“CLINICO EPIDEMIOLOGICAL STUDY OF CONTACT DERMATITIS TO KUMKUM”

Dissertation Submitted in

Partial fulfillment of the University regulations for

MD DEGREE IN

DERMATOLOGY, VENEREOLOGY AND LEPROSY

(BRANCH XX)

MADRAS MEDICAL COLLEGE

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI, INDIA.

APRIL 2015

CERTIFICATE

Certified that this dissertation titled "**CLINICO EPIDEMIOLOGICAL STUDY OF CONTACT DERMATITIS TO KUMKUM"** is a bonafide work done by **Dr. SUBHASHINI S,** Post-graduate student of the Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2012 – 2015. This work has not previously formed the basis for the award of any degree.

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The dissertation entitled **"CLINICO EPIDEMIOLOGICAL STUDY OF CONTACT DERMATITIS TO KUMKUM" "** is a bonafide work done by **Dr. SUBHASHINI S** at Department of Dermatology, Venereology and Leprosy, Madras Medical College, Chennai – 3, during the academic year 2012 – 2015 under the guidance of **Prof. Dr. S. NIRMALA, M.D.,** Department of occupational and Contact Dermatitis, Madras Medical College, Chennai -3.

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DECLARATION

I, **Dr. SUBHASHINI S** solemnly declare that this dissertation titled **"CLINICO EPIDEMIOLOGICAL STUDY OF CONTACT DERMATITIS TO KUMKUM"** is a bonafide work done by me at Madras Medical College during 2012-2015 under the guidance and supervision of **Prof. K. MANOHARAN, M.D., D.D.,** Professor and head department of Dermatology, Madras MedicalCollege, Chennai-600003. This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai towards partial fulfillment of the rules and regulations for the award of **M.D Degree in Dermatology, Venereology and Leprosy (BRANCH – XX)**

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INSTITUTIONAL ETHICS COMMITTEE
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CERTIFICATE OF APPROVAL

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Dear Dr.S. Subhashini,

The Institutional Ethics Committee of Madras Medical College reviewed and discussed your application for approval of the proposal entitled **"CLINICO EPIDEMIOLOGICAL STUDY OF CONTACT DERMATITIS TO KUMKUM"** No. 02112013

The following members of Ethics Committee were present in the meeting held on 13.11.2013 conducted at Madras Medical College, Chennai -3.

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2. Prof. R. Nandini, MD -- Member Secretary
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6. Thiru. S. Govindasamy, BA BL -- Lawyer
7. Tmt. Arnold Saulina, MA MSW -- Social Scientist

We approve the proposal to be conducted in its present form.

Sd/ Chairman & Other members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

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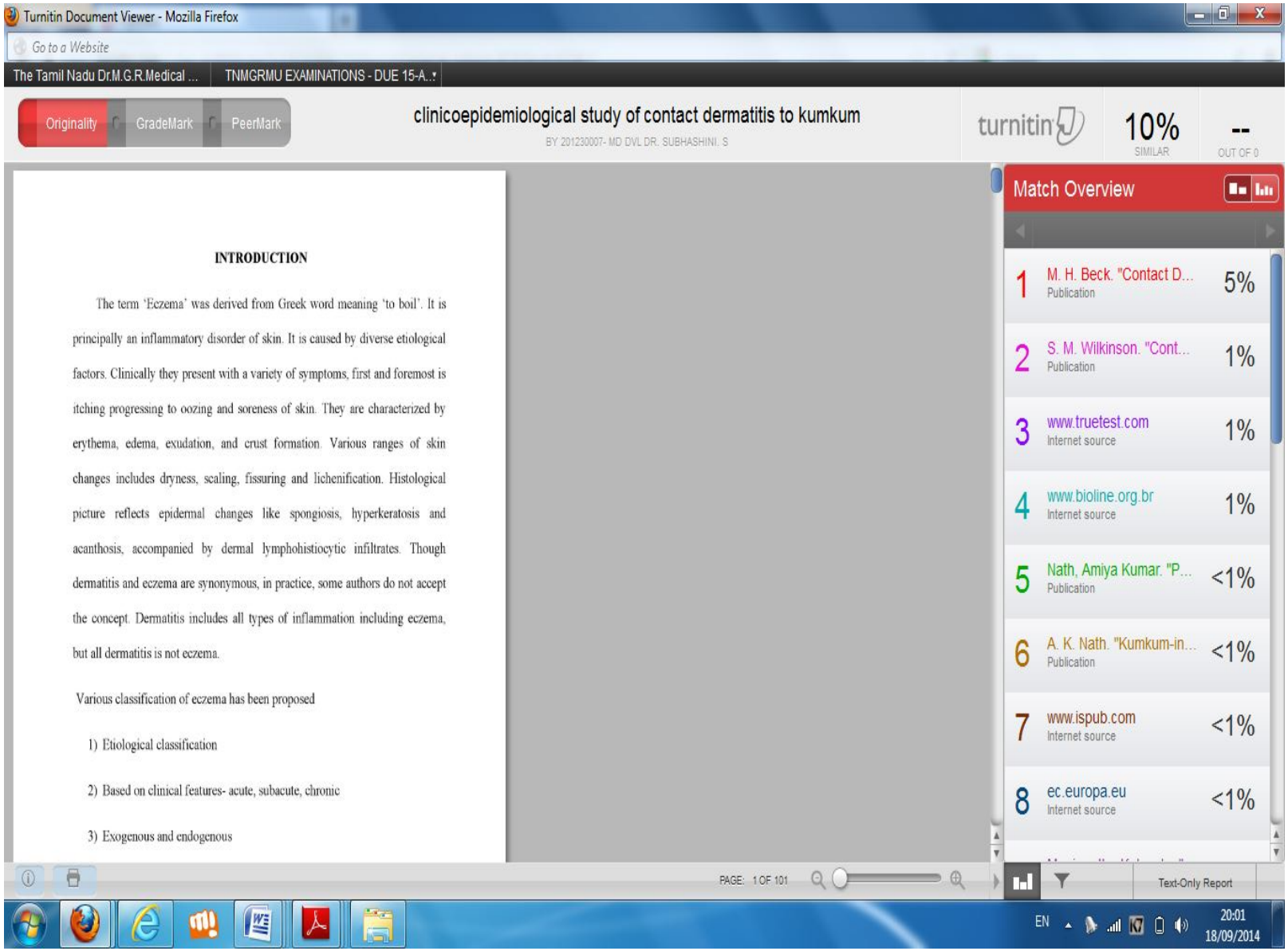
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INTRODUCTION
The term 'Eczema' was derived from Greek word meaning 'to boil'. It is principally an inflammatory disorder of skin. It is caused by diverse etiological factors. Clinically they present with a variety of symptoms, first and foremost is itching progressing to oozing and soreness of skin. They are characterized by erythema, edema, exudation, and crust formation. Various ranges of skin changes includes dryness, scaling, fissuring and lichenification. Histological picture reflects epidermal changes like spongiosis, hyperkeratosis and acanthosis, accompanied by dermal lymphohistiocytic infiltrates. Though dermatitis and eczema are synonymous, in practice, some authors do not accept the concept. Dermatitis includes all types of inflammation including eczema, but all dermatitis is not eczema.
Various classification of eczema has been proposed
1) Etiological classification
2) Based on clinical features- acute, subacute, chronic
3) Exogenous and endogenous
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CONTENTS

ABSTRACT

Introduction:

Kumkum is customarily used by Hindus all over the world for religious belief. It is traditionally prepared by combining turmeric with an alkali. Due to recent entry of commercial kumkum in the market, the chemicals used, sensitize the individuals on chronic exposure and produce contact dermatitis.

Aims and objectives:

The aim is to study the age and sex incidence of kumkum dermatitis among patients attending our OPD, types of clinical presentation, clinical pattern of distribution, association with atopy, association between the duration of exposure to kumkum and the onset of clinical manifestation and to confirm allergic contact dermatitis by doing patch test.

Materials ad methods:

About 50 cases of contact dermatitis with history of exposure to kumkum attending the Occupational contact dermatitis outpatient department were included in the study. A written consent, detailed clinical history, routiee investigations were done. Patch test was performed using allergens in kumkum and the patient used kumkum.

Results:

The incidence of kumkum dermatitis was 4.48% among 33.87% of our OPD. Female to male ratio was 2.8:1 The mean age of distribution was 44.32 years.The mean duration of exposure is 17.64 years. Pigmented contact dermatitis seen in 80% (40 patients), allergic contact dermatitis in 5 patients (10%) and no visible skin changes in 5 patients (10%). Forehead is the common site involved in 19 patients (38%). Forehead & hairparting in 7 patients (14%), glabella in 6 patients (12%), hairparting & glabella in 6 patients (12 %), in 5 patients (10%) had no visible clinical changes. hair parting area only in 2 patients (10%).

Conclusion:

Our patients were treated symptomatically and showed good clinical improvement. Adviced to avoid using kumkum and suggested other alternatives. This study is done to emphasizes

the need for standardization in commercial kumkum manufacturing and to stress the importance of adding these allergens in India standard series.

INTRODUCTION

The term ‘Eczema’ was derived from Greek word meaning ‘to boil’. It is principally an inflammatory disorder of skin. It is caused by diverse etiological factors. Clinically they present with a variety of symptoms, first and foremost is itching, progressing to oozing and soreness of skin. They are characterized by erythema, edema, exudation, and crust formation. Various ranges of skin changes includes dryness, scaling, fissuring and lichenification. Histological picture reflects epidermal changes like spongiosis, hyperkeratosis and acanthosis, accompanied by dermal lymphohistiocytic infiltrates. Dermatitis includes all types of inflammation including eczema, but all dermatitis is not eczema.

Various classification of eczema has been proposed

1) Based on clinical features- acute, subacute, chronic
2) Etiological classification
    - Exogenous eczema
    - Endogenous eczema

EXOGENOUS ECZEMAS

- Allergic contact dermatitis
- Irritant contact dermatitis
- Photoallergic contact eczema
- Eczematous PLE
- Infective eczema
- Post traumatic eczema
- Dermatophytid

ENDOGENOUS ECZEMA

- Atopic eczema
- Asteatotic eczema
- Discoid eczema
- Chronic superficial scaly dermatitis
- Eyelid eczema
- Seborrhoeic eczema
- Pityriasis alba
- Hand eczema
- Venous eczema
- Juvenile plantar dermatosis
- Eczematous drug eruptions

COSMETIC DERMATITIS

Cosmetics are defined as "articles intended to be rubbed, poured, sprayed on or sprinkled, introduced into or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness or altering the appearance."[1]

Cosmetics – induced contact dermatitis are in rising trend in recent years due to use of enumerous number of cosmetic products available in the markets such as hairdye, sticker bindi, commercial kumkum, make-up kits, etc. Kumkum is customarily used by Hindus, all over the world, especially in India by married women. Men and children also wear kumkum as a part of religious belief. Contact dermatitis to kumkum occurs at typical sites such as forehead, glabella, hair parting region, neck and chest. There is gender predilection towards females.

