

## A CLINICAL STUDY ON ALLERGIC CONTACT DERMATITIS TO TURMERIC

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**ABSTRACT:- BACKGROUND:** In south India it is a culture among ladies to use turmeric for beautiful white skin, to remove unwanted hair on the face, in this context I have encountered ladies coming with redness, itching, burning and vesiculation of skin after application of turmeric and also especially on forehead, hair parting after application of kumkum which is prepared from turmeric and which is traditionally followed by Hindu women. **AIM:** To evaluate incidence of allergic contact dermatitis due to turmeric in female by patch testing. **MATERIALS AND METHODS:** 50 clinical suspected cases of allergic contact dermatitis in females of all age groups who were using turmeric were taken and also 20 females who were not using turmeric were taken and patch testing was done with Indian standard series (ISS), kumkum, and prepared turmeric allergens (ethanol extract, sediment, raw turmeric) and commercial preparations. **RESULTS:** Out of 50 cases tested 44 cases were positive for different turmeric antigens (88%). The incidence of kumkum allergy is also high. All the 20 females who were not using turmeric were negative. **Conclusion:** Apart from immense beneficial effects of turmeric, allergic contact dermatitis due to turmeric has been demonstrated and confirmed through patch testing in the present study.

**KEY WORDS:** Allergic contact dermatitis, patch test, ethanol extract, turmeric.

**INTRODUCTION:** Contact dermatitis comprised of 4-6% of all cases in our day to day dermatology out-patient department, among which 2-3% of patients giving history of application of turmeric after which they are developing specific symptoms & signs. In this part of south India people (females) who use turmeric are more, either to remove unwanted hair on the face, for anti-inflammatory purposes, for beautiful glowing skin (or) for religious purposes. More patients complaining of itching, burning, vesiculation, pigmentation in and around the areas (forehead, glabellar region & hair parting) where they apply kumkum (prepared from turmeric), which is universally followed by Hindu women as a traditional symbol and sindhoor on the hair parting by the married Hindu women. There are some studies on kumkum dermatitis but as far as I am aware no work has been done so far on this topic (allergic contact dermatitis due to turmeric) and also only few articles were published in the indexed journals on this study. Hence I took up the study. Allergic contact dermatitis is a classic delayed hypersensitivity (or) a type IV immunological reaction. By definition it is mediated

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by immune cells rather than by antibodies the reaction can be thought of as occurring in two phases, initially a sensitization and then an elicitation response. It is a first (or) sensitization phase that is the basis for its classification as an immune mediated reaction.<sup>[1]</sup> Out of more than 6 million chemicals in the world's environment today, at least 2,800 have been reported to have contact sensitizing properties.<sup>[2]</sup> Most allergens (haptens) are simple chemicals of low molecular weight (<500 1000 Daltons) that contains electrophilic atoms, i.e. positively charged and electron deficient.<sup>[3]</sup> There are two main processes<sup>[4]</sup>: (i) sensitization (induction or afferent limb of contact sensitivity); and (ii) elicitation (or efferent limb) of allergic contact dermatitis. Sensitization presupposes individual susceptibility.<sup>[5]</sup> The capacity for sensitization varies from person to person, but certain individuals are prone to developing sensitivity to particular substance e.g.: nickel.<sup>[6]</sup> Some individuals are resistant to sensitization this resistance may have been acquired by repeated exposure to sub-sensitizing doses of allergen.<sup>[7]</sup> Women have stronger cell mediated immunity responses than men.<sup>[8]</sup> The reason for female preponderance in clinical patch test studies is mainly explained by the large number of metal sensitive females<sup>[9]</sup> which is largely the result of ear piercing<sup>[10]</sup> and the greater exposure to fragrances, cosmetics and hair dyes. Number of positive patch-test reactions tend to increase with age due to accumulation of allergies acquired over lifetime.<sup>[11]</sup> UVB exposure has been shown to diminish the skin's immune response to contact allergens.<sup>[12]</sup> Indian women become sensitized to dyes and adhesives in kumkum and bindi.<sup>[13,14]</sup> Sensitization and subsequent contact dermatitis may result from single exposure to a strong allergen, although usually several or many exposures are necessary before sensitization and dermatitis occur. On first exposure to a strong sensitizer such as DNCB, most subjects develop a local reaction after 5 -25 days. During this period sensitization has been accomplished, and the residues of the allergens in the skin react with newly formed T lymphocytes. If a sensitized person is re-exposed to specific allergen in sufficient concentration, the clinical reaction subsequently develops much more quickly within 24-48 hours, however depending on the degree of sensitivity, penetration and other factors this may vary from few hours to many days. It is possible to develop an allergy to agents after years of contact. Contact dermatitis accounts for 4-7% of all dermatological consultation. Facial allergic contact dermatitis from fragrances, preservatives, skin care products and cosmetics including nail varnish is common.<sup>[15]</sup> Items of religious symbol also affects face. Hyperpigmentation of the face resembling Riehl's melanosis has been frequently reported from Japan. The dominant symptom of Riehl's melanosis is facial hyperpigmentation, most pronounced on the forehead and in the zygomatic or temporal region. At present Riehl's melanosis is synonymous with pigmented contact dermatitis. The most common cause has been sensitizing chemicals in cosmetics. Common allergens causing pigmented contact dermatitis are fragrances, preservatives, hair dyes, lipsticks and kumkum. Tikka/bindi dermatitis is peculiar to India.<sup>[16]</sup> In India depigmentation has been reported due to bindi, the causative agent in bindi adhesive being para-tertiary butyl phenol.<sup>[17]</sup>

