin. A study of 200 patients. *J Dermatol Case Rep* 2017;11:5-8.

12 Dey VK. Misuse of topical corticosteroids: A clinical study of adverse effects. *Indian Dermatol Online J* 2014;5:436-40.

13 Government of India, Census 2011. http://censusindia.gov.in

14 Wong C, Wong S, Tang H, *et al*. Use of skin-lightening products among outpatient attendees in a North Indian Hospital. *Indian J Public Health* 2017;61:137-40.

15 Panda S, Verma S. The menace of dermatophytosis in India: The evidence that we need. *Indian J Dermatol Venereol Leprol* 2017;83:281-4.

16 Nenoff P, Verma SB, Vasani R, *et al*. The current Indian epidemic of superficial dermatophytosis due to Trichophyton mentagrophytes—A molecular study. *Mycoses* 2019;00:1–21.

17 Sinha A, Kar S, Yadav N, Madke B. Prevalence of Topical Steroid Misuse Among Rural Masses. *Indian J Dermatol* 2016;61:119.

18 Balaji A, Velavan J, Raji B, *et al.* A Multicentric Cross-sectional Study to Characterise the Scale and Impact of Polypharmacy in Rural Indian Communities, Conducted as Part of Health Workers Training. *J Family Med Prim Care* 2019;8:2234-2241

19 Coondoo A. Topical Corticosteroid Misuse: The Indian Scenario. *Indian J Dermatol* 2014;59:451-455.

20 Verma SB. Sales, status, prescriptions and regulatory problems with topical steroids in India. *Indian J Dermatol Venereol Leprol* 2014;80:201-3.

Figure legend

Fig. 1 Patient recruitment flow chart

Fig. 2 Patients' perception of causes of their skin conditions

Total number of cases: 211

Fig. 1

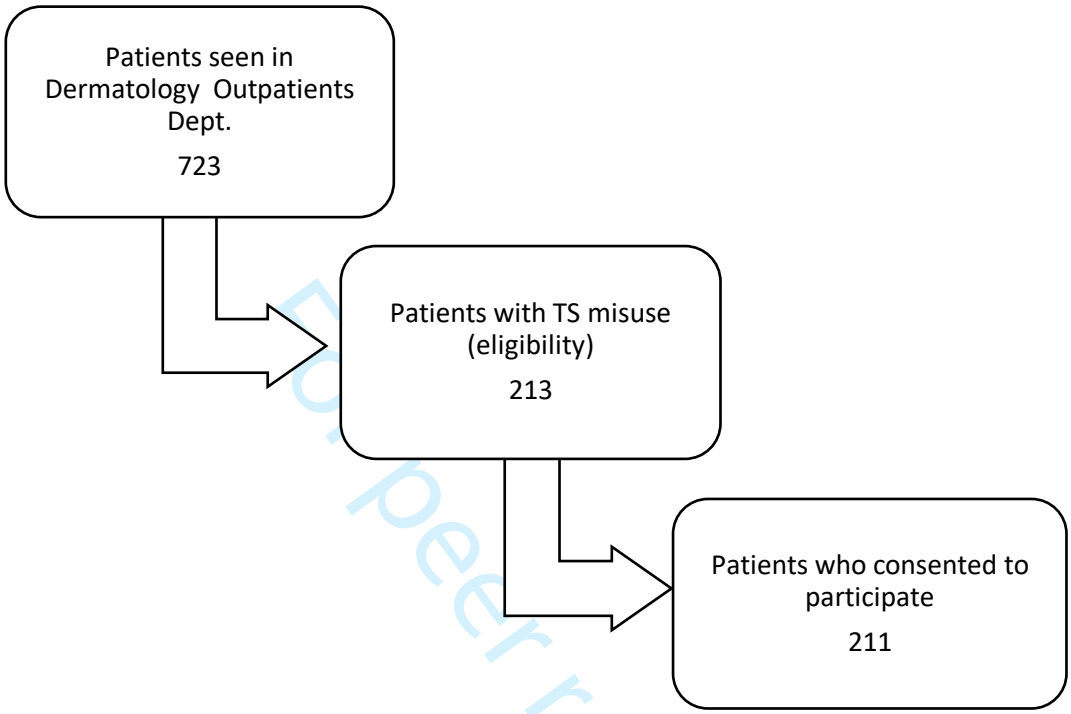
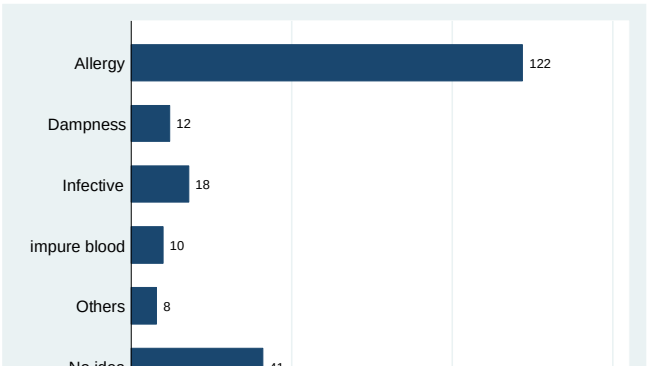


Fig 2.



STROBE Statement

Manuscript title: Magnitude, characteristics and consequences of topical steroid misuse in rural North India - an observational study among dermatology outpatients.
Authors: Molly Thomas, Celestine Wong, Pam Anderson, Nathan Grills

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page, lines 1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	p. 2, line 1 – p.3, line 3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Introduction, p.4, line 3- p.5, line 2
Objectives	3	State specific objectives, including any prespecified hypotheses	p.5, lines 3-5 (*this is an observational study)
Methods			
Study design	4	Present key elements of study design early in the paper	p.5, lines 8-21 (Materials and Methods)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p.5,line 8 – p.6, line 13 (Materials and Methods)
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	p5, lines 17-21;
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	p.7, lines 2-12 (Materials and Methods-Data analysis)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Variables of interests (see Data analysis, p.7, lines 2-10)
Bias	9	Describe any efforts to address potential sources of bias	p.6 Lines 14 -16
Study size	10	Explain how the study size was arrived at	p.5, lines 11-14.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	p.7, lines 2-12 (Materials & methods- Data analysis)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	p.7, lines 2-12 (Materials & methods- Data analysis)
		(*b*) Describe any methods used to examine	NA

		subgroups and interactions	
		(*c*) Explain how missing data were addressed	No missing data
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	NA
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	p. 7 (Fig. 1 Patient recruitment flow chart)
		(b) Give reasons for non-participation at each stage	See fig. 1 (flow chart) on p.7
		(c) Consider use of a flow diagram	Yes, see fig. 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	P.8 (Table 1)
		(b) Indicate number of participants with missing data for each variable of interest	No missing data.
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	p.7 line 16 (95% CI) (this study mainly presented descriptive statistics)
		(*b*) Report category boundaries when continuous variables were categorized	p.11, line 14 – p.12, line 6
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	p.14, line 20- p.15, line 3 (Discussion)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p.18, lines 13-24 (Limitations, with recommendations for future studies)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p. 15, line 4 – p.17, line 21
Generalisability	21	Discuss the generalisability (external validity) of the study results	We recognised this as our limitation (p.18, lines 21-24)

Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p.20, lines 1-2 (Declaration of no funding sources)