Kumkum is traditionally prepared by combining turmeric with an alkali. However, in recent days, this conventional method is not in use. It is manufactured commercially by adding certain chemicals with dyes. These chemicals sensitize the individuals on chronic exposure and produce various types of clinical manifestation including asymptomatic pigmented contact dermatitis to acute irritant contact dermatitis with blister formation.

Though hairdye is incriminated as a primary cause of cosmetic dermatitis in India, a study conducted by Pasricha et al,[2] contact dermatitis due to kumkum is budding as a frequent cause. The prevalence of cosmetic dermatitis represents only the tip of an iceberg. Also, among the patients who experience certain symptoms such as itching, pigmentation, etc., at the contact site either tend to change the brand or stop using the product which favours decrease in prevalence.

Since cosmetics has infiltrated into our life style, contact dermatitis can be prevented by limiting their use and bringing about standardization in manufacturing.

REVIEW OF LITERATURE

CONTACT DERMATITIS

Contact Dermatitis is defined as an inflammatory response of the skin to an irritant or allergic exogenous material. It may be classified as follows:

1. Irritant contact dermatitis.
2. Allergic contact dermatitis.
3. Photo allergic, phototoxic dermatitis.
4. Non-eczematous reactions.

IRRITANT CONTACT DERMATITIS

It is defined as a non-immunological inflammatory reaction occurring at the site of exposure characterized by redness, edema, or erosion following single or multiple application of an exogenous material to the same cutaneous site.

History

In 2000 BC, castor oil extract was used as an irritant to promote hair growth.[3] In the year 1556, deep ulcer of the skin was reported by Agricola among metal workers.

Ramazzini (1633-1714) documented fissures in washerwomen's hand and leg ulcers among salt miners. Willan described dermatitis caused by shoemaker's wax. Bateman reported eruption due to lime in construction workers.[4]

Any agent (physical or chemical) capable of producing cell damage, applied for sufficient time and in a sufficient concentration can lead to irritant dermatitis.

The various factors that contribute to irritation potential are [5,6]

A. EXOGENOUS

1. Chemical characteristics

- Molecular structure
- pH and pK_a
- Concentration and dose
- Inherent toxicity
- Hydrophobicity

2. Penetration characteristics

- Vehicle
- Solubility
- Duration of contact
- Type of contact

B. ENDOGENOUS

- Individual susceptibility
- Site of exposure

1. **Individual susceptibility**

- Atopy
- Race/skin colour
- Age
- Hormonal
- Barrier function
- Repair capacity
- Other skin disease

2. **Site of exposure**

The rate of penetration of chemicals depends on

- Thickness of stratum corneum
- Density of hair follicle
- Presence of sweat duct and sebaceous glands

The skin of the face, scrotum and dorsum of hand is more permeable than skin elsewhere in the body.

C. COFACTORS

- Mechanical
- Thermal and climatic

SPECIFIC IRRITANTS[7]

Acids

Irritant contact dermatitis can be caused either by strong acids (hydrochloric acid, sulphuric acid), weak acids (lemon, vinegar) or acid anhydrides. It depends on the strength of acid used and the integrity of skin barrier. Weak acids are used as preservatives. However, acid anhydrides are more irritant than their corresponding acids. eg., phthalic anhydride. Other list of acids used in various industries are

- Chromic acid - Iron industries as rust proofing
- Hydrofluoric acid – Electronic, glass and petroleum industries
- Hydrochloric acid - Masons for cleaning hands and building stones
- Propionic acid[8] - Animal feed preservation

Alkalis

The mechanism by which alkalis cause contact dermatitis are saponification of surface lipids, breaking the keratin cross linkages and therefore causing swelling up of cells. Soaps, potassium and sodium hydroxide, ammonia, chalks are certain alkalis in common use. Cement cause contact dermatitis in masons and construction workers. Ammonia gas used in copying paper industries produce irritant dermatitis of face.

Alkalis are used in many industries like rubber, dyeing, plastic, tanning and glass industries.

Organic solvents

Organic solvents are aliphatic hydrocarbons and aromatic hydrocarbons that contain benzene ring. They include white spirit, petroleum products and kerosene.

Aromatic hydrocarbons include benzene, toluene, aromatic petroleum solvents, chlorinated compounds and alcohols. Organic solvents are used mainly in textiles, metal industries, dyeing and painting industries and less frequently in the graphic industries and for flooring. Their chemical structure determines the irritant potential.[9]Aromatic solvents are most irritating followed by aliphatic and chlorinated solvents. Esters and ketones are least irritating.

Oxidizing agents

Commonly used oxidizing agents are benzoyl peroxide, sodium hypochloride and ethylene oxide. They are used in bleaching textiles, oils and floors, removing stains from hands by printers and dyers and as sterilizing agents.[10] Ethylene oxide is used as sterilizing agents and may remain on instrument.

Reducing agents

Phenols, thioglycolates and aldehydes[11] are the reducing agents frequently used. Thioglycolates used in cold waving industries act by breaking down the disulphide bonds in keratin thereby increasing percutaneous absorption.

Detergents

The irritancy of detergents grossly varies from other compounds, since its action being unique to the molecular chemistry, pH, oxidizing properties and the enzymes used in detergents.[12] Even in neutral pH, they exert their action by dissolving lipids present on skin surface and by removing water holding substances accompanied by protein degradation and affects cell membrane integrity. They are the source of irritants in domestic as well as in industrial set up.

Oils

Metalworking fluids in increasing order of irritancy are neat oil, soluble oil, semi-synthetic and synthetic oils.[13] Oil acne follows irritation by local application of metalworking fluids. Emulsifier is the principle irritant in water based metalworking fluids.

Skin cleansers

Aromatic waterless cleansers[14] are the major offenders, as they have become habitual among newer generation. Solvents present in soap raises the pH the end result of which dissolve skin lipids. Silica and sand added to this substance perpetuates damage by mechanical abrasion.

Plants[15] and animal products

Citrus peel, flour, flower bulbs, wood dust, spices, corn, pineapple, papaya, garlic and onion are major plant irritants. Mustard family act as irritant and can cause bullous reactions. Caterpillars, carpet beetles can cause irritant dermatitis characterized by papules and vesicles. Onycolysis in butchers occurs due to pancreatic enzymes.

Hard Water

Water is hypotonic and dissolves the protective hygroscopic substance on eroded skin. Hard water containing lime, magnesium and iron can cause mechanical irritation and is more irritant than soft water.[16]

Physical factors

These are heat or cold, humidity, electricity, and UV light.

Mechanical factors

They include friction or trauma produced by rubbing, scratching and srubbing of metal dust, cement, silica and glass spicules. Asbestos, plaster and metal particles in welding industries can cause irritant dermatitis.

CLINICAL FEATURES

The wide spectrum of irritant reaction may be classified into the following types:

1. Chemical (Toxic) burns.

2. Irritant contact dermatitis.

It is of two types acute and cumulative.

3. Non-immune contact urticaria.

4. Symptomatic (subjective) irritant response.

5.Others localized to appendages, granulomatous and pigmentary response.

Chemical burn

It is an irreversible cell damage and necrosis and is characterized by rapid onset of pain, erythema, bulla and ulcer.[17] The onset of symptoms of chemical burn may be delayed for phenol and hydrofluoric acid.[18]

Burns are classified according to the depth of cutaneous involvement:

1. **Superficial partial thickness burn**

It extends up to dermal papilla and appears pink to red and wet as a result of capillary leakage. Dermal capillaries are intact and blisters may be present. Sensation is preserved. It heals within 10-14 days without scaring.

2. **Deep partial-thickness burns**

It extends into dermis and appendages are spared. It appears white or pale pink and odematous. There is partial loss of sensation and only deep pressure sensation is retained. Processes of healing begin from the residual adnexal structures and completed by 6 weeks with scaring.

3. **Full-thickness burns**

It extends up to subcutaneous fat and appears brown/black or pale white, with a leathery eschar. Sensation is completely lost**.** Healing occurs slowly with scaring and formation of contractures are present.

4. **Fourth degree burns**

It involves deeper structure like tendon, muscle, bone and joints.

Irritant contact dermatitis

"Irritant contact dermatitis represents the cutaneous response of skin to physical or toxic effects of wide range of environmental exposure"

It closely resembles allergic contact dermatitis or other endogenous eczema thus delineating these clinical conditions is a challenge. Therefore, its essentially a diagnosis of exclusion.

Acute irritant contact dermatitis[19]

"Acute irritant contact dermatitis results from single overwhelming or a brief repeated physical or chemical contact to an irritant leading to acute inflammation of skin." The clinical spectrum widely ranges from immediate burning or stinging sensation with transient erythema followed by edema, vesicule, bullae and necrosis of tissue. The evolution of lesions are strictly restricted to the site of application and is invariably associated with pain. The signs and symptoms can further be worsened by occlusion. Complete resolution may be acquired within few days to several weeks depending on the severity of irritant response. Irritants such as propylene glycol and diacrylates shows delayed irritant response.

Cumulative irritant dermatitis[20]

It occurs due to repeated and damaging insults to the skin. Both physical factors (trauma and friction) and chemicals combine together and play a role in skin damage. It begins as a localized dry patch progressing to inflammation and chapping. Sites commonly affected are fingertips, web spaces and dorsum of hands. Various occupations associated with irritant contact dermatitis are hairdressing, painting, printing, construction industries, mechanical industries, agriculture and fishing.

Non-immune contact urticaria

Non-immune contact urticaria typically occurs as transient erythema or urticarial wheal and flare that develops within minutes of exposure and fades quickly within hours.[21] They affect both normal and eczematous skin of unsensitized individuals. A vast list of agents cause contact urticaria, some of them are animals (arthropod, caterpillar, jellyfish, etc) foods (mustard, cayenee pepper), fragrances (cinnamic acid and aldehydes, balsam of peru, thyme, etc), medicaments (benzocaine, cantharidin, camphor) and preservatives such as benzoic acid.