Turmeric contains upto 5% essential oils and upto 3% curcumin a polyphenol, it is the active substance of turmeric and it is also known as C-175300 or

Natural yellow 3. Curcumin, a polyphenol compound is responsible for the yellow colour of the turmeric and is the most active Pharmacological agent. <sup>[18]</sup> The oleoresin is prepared via extraction from the turmeric with one of the approved organic solvent, following the evaporation of

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the solvent turmeric oiloresin may contain 15-40% curcuminoids, of which curcumin predominates (which I have followed in the present study to prepare the antigen). The other two curcuminoids being demethoxycurcumin, and Bis – dimethoxycurcumin.<sup>[19]</sup> The dried root of turmeric reportedly contains 4-8% curcumin of which curcumin I is the most abundant.<sup>[20]</sup>Hata et al described a woman who developed erythema, papules and vesicles on the dorsa of her hands after applying a medicament containing *Curcuma longa*; on the skin she had positive patch test to curcumin 1%, 0.5% and 0.1% in petrolatum.<sup>[21]</sup>Goh et al described a spice miller who developed dermatitis on the hands to curry powder and curcuma longa, he had positive patch test to *Curcuma longa* 25% in petrolatum.<sup>[22]</sup> Curcumin is also used to color the chlorhexidine solution used for disinfection prior to surgery; curcumin allergy in relation to Yellow chlorhexidine solution used for skin disinfection has been documented. The concentration of curcumin in the yellow chlorhexidine is 0.05%. Patch test with European stranded series of allergens, supplementary standard series, and curcumin in petrolatum at 1% and in ethanol at 0.01% were done. Both tests with curcumin showed a ++ reation at day 2 and day 4. It was concluded that the contact dermatitis was due to curcumin allergy.<sup>[23]</sup>Allergic contact dermatitis to turmeric in kumkum has been reported.<sup>[24]</sup>Kumkum is a commonly used cosmetic in India, traditionally based on turmeric powder, and its ingredients can cause various types of dermatoses. Tetrahydrocurcumin (THC) is a halogenated form of curcumin. It is colorless and can be added to skin care products to function as antioxidant, to prevent lipids in the moisturizers from becoming rancid. Allergic contact dermatitis to THC has been reported. <sup>[25,26]</sup>

For patch testing of unknown substances, the following steps should be taken.

- Search for the safety data on the given substance.
- Dissolve the substance in water, petrolatum, acetone, methyl ethyl ketone, ethanol etc.
- In case of leave on products, use them as such for patch testing.
- In case of wash off products, use 10 and 100 times dilution.
- In case of industrial products, 100 and 1000 dilution should be used.
- In case of positive reaction is obtained, do atleast 10 controls to rule out false positive reactions.

**METHODS:** The study comprised of 50 clinically suspected cases of Allergic Contact Dermatitis in females of all age groups who attended Outpatient department of Dermatology, Venereology and leprosy, Vinayaka Missions Medical College and Hospital from 1-1-2011 to 1-1-2012 (1year) At the same time 20 females (controls) who were not using turmeric were also tested.

## INCLUSION CRITERIA

All female patients who presented with allergic contact dermatitis who were using topical turmeric, after taking informed consent

## EXCLUSION CRITERIA

1. Subjects with active disease during the visit (they were treated and patch testing was done at a later date after remission).
2. Patients on steroids / antihistamines / immunosuppressants /UVA, UVB phototherapy (here patch tests were deferred until a fortnight after stopping the treatment).

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3. Non consenting patients.
4. Pregnant women.

A detailed history of the patients included in the study was taken. Complaints, duration, evolution, progress were noted. Morphology of the lesions and the sites of involvement were noted. Past history of patients for similar complaints was asked and also past history and family history of allergies (atopy) was evaluated. History of any drug intake prior to and after onset of lesions is noted down. History of topical application of any medicaments was noted. History of allergy to any other cosmetics (kumkum, etc.,) used by the patient was noted down. Dermatophyte infections, Seborrhoeic dermatitis, Psoriasis, Atopic dermatitis were ruled out clinically as a part of differential diagnosis. All the active dermatitis if present was brought under control by topical steroids and wet compressors.

Additionally routine general and systemic examination and routine blood investigations namely routine haemogram and blood sugar were done. Patients were taken for patch testing with **Indian Standard Series** of allergens (approved by CODFI), prepared **TURMERIC** allergens (100 gms of pure turmeric root crushed into small pieces was mixed with 150 ml of ethanol and tightly corked. The cork was removed after 3 days and the mixture was filtered with the help of filter paper in to a fresh beaker, the substance which was filtered into the beaker was taken as ethanol extract and the substance which was left out in the filter paper was taken as sediment. 1gm each of ethanol extract and sediment were mixed separately with 10gms of petrolatum to make 0.1% non-irritant concentration and patch tested), and any of the cosmetics (kumkum) used by the patients to which she is allergic

## INDIAN STANDARD SERIES OF PATCH TEST ALLERGENS

(Approved by Contact and Occupational Dermatoses Forum of India) (CODFI)

S.No	Allergen
1	Vaseline 100%(Control)
2	Balsam of Peru 10%
3	Formaldehyde 2%
4	Mercaptobenzothizole 1%
5	Potassium dichromate1%
6	Nickel sulphate 5%
7	Cobalt sulphate 5%
8	Colophony 10%
9	Epoxy resins 1%
10	Parabens mix 15%

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11	Paraphenylenediamine 1%
12	Parthenium 15%
13	Neomycin sulphate 20%
14	Benzocaine 5%
15	Wool Alcohol 30%
16	Chlorocresol 1%
17	Fragrance mix 8%
18	Thiuram mix 1%
19	Nitrofurazone 1%
20	Black rubber mix 0.6%

S.NO	ALLERGEN (turmeric)
1	Ethanol extract of turmeric in petrolatum
2	Sediment of ethanol extract in petrolatum
3	Turmeric as is [water based]
4	Turmeric face cream [Commercial]
5	Other cosmetics and topicals used by patient (KUMKUM, etc.,)

### PROCEDURE OF PATCH TESTING:

#### PREPARATION OF THE PATIENT:

The patch test procedure and common side effects were explained to the patient and informed consent was taken in every case. A clean bath was advised before coming. Any hair on the back was advised prior removal with razor (without use of shaving cream or soap).

The back of the patient was ensured of absence of any dermatitis. An interval of atleast a fortnight was ensured following treatment of a dermatitis involving the back. The back was prepared by gentle cleaning avoiding excess rubbing.