Symptomatic irritant response

It is the subjective feeling of stinging or burning sensation caused by an irritant, yet without any obvious clinical skin changes. Many a times,

this response is attributed to cosmetic intolerance as it occurs usually over head and neck. These individuals are termed to have ‘sensitive skin’. Though the mechanism is unclear, it’s presumed that the irritants penetrates via sweat duct and hair follicle opening thus stimulate sensory nerve endings.[22] Factors predisposing to sensitive skin include young females with fair skin, hormonal status, exacerbates in summer, thin stratum corneum, increased sweat glands, increased nerve innervation and impaired barrier function. Two types of responses are noted

1. Immediate type stinging caused by chloroform, methanol, 95% ethanol within seconds of contact

2. Delayed type stinging develops within 1-2 min of contact reaching a maximum at 5-10 min and fades slowly by half an hour. This is caused by salicylic acid, resorcinol, benzoyl peroxide, propylene glycol, lactic acid.[23]

Other irritant responses

1) Folliculitis - Tar, oils and arsenic
2) Acne by Halogenated aromatic hydrocarbons.
3) Miliaria – Alluminium chloride, chronic occlusion.
4) Hyperpigmentation – Arsenic, gold, silver, mercury, bismuth.
5) Hypopigmentation – Phenols and catechols.

6) Granulomatous – Silica, talc, beryllium & Alopecia by Borex, chloroprene dimmers.

ALLERGIC CONTACT DERMATITIS

Allergic contact dermatitis is due to delayed type of hypersensitivity reaction or cell mediated immunity to various allergens.

History

The term "ALLERGIE" was first coined by Von Pirquet in 1906.[24]In Greek "Allos" and "ergon" means other or different work. Bloch and Steiner-Woerlich first prooved allergic sensitization of human skin to Primula extracts. Jacob and Landsteiner explained the basic pathogenesis of allergic contact dermatitis.

The various substances causing allergic contact dermatitis are cement, hairdye, nail varnish, kumkum, fragrances, rubber, metals (nickel, chromium, cobalt,etc) clothing (dyes), topical medicaments, preservatives, leather, colophony, plants and woods. Among these allergens kumkum was chosen for our study.

Patch testing is the tool to diagnose allergic contact dermatitis. In 1847, Stadeler developed a rudimentary patch test by using blotting paper and reproduced the lesions provoked by Anacardium occidentale. It was

Josef Jadassohn, in 1895 described the conventional method of patch testing while he was working in Breslau university.[25] Brono Bloch in who is a pioneer in dermatology expanded Jadassohn's patch test technique in 1911. He also introduced grading for patch test reactions and explained standard series concept, cross sensitization and systemic contact dermatitis.[26] Marion Sulzberger who works as an assistant to both Jadassohn and Bloch introduced patch test in New York. He further strongly advocated and promoted the use of patch to New world. Our present day standard patch test series was an expanded form of the prototype, given by Paul Bonnevie, former assistant of Bloch.

PATHOGENESIS

Two main process are involved

1. Sensitization (induction or afferent limb)
2. Elicitation (efferent limb)[27]

SENSITIZATION

The main events are

1. Binding of allergen

An allergen binds covalently to a skin peptide to result in reaction product which comes in contact with langerhan's cell and associates with

MHC class II molecule on HLA-D locus.[28] This process occurs within 6 hours for epicutaneously applied allergen. Costimulatory factors such as IL 1β, TNFα and GM-CSF are required for activation, maturation and migration of Langerhans' cell.[29]

2. Recognition of complete or conjugated antigen

The langerhan's cells carries the antigen to regional lymphodes and it is apposed to T lymphocytes in paracortical area.[30] Various factors that favors binding are first, by the ruffled membrane and the dendritic nature of Langerhans' cells and intricate structure of the paracortical area, secondly, by the interaction of cellular adhesion molecules like LFA-1(CD4 cells) with ICAM-1(Langerhans' cells) and CD2 on T cells with LFA-3 on nucleated cells. Recognition of antigens releases mediators or cytokines like IL-1 by antigen presenting cells and IL-2 by T lymphocytes.

3. Proliferation and dissemination of sensitized T lymphocytes

The cytokines leads to activation, maturation and proliferation of cytotoxic CD8 and CD4 cells. These T cells travel all over the body and interact with antigen present in the skin leading to localization to the sensitization site. As a result keratinocyte death occurs by Fas ligand and perforin mediated pathways induced by cytotoxic T cells.

ELICITATION

Re-exposure to specific allergen in a sensitized individual results in clinical reaction within 24-48 hrs. Antigen may be presented not only to langerhan's cell but also IL-1 secreting keratinocytes. It results in cytokine release leading to inflammatory response. A delayed reaction time is found with low degree of sensitivity following exposure to small amount or delayed penetration of allergy.

PREDISPOSING FACTORS

INDIVIDUAL

1. Constitution

Sensitization requires individual susceptibility. Some individuals are resistant to sensitization as a result of repeated exposure to the allergen through sub-sensitizing doses or via the oral route with the development of tolerance.[31] False positive reactions in patch test are seen to metals like nickel, cobalt and chromate frequently in atopic individuals.

2. Sex

Cell mediated immunity is stronger in women than men.[32] Females are exposed more to metals, cosmetics, fragrance and hair dyes. Positive results in patch test are seen more in females than males.

3. Hormones

Oral contraceptives increases DNCB response. Premenstrual exacerbation of nickel allergy has been described. Pregnancy either improve or aggravate contact dermatitis.[33]

4. Race

Racial differences exist but it is not due to predisposition. It occurs as a result of difference in exposure in different races.[34] Afro-Caribbean are more resistant than white people.

5. Age

Age plays little role in sensitization. Positive patch test reactions are increased in old age due to more allergies and medicaments exposure in their lifetime. Increased prevalence in children is due to ear piercing.[35] Chromates and resins present in footwear also responsible for increased sensitization in children. Young adults test positive more for occupational and cosmetic allergens.

6. Medication

Immunomodulators, prednisolone more than 15 mg/day and potent topical steroids, UVB, PUVA therapy gives negative patch test reaction.[36] Antihistamine and sodium cromoglycate have only little influence on patch test reaction.

7. Coincidental disease

Contact sensitization is impaired in both cutaneous and internal malignancies.[37]

8. Local factors

Irritant dermatitis increases absorption of allergen and chances of secondary sensitization because of the presence of immunocompetent cells and cytokines at the site of damaged skin .Chromate, nickel and cobalt sensitivity is increased in patient with hand eczema.[38]

9. Atopy

Atopic dermatitis increased the chances of developing hand eczema by 3 folds. Atopy doubles the effect of irritant exposure. They also have a poor prognosis than non atopics, as they have persistent dermatitis even if they change their jobs.

ENVIRONMENTAL

1. Climate

Heat, UV rays and humidity have a role in contact sensitization. UVB exposure depletes langerhan's cell and reduce skin contact allergy.[39] Chapping of skin in winter leads to irritant contact dermatitis.

2. Flora and fauna

Allergic plants of compositae family[40] are destroyed during winter and return during summer. Spread of allergic plant material is caused by dry wind. Animals doesn't have major role in seasonal cause.

3. Socioeconomic and cultural

Socioeconomic status will determine the pattern of cosmetic, perfumes and jewelry exposure. Hair dyes, kumkum and bindi allergy is common in Indians.[41]

CHEMICAL

Skin cells binds to haptens to form hapten-protein complex or complete antigen.[42] Covalent bond is formed between skin protein and hapten.

PATCH TESTING

The patch test is the only practical test for demonstrating contact type of allergy. It is a proof for diagnosing allergic contact dermatitis. Patch test

helps in identifying the allergens causing delayed type hypersensitivity in a patient which may not be identified by blood test or skin prick test.

The aim of patch test is to decide whether the test is positive or negative, whether it is an allergic reaction or as an irritant reaction and finally to quantitate the degree of sensitivity. Activated T lymphocytes present at the site of patch test will produce delayed hypersensitivity reaction. A positive patch test reaction indicates allergic contact sensitivity.

Indications[43]

1. Eczematous disorders in which contact allergy is suspected or is to be excluded.
2. Eczematous disorders not responding to treatment.
3. Eczema of the eyelids, face, ears and perineum (intermittent or persistent).
4. Chronic foot and hand eczema.
5. Stasis eczema.
6. Asteatotic eczema
7. Eczematous lesions around leg ulcer
8. Atopic dermatitis
9. Pompholyx or dishydrotic eczema
10. Lichenification
11. Seborrhoic dermatitis (acute inflammatory stage)

12. Nummular dermatitis

Methods

Patch testing elicit an immune response in sensitized persons to a defined amounts of allergen and is useful in assessing the degree of response. The amount of allergen used depends on its concentration present in the vehicle.[44] The fixing tape to which the chambers or discs attached should be non - occlusive, non-irritant and non-allergenic.

- The procedure should be delayed
    - For 15 days if acute eczema present at test site
    - for 4 weeks following sun bathing
- Stop immunosuppressive drugs
- UV light exposure to the test site should be avoided.
- Systemic corticosteroids dose equivalent to less than 15 mg of prednisolone[45]
- Avoid patch test in pregnant patients for any adverse event.

Test material

Various patch test chambers recommended by International Contact Dermatitis Research group are:

a) Finn chamber

b) AL-test Unit

c) Duhring chamber

d) Van der bend square plastic chamber

e) Oval plastic chambers (epicheck)

f) TRUE – thin layer rapid use epicutaneous test

Finn chamber

Finn chamber was devised by Pirila (1975). The chambers are made up of stiff aluminium with a diameter of 8mm and a depth of 0.5mm.[46] A filter paper is required when testing with solutions.

AL-test unit

Fregert (1972) introduced the AL-test unit which was recommended by International Contact Dermatitis Research Group and the North American Contact Dermatitis Group (1973). It is now rarely used. It consists of aluminium foil covered with polythene and 10mm central disc of filter paper adhered by heat and not by glue.[47]

Duhring chamber

Duhring chamber was designed by Frosch Kligman (1975). It is an enlarged aluminum unit measuring 18mm across and a capacity of 250 microlitres and six to eight patches can be fixed to the flexor surface of each forearm.[48]

Van der bend square chamber

Van der bend square chamber was first introduced by Malten and Nater et al (1976). A square application area makes it easier to

differentiate between allergic test reaction and toxic reaction since the later corresponds exactly to the shape of chamber. The adhesive tape used not only keep the tests in place, but also provide some degree of occlusion which aid in hydration of horny layer thus providing better penetration. Some may be sensitive to colophony-based adhesive tape to whom an alternative acrylic based or plastic based adhesive tape can be used.