#### PREPARATION OF PATCHES AND APPLICATION

Indian standard series of allergens (ISS), and prepared turmeric allergens (ethanol extract of turmeric and sediment in petrolatum.) were stored in refrigerator at 4-degree C to 8 degree C. Patch test units were kept at room temperature

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1. Allergens were taken out of refrigerator 15 min before testing and required amount is placed over the aluminum chambers (contact and occupational dermatitis forum of India guidelines were followed)
2. Patch test units were applied to the back of the patient, and the patches were labeled and numbered accordingly
3. Patients were told that the patches will be kept in place for 48 hrs., and they were instructed not to wet the patches during this period, to avoid exposure of patches to sun light and to report if there is sever itching or irritation

**PATCH TEST READING:** Patches were removed after 48 hours, circles were marked around the grooves with marking pen and patches were numbered. Readings were taken 45-60 minutes after removal of patches. Second reading was taken on day 4 to confirm the presence of allergic reaction that will persist or increase and irritant reactions shall tend to decrease.

**READING AND INTERPRETATIONS:** Recording of patch test reactions is done according to the International Contact Dermatitis Research Group (ICDRG).

-	Negative
?+	Doubtful reaction, faint erythema only
+	Weekly positive reaction; palpable erythema, infiltration, possibly papules.
++	Strong positive reaction; erythema, infiltration, papules and vesicles.
+++	Extreme positive reaction; intense erythema and infiltration and coalescing vesicles
IR	Irritant reaction
NT	Not tested

## RESULTS

### 1. Tested Patients(n)

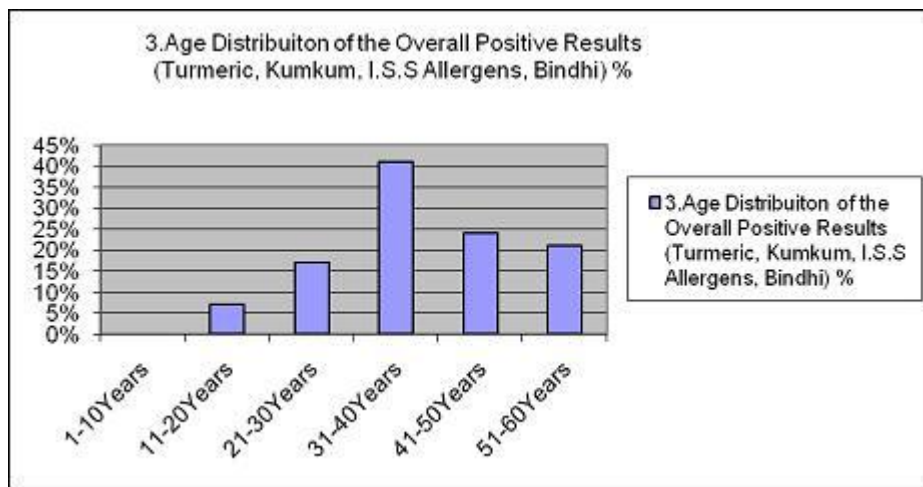
	Total	Total Positive Results	Negative Results
Number of Patients(n)	50	29	21
Percentage%	100%	58%	42%

### 2. Age Distribution of the Patients

Age Group	Total	%
1-10Years	0	0%
11-20Years	4	8%
21-30Years	12	24%
31-40Years	20	40%
41-50Years	12	24%
51-60Years	2	4%
Total	50	100%

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### 3. Age Distribuiton of the Overall Positive Results (Turmeric, Kumkum, I.S.S Allergens, Bindhi)



### 4. Age distribution of the positive cases of Turmeric ( For Individual Allergens: Ethanol extract , Sediment, Raw turmeric and Commercial Preparation

Age Group	Ethanol Extract (EE)	Sediment after Ethanol extract (SED)	Raw Turmeric	Commercial Preparation	Maximum Number of cases
1 - 10 yrs	0	0	0	0	0
11 - 20 yrs	1	0	0	0	1
21 - 30 yrs	4	4	4	1	13
31 - 40 yrs	5	4	5	0	14
41 - 50 yrs	5	3	3	1	12
51 - 60 yrs	2	0	2	0	4
<b>Total</b>	<b>17</b>	<b>11</b>	<b>14</b>	<b>2</b>	<b>44</b>

## 5. Turmeric Cases ( For Individual Turmeric Allergens)

Individual Cases	Number	Percentage
Ethanol Extract (EE)	17	38%
Sediment after Ethanol extract (SED)	11	27%
Raw Turmeric	14	31%
Commercial Preparation	2	4%

## 6. Age Distribution of the Positive Results (I.S.S Allergens Only)

Age Group	Total	%
11-20Years	1	7%
21-30Years	2	14%
31-40Years	7	46%
41-50Years	4	26%
51-60Years	1	7%
Total	15	100%

## 7. Type of I.S.S Allergens according to frequency of Positive Patch results

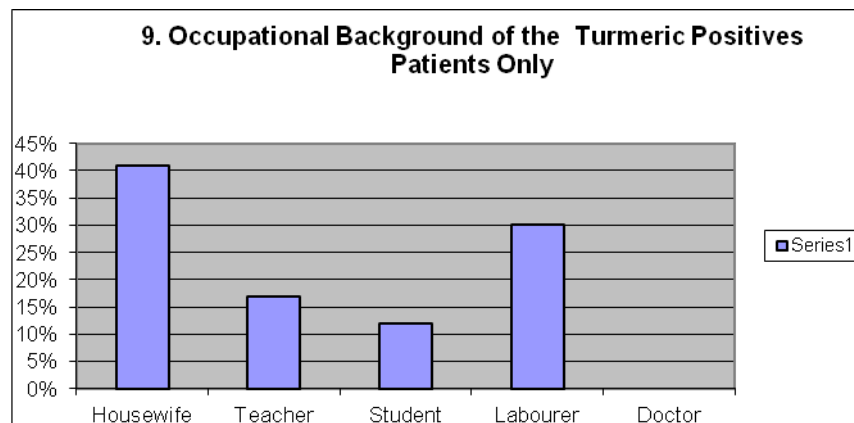
Allergens	Cases	Percentage
Nickel Sulphate	8	43%
PPD	3	17%
Black rubber Mix	1	5%
Parthenium	1	5%
Neomycin	1	5%
Cobalt Sulphate	1	5%
Colophony	1	5%
Pot. dichromate	1	5%
Fragrance Mix	1	5%
Balsam of peru	1	5%
Total	19	100%



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## 8. Occupational Background of the Patients

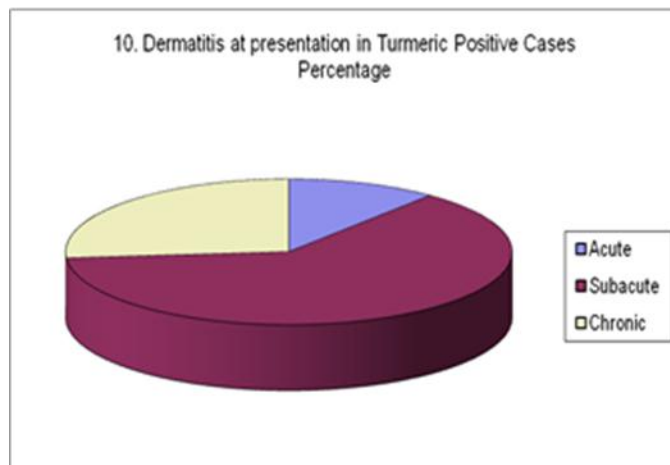
Occupation	Total	%
Housewife	26	52%
Teacher	6	12%
Student	7	14%
Labourer	10	20%
Doctor	1	2%



## 10. Sites Affected in the Positive Cases (Turmeric)

Site	Total	%
Face, Neck	4	23%
Face, Neck, Hands	1	6%
Forehead, Face, Neck	2	12%
Face	7	41%
Face, Hands	1	6%
Forehead, Face	2	12%
Total	17	100%

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**12.Total duration of the Disease in the Patients**

Duration	Total	Percentage
< 6 months	25	50%
> 6 months	3	6%
1-3 Years	16	32%
>3-10 years	5	10%
>10 years	1	2%
Total	50	100%