Pasricha in 1981 described an indigenous method of patch testing. The patch test unit consists of a 4cm square adhesive plaster, the centre of which 4-8 layers of 2.5cm square ordinary clean cotton gauze is stuck with. In the centre of the gauze one cm square piece of filter or cotton paper is placed. Allergen is soaked into or placed on the central piece before placing the unit on the patient's skin.

The disadvantages of this chamber are:

1) It is time consuming.

2) It occupies a large surface area, hence not ideal for testing more than 25 substances at one sitting.

3) Severe reactions may spread beyond the patch test site, because of lack of limiting device.

The antigen-impregnated-discs (AID) described by Pasricha (1981) can be used for patch testing by the patch test unit. An antigen impregnated- disc consists of 1 cm square piece of Whatman-3 filter paper

impregnated with a standard amount of the water soluble antigen. Antigen-containing-saucers are made of an antigenically inert material with 1cm diameter and 0.5mm in depth saucers filled with a standard quantitiy of the antigen in ointment form.

These ready-made materials offer certain advantages. In the case of antigen impregnated discs :

1) The antigen discs are more stable, being in the dried form.

2) No risk of increase in the concentration of the solutions by which may caused by evaporation of the solvent.

3) There is no risk of contamination since each unit is independent of each other.

4) There is no need to measure the antigen solution for every test.

Antigen-containing-saucers (ACS) have the same principle as Finn chamber, except the antigens are already placed in required quantity. The antigen containing saucers also have the same advantages as that of antigen impregnated discs, since there is no risk of antigen contamination in both, because each saucer are placed as independent units. Quantitation of allergen for each test is also not required.

An indigenous patch test unit resembling Finn chamber was described by Surinder Kaur and Sharma (1986).[49] The aluminium disc of size 7.0 – 7.5 used in this test are obtained from the tops of discarded

injection vials. The disc has smooth edges. They were placed on adhesive tapes of size 12 x 5 cm in two parallel rows of five each. The distance between the centre of two adjacent discs are maintained at 2 cm.

For aqueous antigens, a wisp of cotton wool touched with the antigen was placed in the chamber with a forceps.

The advantages of this chambers over other indigenous units are:

1) Having high value of ratio between volume / area; it gives a better response.

2) Need less time to prepare.

3) Tight apposition to the skin which is apparent from the indented ring on the surface when the unit is removed.

4) This can be washed and reused.

5) It occupies a small surface area, hence ideal for testing more substances in one sitting.

6) Reactions will not spread beyond the patch test site, because of the limiting device.

TRUE (Thin layered Rapid Use Epicutaneous test)[50] test consists of prepackaged allergen in a hydrophilic polymer and can be readily used. It is available in a standard series containing 24 allergens. The results

obtained were comparable with that of Finn chamber system. Its advantage over other methods are

1) Portable
2) Convenient usage
3) Gives consistent results

Vehicle

The aim of patch test is to reproduce allergic reaction and not an irritant reaction. Uniform dispersion of allergen and its particle size is important in obtaining good results. Hence, the allergens are dissolved in a solvent (vehicle) to achieve a desirable test concentration. The molecular nature of petrolatum like being more stable and hypoallergenic makes it the most suitable vehicle. It also has an added property of being occlusive thus preventing oxidation of allergens and prolongs its shelf life.[51] However, it is not the ideal agent in hot climates. Other substances used as vehicles are water, acetone, alcohol, methylketone and olive oil.

When organic solvents are used as vehicle, it should be allowed for a few minutes to evaporate before applying the patch test to prevent from irritant reaction. Modified Plastibase has been recently developed for the Indian Contact Dermatitis Group.[52]

Patch test concentrations

Higher concentration of allergen than that produces contact dermatitis is usually used for patch testing. It is advisable to start with low concentration of allergen and to gradually increase the concentration if doubtful. Open test can also be employed before performing closed patch test as occlusion enhance irritant potential of allergen.

Medicaments and cosmetics can be tested 'as is', whereas 'rinse off' products are tested at 5% concentration. Detergents, soaps and shampoos are tested at a concentration of 1% or less.

Patch test dose

The dose is 5 mm length of test substance if petrolatum is used as the vehicle in disposable syringe containers.[53] If the vehicle is a fluid, a drop of fluid or 15 μL in a pipette is placed on a filter paper in the chamber.

Storage of allergen

Allergen should be stored at 4°C in dark to prevent oxidation. Allergens stored in small jars results in evaporation of volatile substances. Homogeneity of allergens in the vehicle is lost in hot climate.

Test site

Upper back[54] is generally preferred for patch testing, because

(1) It provides a large skin area for testing

(2) Pressure on the back during lying down helps a better contact of the allergen with the skin

(3) Least mobile area

(4) Less hairy

(5) Easy to do and read patch test

Other sites are upper arm and thighs, lower back, less commonly flexural aspect of the forearm and abdomen.

Marking

Margins of patch test site are marked preferably with skin marking pencil or with ink and stains. The patient is advised to avoid taking bath, sun exposure, excessive sweating, strenuous work and exercises which may dislodge the patch from its original position.

Exposure time

After 48-h of application, readings are taken 1 h after removal and again 48 hours later as allergens such as neomycin and topical steroids will produce delayed reaction, with the same observer taking both the readings.[55]

Erythema produced by stripping the tape is allowed to resolve and some reactions and infiltration will take 30 min to 1 hr to appear after release of pressure from the strips.

READING AND INTERPRETATION

According to **Contact and occupational dermatitis forum of India (`CODFI),** the patch test reactions are recorded as follows,[56]

-	Negative.
?-	Doubtful reaction; Only faint erythema seen.
+	erythema and papules (non-vesicular)
++	erythema, papules and vesicles (vesicular)
+++	erythema, edema and vesicles/bulla/ulcer (bullous or ulceration)
IR	Irritant reaction
NT	Not tested

Patch-test results are recorded objectively and interpreted separately. The difference between allergic patch-test reactions and non-allergic irritant reactions are,

S. No	**Allergic reaction**	**Irritant reaction**
1.	Infiltration present	No Infiltration
2.	Itching present	No itching
3.	Erythematous	Deep red or brown hue
4.	Reaction may extend beyond margin of the patch	Sharp line corresponding to margin of patch test

Non-invasive measurement techniques

Several non-invasive techniques used to quantify patch are laser Doppler flowmetry, high-frequency ultrasound, thermography, transepidermal water loss and skin reflectance method. But these tests are considered inferior to conventional patch testing.

FALSE POSITIVE REACTION

False-positive reactions occurs due to

- Increased concentration of allergen
- Irritant nature of vehicle
- Impure substance or contaminants present in test substance
- Uneven dispersion of allergen in vehicle
- Application of Excess allergen
- Active dermatitis at the site of patch test
- Active dermatitis at any other sites
- Pressure effect of Finn chamber
- Artefact
- 'Angry back' reaction[57]
- Reactions due to adhesive tape

FALSE NEGATIVE REACTION

- Insufficient concentration of allergen in vehicle
- Inadequate amount applied
- Substance degraded due to oxidation or loss of self life
- Poor adhesion of patches due to increased sweating
- Patches applied at wrong site where it is more likely to be disturbed
- Inappropriate vehicle
- Readings performed before 48 hours
- Pretreatment of patch-test site with topical corticosteroids
- UV irradiation or sun exposure of patch-test site
- Immunosuppression due to infection or systemic drugs[58]

COMPOUND ALLERGY

Finished product shows a positive patch-test reaction but the ingredients shows negative reaction. This concept proposed by Calnan was called as compound allergy.[59] In Hirudoid cream, a new allergen was formed as a result of combination of two preservatives in the cream.[60]

Quenching

Theoretically, combination of chemicals sometimes results in negative patch test reaction. This effect is called quenching effect.[61] It is seen in fragrance material containing aldehyde. Triclosan due to its anti inflammatory action cause quenching effect on nickel dermatitis.[62]

PHOTOPATCH TESTING

Indication[63]

- Eczema of light exposed site
- History of exacerbation of eczema following sun exposure
- History of reactions to sunscreens

Procedure[64]

- Two sets of antigens are applied on either side of the vertebral column
- Patch tests are removed after 48 hours and readings are taken
- One side of the test site is irradiated with $5J/cm^2$ of UVA with patients back positioned at 15 cm from the lamps
- Other side is kept as control
- The control site and the rest of the body are covered with opaque material during irradiation
- Steps to be taken to avoid any incidental irradiation by natural light of both the irradiated and control set of allergens
- Second reading is taken after 48 hours and noted

Readings

Readings are noted similar to routine patch test with the prefix Ph.

Results	**Readings**
Ph+	Weak positive reaction
Ph++	strong positive reaction
Ph+++	Extreme positive reaction

The results are interpreted as follows,

- Positive on irradiated side only indicates photoallergic dermatitis
- Strongly positive on both sides indicates contact dermatitis
- Positive on both sides but stronger on the irradiated sites indicates combined contact and photoallergic dermatitis

Complication

- Pruritus
- Folliculitis
- Infection
- Active sensitization
- Localized flare of dermatitis and other skin disorders
- Flare of dermatitis at previous contact sites
- Generalized flare of dermatitis
- Irritant reactions

- Persistence of patch test reaction
- Pigmentation or depigmentation
- Caustic burns and scaring
- Urticaria and
- Anaphylaxis[65](very rare)

MULTIPLE PATCH TEST REACTION

Causes of multiple patch test reactions are

1. Non specific hyperreactivity
2. Multiple primary hypersensitivities
3. Cross reaction

Non-specific hyperreactivity

It is proposed that, in patch test, the allergen is added at a concentration such that it never induces false positive reactions. Yet, some allergens requires a higher concentration to provoke a positive reaction. This threshold for a false positive irritant reaction varies among individuals.

When patch testing is done at active dermatitis stage or in 'status eczematicus' period, even uninvolved skin at distant site show features of irritant reaction.[66] It is stated as 'stochastic resonance' by Rietschel. He

proposed the reaction is due to “signal amplication of immune-mediated events by neurological influence”. If the same reaction is noted in adjacent patch test site it is called by various names like ‘spillover’, ‘excited skin’ or ‘angry back’.

To avoid non-specific weak false positive reaction, ideally patch test should be done after weeks or months, even when dermatitis has resolved.

Multiple primary hypersensitivity

Patients with long history of contact dermatitis will likely develop multiple sensitivities to unrelated chemicals. Sensitivity to one allergen will predispose the individual to acquire sensitivity to other allergens. Some may also exhibit genetic predisposition. It occurs due to application of allergens on eczematous skin which facilitates sensitization.[67] In such situation one allergen initiates a primary response, subsequent allergens maintain the eczematous state.

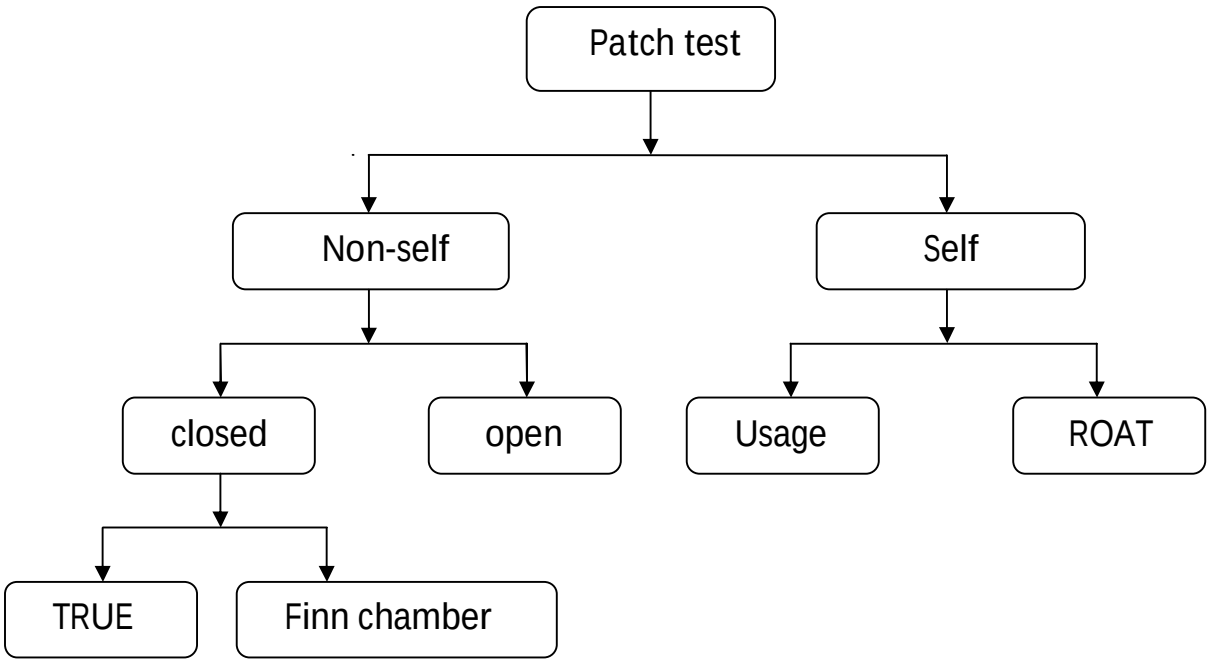
For example, if a person test positive for nickel he/she is more likely to test positive for palladium, as they both are placed closely in periodic table.

- Cobalt and chromate allergy is more common in cement workers.
- Positivity to topical medicaments, will show positive reaction to unrelated vehicle component.

- In foot dermatitis, concominant allergy to rubber and dyes in shoes and shocks occur. In contact dermatitis to cement, combined cobalt and chromate allergy will occur.

Cross reaction

The phenomenon of extention of sensitization of one allergen to another structurally related allergen is called cross-reaction. It is hypothesized that sensitized T cells are unable to differentiate between the closely related allergen, and thus exhibits an allergic reaction. Aromatic compounds like *p*-phenylenediamine, benzocaine, procaine, sulphonamides and para aminobenzoic acid will show cross reaction. Contaminants[68] may cause 'false' cross - sensitivity due to presence of traces of one substance in another.



Other tests for contact allergic dermatitis

Open test

In open patch test, allergens are applied over 1 cm^2 area of skin and allowed to dry. Readings are taken after 48 hours and interpretation of result is similar to closed patch test. When allergens with good penetration is used in sufficient concentration produce a positive reaction in sensitive individuals.[69] for example.,

- In Primula dermatitis, patients show positive, even bullous reaction when comes in contact with leaf.
- Its widely used before applying hair dye.
- They are sometimes used as preliminary screening test with unknown substances.

Usage test

This test is employed when both open and close patch test are negative, yet the history suggestive of or when you suspect contact dermatitis. Patient is advised to use the suspected product again. It is more useful to diagnose cosmetic and clothing dermatitis. However, it is difficult to differentiate between an allergic and a non-specific or irritant response.

Repeat open application tests (ROAT)

Substances are applied two times daily over 5 cm^2 area of skin for 4 weeks or until an allergic reaction develops. The most commonly used sites

are the upper part of arm or flexor aspect of the forearm.[70] A scale to record the results has also been proposed.[71]

Intradermal tests

Intracutaneous tests are performed with simple chemicals.

- On the first day erythema followed by swelling develop at the site of injection
- Papules or vesicles may develop after 2 to 4 days

The chemicals are used at 10-100 times lower concentrations than epicutaneous test.[72]

In vitro test

It includes Migration inhibition test, Lymphocyte transformation test and Leukocyte procoagulant activity. It measures products from T cell activation that are helpful in elucidating immune cascade.

PHOTO ALLERGIC AND PHOTOTOXIC REACTIONS:

The mechanism of photosensitization was reviewed by Thune.[73] Photoallergic reaction is a delayed hypersensitivity reaction in which photoallergic substances like sunscreens, fragrances, NSAIDS, quinolones, sulphonamides etc gets activated with UV radiation. Phototoxic reactions are non allergic cutaneous reaction induced by various topical and systemic drugs.

NON-ECZEMATOUS DERMATITIS:

Contact dermatitis are usually eczematous but occasionally it may be noneczematous and can present as follows,

1. Contact urticaria
2. Erythema multiforme-like
3. Purpuric contact dermatitis
4. Lichenoid contact dermatitis
5. Lymphomatoid eruptions
6. Pigmented contact dermatitis
7. Leukoderma
8. Contact granulomatous
9. Onycholysis

CONTACT DERMATITIS TO KUMKUM

Kumkum means saffron (Sanskrit=Saffron, a spice derived from the flower of Crocus sativus). Application of kumkum for religious purposes over the forehead and hair parting area was in practice since ancient times. Cosmetics such as kumkum or thilak are most commonly used by Hindus in India and in few other countries.[74] In olden days home-made kumkum was in practice. This is prepared by treating powdered turmeric with an alkali which imparts the characteristic red color to kumkum.[75] Whereas in

recent times, this has been replaced by commercial preparations with the advent of synthetic chemicals and dyes.[76] The knowledge of kumkum dermatitis and the allergens available for patch testing is very limited.[77] There is also paucity of data available from the manufacturers about the constituents of kumkum. There are only limited studies conducted in Indian population since many of them either remain asymptomatic or change their brand for which they may become allergic later on. With the available studies the most common allergen is red kumkum.[78]

ALLERGENS IN KUMKUM[79,80]

The various allergens in kumkum are

1) Thimerosal
2) ter-Butyl hydroquinone
3) Gallate mix
4) Para-phenylenediamine
5) Brilliant lake red R
6) Benzotriazol
7) Sudan I
8) Aminoazobenzene
9) Kathon CG
10) Parabens mix
11) canaga oil

THIMEROSAL

Thimerosal is an organic mercurial compound containing mercury and thiosalicylate with formula C9H9HgNaO2S and molar mass 404.81 g/mol. It has both antiseptic and antifungal property. Its bacteriostatic property is used in

- Multidose vaccine vials
- Kumkum
- Make-up removers
- Eye moisturizers, eye shadows and mascaras
- Soap free cleansers
- Ophthalmic drops

CLINICAL PRESENTATION

- Localized allergic contact dermatitis
- Redness and swelling at the injection site
- Hypersensitivity reactions
- Hand eczema
- Palmar and fingertip dermatitis
- Isolated conjunctivitis
- Corneal neovascularisation from contact lens

Patch test

0.1% thimerosal is used for patch testing

Thimerosal is reported as the most common allergen in recent years. Patients develop allergy either to mercury moiety alone or to thiosalicylic acid. False positive reactions noted in mercury sensitive individual.

TERTIARY-BUTYL HYDROQUINONE

ter-Butyl hydroquinone (TBHQ) is an organic aromatic compound. It is a hydroquinone derivative substituted with *ter*- butyl group. TBHQ has unique properties such as

- antioxidant
- preservative
- corrosion inhibitor in biodiesel
- Stabilizer - inhibits auto polymerization of organic peroxides
- Fixative

SOURCE

- Vegetable oil
- Kumkum
- Lipsticks, eye shadows, blushers

- Varnishes, lacquers and resins
- Perfumes

It is used in concentrations ranging from 0.1% to 1.0% as preservatives in cosmetics and in concentrations upto 0.02% is used to prevent rancidity of fats, oils and polyesters.

Patch test

1% ter-butyl hydroquinone is available for patch testing

GALLATE MIX

Gallic acid is a trihydroxybenzoic acid, an organic acid of chemical formula is $C_6H_2(OH)_3COOH$. Gallates are salts and esters of gallic acid and differ from each other in length of their side chains.[81]

Propyl gallate 0.5%

Octyl gallate 0.5%

Dodecyl gallate 0.5%

This Gallate mix was in use as an antioxidant since many years in cosmetic products. Multiple studies have reported sensitivity to octyl gallate, doceyl gallate and propyl gallate in descending order.[81,82] But

allergy to propyl gallate is reported more as it is the most commonly used in industry. These gallate mix are added as a part of other constituents in

- Lip balms and lip sticks
- Salves
- Cosmetic creams and lotions

Patch test

The ideal patch test concentration used is[83]

- Propyl gallate 1%
- Octyl gallate 0.25%
- Dodecyl gallate 0.25%

All diluted in a petrolatum or olive oil vehicle.

PARA - PHENYLENEDIAMINE (PPD)

It is an organic compound with the formula $C_6H_4(NH_2)_2$. It is an aniline derivative. It occurs naturally as a white solid that becomes dark on exposure to air due to oxidation. It has a high melting point and boiling point. PPD is allergenic in its reduced state, once it is oxidized and polymerized it's no longer allergenic.[84] PPD may cross react with various

other compounds such as aniline and azo dyes, local anaesthetics, esters, hydroquinones, PABA and phenylhydrazines etc.[85] Source of PPD are

- hair dyes
- kumkum
- henna tattoo
- photocopiers and printing inks
- petrol, oils, and greases

Patch test

1% PPD in petrolatum is used for routine patch testing.