**13. Duration of disease in positive cases (Turmeric only)**

Duration	Total	Percentage
< 6 months	7	41%
> 6 months	2	12%
1-10Years	8	47%
11-20Years	0	0%
Total	17	100%

**14.Duration of turmeric use in patients**

Years	Total	%
1-10Years	15	30%
11-20Years	19	38%
21-30Years	13	26%
1-40Years	3	6%
	50	100%

## 15. Duration of Turmeric use in Positive cases

Years	Total	%
1-10Years	7	41%
11-20Years	4	24%
21-30Years	4	24%
31-40Years	2	11%
	17	100%

## 16. Duration of Application in Positives Cases and onset of Dermatitis

Duration of Use	Onset of Dermatitis	Time Interval
25years	6months	24years 6months
15years	15days	14years,11months,15d
30years	1months	29years,11months
10years	1years	9years
10years	8months	9years,2months
35years	10years	25years
9years	6months	8year, 6months
20years	8years	12years
8years	3years	5years
40years	7years	33years
25years	8years	17years
5years	2years	3years
5years	8months	4year,4months
25years	1years	24years
20years	2months	19Years,10months
10years	6months	9year, 6months
15years	5months	14years,7months

The Average duration between the exposure of the Allergen(turmeric) and manifestation of ACD was 15 Years

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## 17. Single/Multiple Sensitivities (Turmeric Only)

No of Antigens positive	Total	%
1	3	18%
2	3	18%
3	9	53%
4	2	11%

## 18.Both turmeric & I.S.S Positivity

Age Wise	Number	%
21-30 years	1	33%
41-50years	2	67%
Total	3	100%

## 19.Individual Positive Cases for the Allergens Tested

Positive Cases	Patients	%
Turmeric Cases	17	39
I.S.S Cases	15	35
Kumkum	9	21
Sticker-Bindi	2	5

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fig :1 i.s.s allergens and prepared turmeric allergens

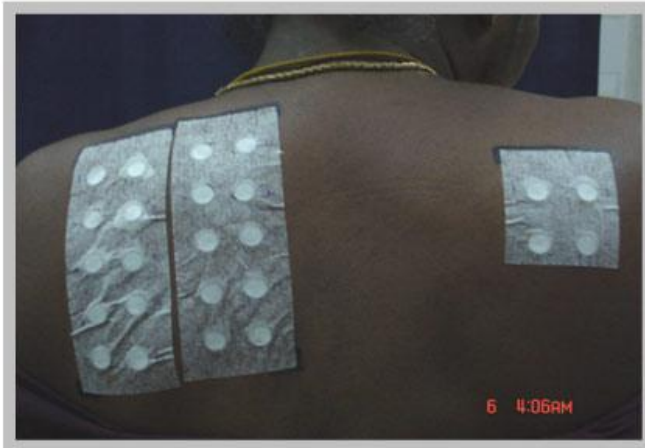


Fig-2 Method of Application of Patch Test

## CONTACT DERMATITIS

### DIFFERENT PRESENTATION



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ETHANOL EXTRACT++  
SEDIMENT AFTER ETHANOL  
EXTRACT++  
RAW TURMERIC++



ETHANOL EXTRACT++  
SEDIMENT AFTER ETHANOL  
EXTRACT-  
RAW TURMERIC++  
KUMKUM+



ETHANOL EXTRACT-  
SEDIMENT AFTER ETHANOL  
EXTRACT+  
RAW TURMERIC-  
COMMERCIAL PREPARATION-  
KUMKUM+



KUMKUM+  
STICKER BINDI+

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**DISCUSSION:** The purpose of my study was a clinical study of allergic contact dermatitis to turmeric in females along with patch testing with ethanol extract of turmeric; sediment after ethanol extract, raw turmeric paste, commercially available turmeric preparation, and also with kumkum as allergic contact dermatitis to turmeric in kumkum was reported. Along with these allergens they were also tested with Indian Standard Series (I.S.S) allergens so that the common allergens are not missed. At the same time 20 individuals (females) who were not using turmeric were also tested, with the prepared turmeric allergen to observe whether it is causing any allergic reactions in females who were not using turmeric and also to rule out the occurrence of irritant reactions if any. To find a non irritant concentration most chemicals can be tested with three concentrations 10%, 1% and 0.1% in aqueous solution or in petrolatum. I have followed the same, and I have made ethanol extract in petrolatum and sediment after ethanol extract in petrolatum. A positive reaction should not be accepted allergic unless at least 20 controls are negative.<sup>[27]</sup> In the present study all the tested (20) controls were negative to prepared turmeric allergens. During the period of my study allergic contact dermatitis cases accounted for 4-6% of the total out patient attendance at the department of dermatology.