KATHON CG

Kathon CG (isothiozolinones) are heterocyclic compounds. They are commonly used as preservatives in cosmetics and toiletries. It is a mixture of [86,87]

- methylisothiazolinone (1.125%)
- methylchloroisothiazolinone (0.375%)
- magnesium nitrate and magnesium chloride (23%)
- Water (75%)

Kathon CG is used as a biocides because of their extended antimicrobial properties against gram–positive and gram- negative bacteria, algae and fungi.[88,89] It is available as cosmetic grade at 1.5% active ingredient stabilized with magnesium nitrate. It is used as a cosmetic

preservative at a maximum permissible concentration of 15 ppm for rinse-off products and 7.5 ppm for leave-on products.

Source

- Shampoos and hair conditioners
- Surfactants
- shower gels and body washes
- bubble baths, liquid soaps and wipes
- cutting oils, military fuels
- paints, wallpaper pastes, glues
- household cleansers
- printing inks, fountain solution, as slimicide in paper mills

Clinical presentations

- hand dermatitis in hairdressers
- perianal dermatitis using moist toilet paper and wipes[90]
- exposure pattern of dermatitis seen in sensitized subjects staying in newly painted rooms[91]
- chemical burns from spillage of concentrated oils
- secondary delayed dermatitis from active sensitization[92,93]

Patch test

A concentration of 100 ppm in water is used for patch testing. A higher concentration of 200 ppm may identify sensitized individuals missed by 100 ppm.

PARABENS MIX

Parabens are ester derivatives of *para*-hydroxybenzoic acid. Parabens mix is colourless, odourless, stable and poorly soluble in water.[94] It contains the following substances such as Methyl para - hydroxybenzoate, Ethyl para - hydroxybenzoate, Propyl para - hydroxybenzoate, Butyl para - hydroxybenzoate, Benzyl para - hydroxybenzoate. They are the common chemical preservatives used in cosmetics since 1920s.

Source

At home

• Lipsticks and lip balms

• Pet care and grooming products

• Soaps and shaving products

• Topical anaesthetics

• Skin ointments, lotions, moisturizers and sunscreens

• Food preservative

• Shampoo, conditioner, hair colouring and hair care products

• Cosmetics such as foundations, blush, mascaras, eye shadows and eyeliner, lipsticks, nail varnish and makeup removers

At work

• Metalworking oils and fluids

• Cosmetics and hair care products

• Agriculture, food production and processing

• Veterinary medications

• Antiseptic topical medication

It is used as antibiotic conservator. They act against gram positive bacteria, moulds and yeast. It also possesses weak estrogenic activity.[95] It precipitates tumor formation by interacting with melanocytes through estrogen receptors in melanoma. They may also potentiate photo induced damage of keratinocyte by increasing the oxidative stress.

Parabens in food are orally absorbed and metabolized by esterases in liver to para-hydroxy benzoic acid and eliminated in urine as glucuronide, glycine and sulfates.[96,97] Parabens in skin care products are metabolized by skin esterases and only a few amounts is available to cross systemic circulation.[98]

Parabens paradox

Though individuals show patch test positivity to Parabens mix, they can very well tolerate the allergen containing personal products. This is called as Parabens paradox. It is weakly sensitive allergen and the prevalence is also low among general population.

Patch test

Patch testing can be done for individual allergen to detect whether it is truly allergenic. Parabens mix 12% in petrolatum is used for patch testing.

BENZOTRIAZOLE

Benzotriazole is a heterocyclic compound with three nitrogen atoms and a fused benzene ring. Its chemical formula is $C_6H_5N_3$. It is colourless and a polar compound. It is synthesized by combining benzene-1, 2-diamine and carboxylic acid. It has antibacterial, antifungal, antiviral and anti-inflammatory. It also exhibit mild antihypertensive and analgesic properties.

Uses

- photographic emulsions fixator
- anti-tarnish agents
- corrosion inhibitor
- antifreeze in water coolant systems
- cosmetics- to prevent photo degradation
- anti- ageing

Benzotriazole has very low sensitization potential. It is used in concentration of 1% in petrolatum.

SUDAN I

Sudan I (1-phenylazo-2-naphthol) is an organic compound, which is classified under azodyes. It is also known as CI Solvent Yellow 14 and Solvent Orange R. It is added to various products such as waxes, oils, petrol, solvents and polishes to impart characteristic orange-red colour. It is also used as colouring substance in various foodstuffs. Sudan I is found to be genotoxic and carcinogenic in animal studies.[99] Comparisons between experimental animals and human Cytochrome P450 (CYP) strongly suggest animal carcinogenicity data can be extrapolated to humans[100] It is used in cosmetics in various concentrations ranging from 2.789 mg/gm to 8.694 mg/gm. Sudan I have also been implicated as the cause of pigmented allergic contact dermatitis

in red "kumkum"[101]. A metabolite of sudan I which is obtained by *para*-hydroxylation of its phenyl group may play major role in its allergic potency.[102]

Patch test

Sudan I 0.1% in petrolatum

LANOLIN

Lanolin is a natural product obtained from sheep fleece. It's a complex mixture of fatty acids, fatty alcohols and their esters. Hydrolysis of the wax portion of the fleece yields wool wax alcohol also called lanolin alcohol.

Allergenic potential of lanolin can be modified by various chemical processes such as acetylation, transesterification, hydrogenation, ethylenation and finally the allergens thus obtained are removed by purification.[103] They can also be made hypoallergenic by reducing the alcohol levels to less than 3% (w/w).[104]

Source of exposure

- paints and polishes
- adhesive plasters, sealants
- textile industry
- cosmetics
- pharmaceuticals
- anticorrosive coatings and cutting oil emulsions

Lanolin is used as an emulsifying and stabilizing agent in cosmetics and in pharmaceutical bases. It is also used as an emollient. Symptoms of contact dermatitis to lanolins negligible in healthy population, but sensitization is accomplished more easily because of prior subclinical sensitization and conditioning exposure.[105]

Patch test

Patch test is done with wood alcohols 30% in petrolatum. Identifying the individuals with allergy can be improved by patch testing with wider range of lanolin derivatives. Amerchol L 101 50% in petrolatum and lanolin 'as is' can also be used to increase the number of positive cases.[106]

BRILLIANT LAKE RED

Brilliant lake red is an azodye with molecular formula C34H22CaN4O6. Commercial preparations contain ethyl extractable impurities, among which sudan I is considered as potent sensitizer. It is used in lipsticks, lipslaves, enamels and as food additives. It is the most important agent in causing pigmented contact dermatitis.[107] Patch test is done at concentration of 1% petrolatum.

CANAGA OIL

Canaga oil also called ylang-ylang oil is obtained from the flowers of Canaga odarata. The yellow flowers are subjected to various chemical processes including steam distillation and various allergens are separated.

Dihydro di-isoeugenol is the main sensitizer.[108] It was first described as a common sensitizer in 1971.[109]

Uses

- aromatherapy and perfumes
- anti-hypertensive
- normalize sebum secretion
- treating insect bites and wounds
- aphrodisiac
- Body lotions, Scented sprays
- creams and shampoos

Other known allergens in kumkum include various dyes such as coal tar dyes, toluidine red, erythrosine, lithol red, calcium salt, groundnut oil, tragacanth gum and turmeric powder.

The various clinical manifestation caused by these allergens in kumkum are

- Pigmented contact dermatitis
- Allergic contact dermatitis
- Irritant contact dermatitis
- Contact urticaria

PREVENTION OF CONTACT DERMATITIS

Prevention can be divided into primary, secondary and tertiary.

1. Primary – prevention of sensitization induction and control of exposure

2. Secondary - prevention of elicitation

3. Tertiary - measures to control established and on going dermatitis

Various steps that can be taken for prevention of contact dermatitis are

1. Allergen containment and replacement

2. Legal and regulatory measures

3. Corporate responsibility

4. Domestic precaution and hygiene

5. Proper education

Regulatory measures followed in various countries across globe are

- Release of nickel is restricted to 0.5µg/cm^2/week
- Amount of hexavalent chromium in cement should be <2ppm
- Preservatives like MCI/MI not allowed above 15 ppm in cosmetics
- Formaldehyde >0.2% is not permitted
- Use of fragrance >10ppm for 'leave-on' products and >100ppm for 'wash-on' products should be labelled
- Use of acrylates is limited to 0.5-2%
- Products with skin sensitizer >1% should be labelled as "R43-may cause sensitization by skin contact"

- Persulphate use is prohibited in baking industry
- Finland limits the use of formaldehyde for clothing
- Turpentine use in paints strictly limited in Germany

TREATMENT

Avoidance advice

Possible sources causative allergen(s) should be identified, advised and motivated to avoid further exposure and other related allergens. Appropriate protective clothing or changes in handling technique may be advised. In some patients continued exposure is unavoidable, but can be reduced to a sufficient degree to keep the dermatitis at an acceptable level. It is advisable to stress that allergy does not disappear when the dermatitis clears, but that the risk of relapse after further contact with the allergen persists throughout life.

Active treatment

The main treatment consists of avoidance of the causative factors, but topical corticosteroids are necessary to control the disorder.[110]

Other treatments are

1. Emollients should be used adequately and regularly

2. For acute eczema wet dressing is done with saline, aluminium acetate, potassium permanganate 1in 8000 dilution or silver nitrate

3. Antibiotics for Secondary infection

4. Antihistamine for itching

5. In severe cases or dissemination, systemic steroids are used

6. Topical tacrolimus and pimecrolimus is used in atopic eczema

7. Immunosuppressive drugs such as azathioprine and cyclosporine for recalcitrant cases

PROGNOSIS[111]

The prognosis of allergic contact dermatitis is determined by its cause and avoidance of repeated and continuous exposure of allergens. Once a person acquires sensitivity to an allergen, it tends to persist. Sensitivity to ubiquitous allergens eg., chromate, nickel, PPD persists whereas, sensitivity to weaker allergens may disappear. Cross-sensitization also reported to remain as such. A chronic dermatitis patients, atopics and older age persons have poor prognosis and may affect quality of their life. Chronicity is attributed to the following factors

1. Impaired barrier function of the skin

2. Inappropriate treatment

3. Ingestion of allergens

4. Infection

5. Stress

6. Auto sensitization[112]

7. Constitutional factors

8. Inherent tendency to become continuous and chronic

9. Atopy

AIM OF THE STUDY

(1) To study the age and sex incidence of contact dermatitis to kumkum among patients attending our OPD.

(2) To study various types of clinical presentation among the patients.

(3) To study various clinical pattern of distribution of kumkum dermatitis.

(4) To study the association of contact dermatitis to kumkum and atopy.

(5) To confirm allergic contact dermatitis by doing patch test.

(6) To study the association between the duration of exposure to kumkum and the onset of clinical manifestations in the study group.

STUDY DESIGN:

Prospective and observational study.

INCLUSION CRITERIA:

(1) Patients with symptoms suggestive of irritant/allergic contact dermatitis who give history of exposure to kumkum.

(2) Patients who are able to understand the value of the patch test, ready to give consent and can come for follow up are included in the study.

EXCLUSION CRITERIA:

(1) Patients with irritant/allergic contact dermatitis without history of exposure to kumkum.

(2) Age less than 18 years

(3) Pregnancy and lactation

(4) Active disease at the site of patch test

(5) Recent history of patch test

(6) Patients who are immunocompromised due to disease or drugs.

(7) Patients on steroids (T. Prednisolone or equivalent to >15 mg) for any other medical illness

(8) History of topical steroid application on back for 1 week prior to patch test

(9) Patients with sunburn on back within last 2 weeks

MATERIALS AND METHODS

SAMPLE:

About 50 cases of contact dermatitis with history of exposure to kumkum attending the Occupational contact dermatitis outpatient department, Department of Dermatology, Rajiv Gandhi Government General Hospital and college, Chennai from November 2013 to August 2014 were included in the study. The study was approved by the institutional ethical committee, Rajiv Gandhi Government General Hospital and college, Chennai. A written consent form was obtained from all patients included in the study.

METHODS:

A detailed history of the patients including the age, sex, chief complaints, the type of occupation were noted. Their duration of exposure to kumkum and the duration of complaints were noted. Based on the morphology and distribution of the lesion patients were diagnosed as having either pigmented contact dermatitis, allergic contact dermatitis, irritant contact dermatitis, contact urticaria or a combination of these were documented. Clinical pattern and the site of distribution of the contact dermatitis were recorded. Any history, symptoms and signs suggestive of atopy were noted family history of atopy was also inquired. A thorough past history of similar illness and any history of drug intake prior to and

after the onset of lesions were noted. Any history of topical application over the site of contact dermatitis were recorded.

All the patients were subjected to blood investigation namely complete hemogram, liver function test, renal function test and absolute eosinophil count. Patients with history and clinical features suggestive of contact dermatitis due to kumkum were patch tested with allergens in kumkum and patient used kumkum ‘as is’

PROCEDURE

Patch testing was done for all the patients with the following allergens available in the Indian standard series approved by the Contact and Occupational Dermatitis Forum of India (CODFI) marketed by Systopic laboratories limited.

a) para- Phenylenediamine (PPD) - 1.0% pet
b) paraben mix 12.0% pet
c) Gallate mix 1.5% pet
d) Benzotriazole 1.0% pet
e) ter- Butyl hydroquinone 1.0% pet
f) thimerosal 0.1% pet
g) patient used kumkum ‘as is’

Patch testing was done as follows

1. Allergens were stored in the refrigerator at 4 degree C to 8 degree C. It is taken out from refrigerator 15 min before testing.

2. The patch test unit was marked with the name of the allergen to be tested.

3. The protective foil of the Finn chamber was removed and the patch test unit was placed on the table with the aluminium chambers facing up.

4. Vaseline (used as control) and other allergens were applied on their respective marked Finn chambers.

5. 5mm length of the allergen from the syringe was put in the centre of the aluminium chambers.

6. The kumkum which the patient uses is included ‘as is’ in patch test.

7. The upper back of the patient was gently cleaned with sterile gauze before appliying the patch test.

8. Patches were removed after 48 hours.

9. Reading was taken after 30min.

INSTRUCTIONS GIVEN TO THE PATIENT:

1. Patch test to be left in place for two days and two nights.

2. Not to take bath or wash the back during that period.

3. To avoid tight garments.

4. To avoid exercise or any other activity causing sweating.

5. To avoid friction or rubbing, scratching the patch test site.

6. To avoid exposure to sunlight or artificial UV light

7. To report immediately if there is any severe itching or irritation.

8. To come for patch test reading after 48 hours.

The readings were compared with the control and were interpreted according to the guidelines devised by the Contact and Occupational Dermatitis Forum of India (CODFI).

OBSERVATION AND RESULTS

A total of 50 patients attending our occupational contact dermatitis OPD with the history of contact dermatitis to kumkum with variable duration of exposure were included in the study. Based on history and clinical morphology, they were diagnosed as allergic contact dermatitis, irritant contact dermatitis, pigmented contact dermatitis and contact urticaria. All the cases were patch tested with standard allergens specific to kumkum. The patients were adviced to bring the kumkum which they are using and it is included in the patch test. The kumkum is used 'as is' under occlusion.[113]

TABLE 1 - INCIDENCES OF KUMKUM CONTACT DERMATITIS

Gender	Total OPD	Contact Dermatitis	Kumkum Dermatitis
Males	2018	703	13
Females	1276	413	37
Total	3294	1116	50

Among 3294 patients attending occupational contact dermatitis department, 1116 patients (33.87%) comes with the complaints of contact dermatitis. In this group about 50 patients (4.48%) had history of contact dermatitis acquired by using kumkum.

CHART 1 - INCIDENCES OF KUMKUM

CONTACT DERMATITIS

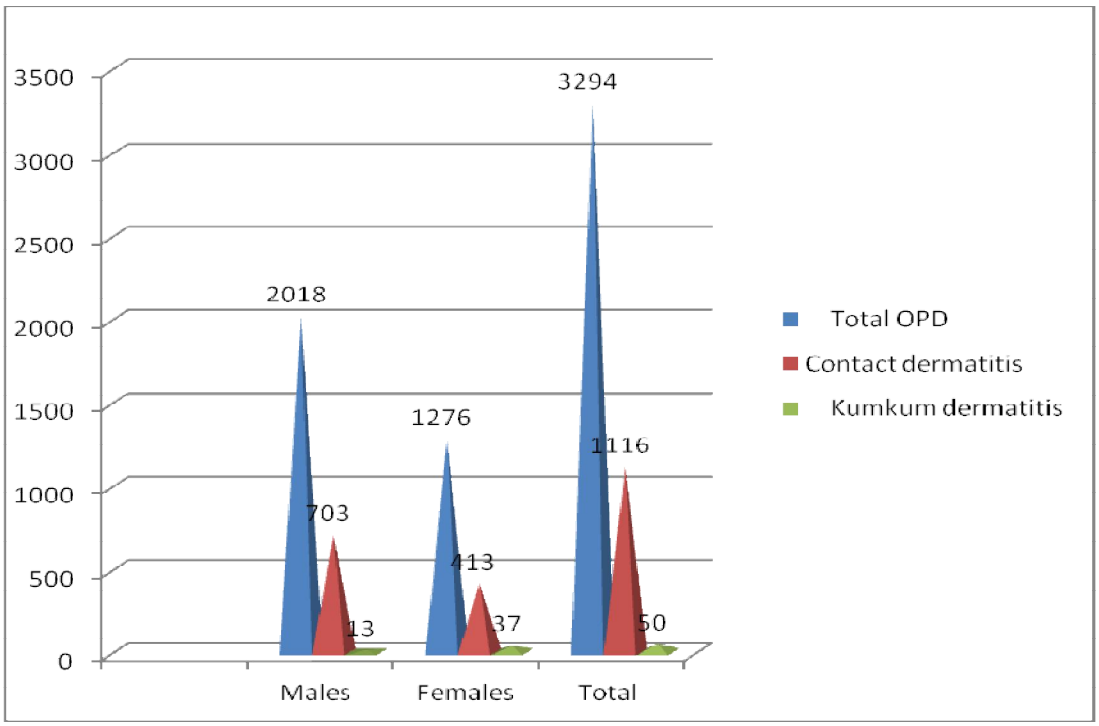


TABLE 2 – SEX DISTRIBUTION

Gender	Frequency	Present
Males	13	26 %
Females	37	74 %

Out of the 50 patient, 37 cases (74%) were females and 13 cases (26%) were males. The same is represented in chart.