Out of 50 patients tested I found

- 17 positive cases to ethanol extract of different gradings
- 11 positive cases to sediment
- 14 positive cases to raw turmeric
- 2 positive cases to commercial preparation
- 9 positive cases to kumkum
- 2 positive cases to bindi
- 15 positive cases to I.S.S
- 3 Positive cases for both I.S.S. and Turmeric

The high positivity to ethanol extract of turmeric when compared to I.S.S may be due to the specific cases (suspected ACD to turmeric) and all the positive cases are of current relevance. 15 patients were positive to I.S.S among which 3 patients are positive for both I.S.S and turmeric, where positivity to turmeric is considered as of current relevance and in the other 12 patients the particular I.S.S allergen (s) are relevant. 2 cases of contact urticaria to curcumin were reported in the literature where one among them is non-immunologically mediated and the other is immunologically mediated.<sup>[28]</sup> In the present study we have not encountered any case of contact urticaria to curcumin. 2 patients with I.S.S. allergy gave family history of allergic contact dermatitis. None of the patients gave history of atopy either personal (or) family. The highest positivity of turmeric allergy is seen in 31-40 yrs age group. Surprisingly the highest positivity for I.S.S is seen in the same age group 31-40 years. 1 case of positivity to turmeric in 11-20 yrs and 2 cases in 51-60 age group. The less number of cases in 11-20 yrs age groups may be due to less exposure and the less number of cases in 51-60 yrs age group may be due to fading immunity in old age. There is also high incidence of ACD to Kumkum 9 patients were positive to Kumkum, apart from turmeric in kumkum the other ingredients in kumkum are Brilliant lake Red R, Sudan I, Aminobenzenes and Canaga oil. As allergies to these ingredients are reported <sup>[29-33]</sup> they should also be tested. Positive reaction to sediment may be due to a possibility of near total extraction (or) any other unknown allergen in the sediment which has to be evaluated. Only 2 positive patch test reactions to commercial preparation is explained by its refined nature of preparation. The high sensitization to turmeric is explained due to frequent contact by applying to face and body for cosmetic, religious and medicinal purposes. Apart from applying turmeric topically, females may also get exposed to it in the form of spices during cooking <sup>[34]</sup>.

## LIMITATIONS OF THE STUDY

1. Preparing the ethanol extract of turmeric and appropriate concentrations.
2. Unable to know whether the extract is complete or not.
3. Unacceptability, (ie) avoidance of bathing for the concerned test period and review after 48 and 96hrs.
4. Apart from getting exposed to turmeric topically, in India everybody is exposed to oral ingestion of turmeric. We have to also look into the aspect of systemically reactivated contact dermatitis.

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5. Small sample size.

**CONCLUSION AND SUGGESTIONS:** Apart from the immense beneficial effects of turmeric, allergic contact dermatitis due to turmeric has been demonstrated and confirmed through patch testing in the present study. There is also high incidence of Kumkum dermatitis. As turmeric and kumkum has a wide popularity in people for their medicinal, cosmetical, traditional and religious properties and beliefs application of them is inevitable, so an alternative should be found in making turmeric non allergenic. As the positive cases of turmeric allergy are more compared to I.S.S allergy in my study and also as the incidence of kumkum dermatitis is raising we can think of inclusion of Turmeric and Kumkum in I.S.S allergens.

**ACKNOWLEDGEMENT:** I acknowledge my professor Dr. Sri Venkateshwaren for helping me during the course of study. I am also thankful to my patients without whose co operation this work would not have been completed.

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