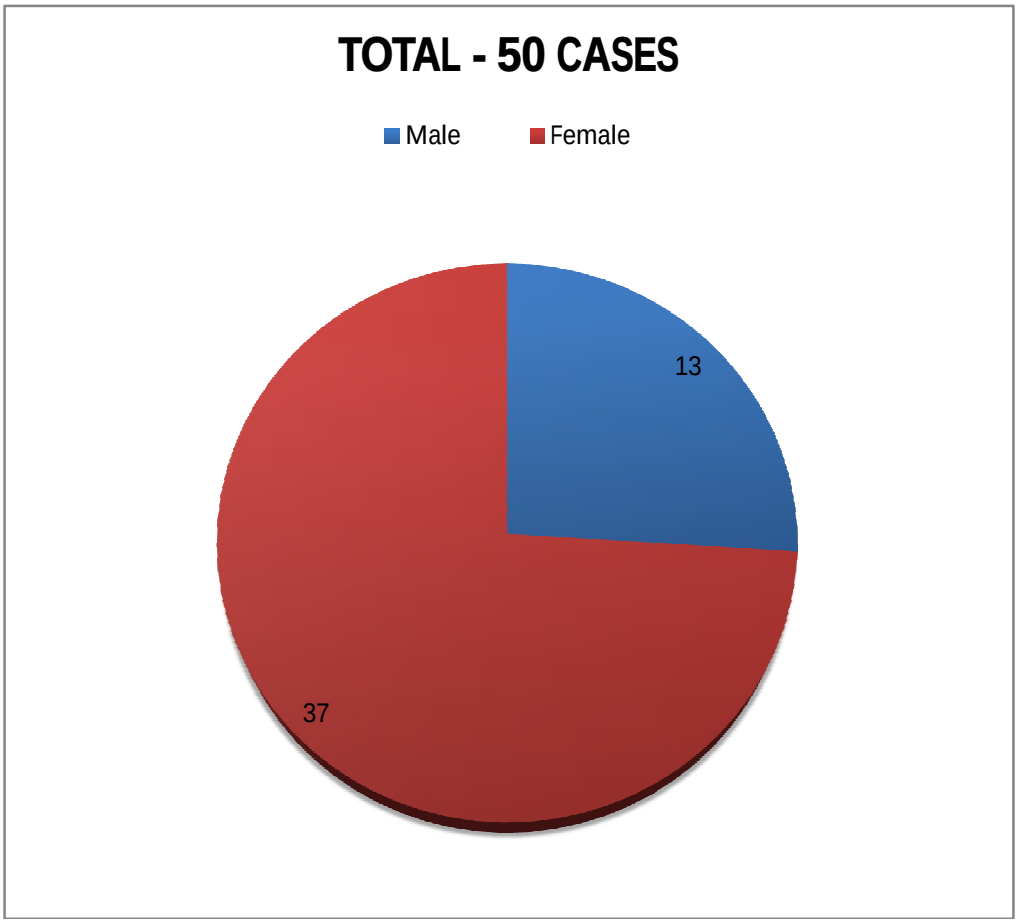
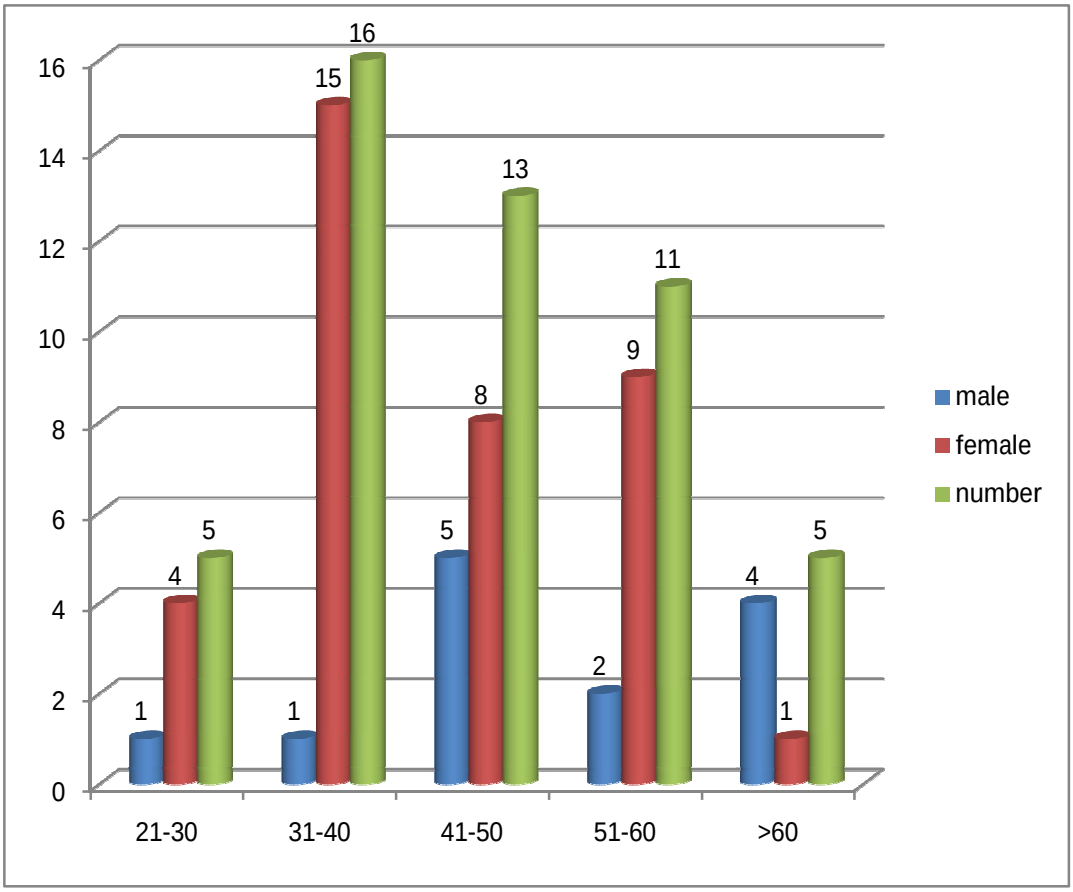


TABLE 3- AGE AND SEX DISTRIBUTION

Age group	Sex		Number	Total (%)
	Male	Female		
21-30	1	4	5	10%
31-40	1	15	16	36%
41-50	5	8	13	26%
51-60	2	9	11	22%
>60	4	1	5	10%

Majority of the patients (29 cases) were in the age group of 31 – 50 years. They formed 62% of the total. Age group of 51 – 60 had 11 patients with 22 percentage. 5 patients each about 10 % were in the age group of less than 30 years and more than 60 years. The youngest patient in the study was 21years old female and the oldest was 71 years old male.

CHART 3- AGE AND SEX DISTRIBUTION



This chart shows that maximum number of patients were in the age group of 31-40 years wich includes total of 16 patients (15 females and 1 male). The second most common age group was between 41-50 years with 13 cases in total (8 females and 5 males). The ratio of males were more in number in the age group of more than 60 years.

TABLE 4- INCIDENCE OF ATOPY

Atopy	Number	Percentage
Present	20	40%
Absent	30	60%

Among 50 cases, 20 patients (40%) had history of atopy whereas 30 patients (60%) had no history of atopy.

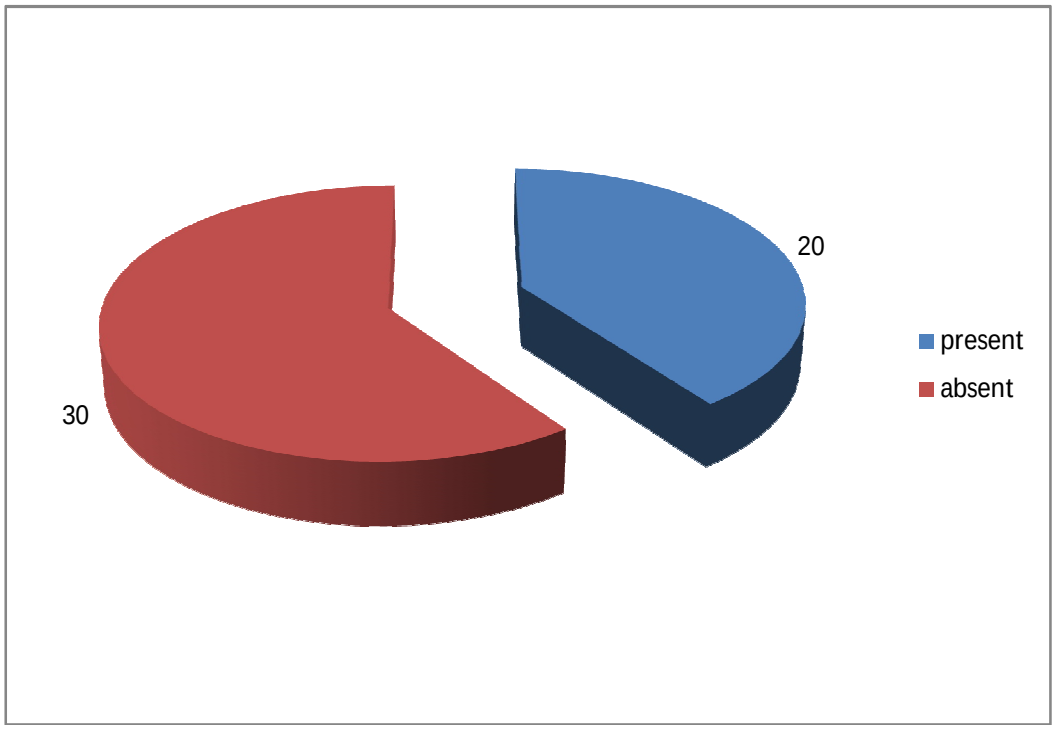
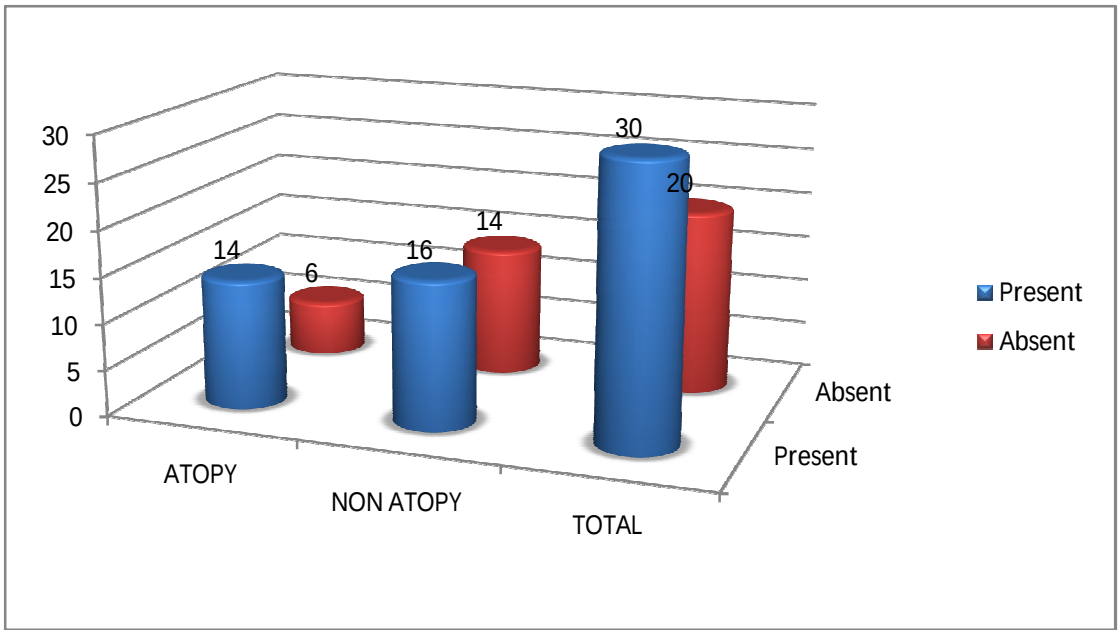


TABLE 5- COMPARISION OF ABSOLUTE EOSINOPHIL COUNT Vs ATOPY

AEC>440 cells/cu.mm	Atopy		Non atopy	
	Number	Percentage	Number	Percentage
Present	14	70	16	53.3%
Absent	6	30	14	46.7%
Total	20	100	30	100%

Among 30 patients with the history of non atopy, Absolute eosinophil count of >440cells/cu.mm was seen in 16 patients (53.3%) and absent in 14 patients constituting 46.7%. In 20 patients, with positive history of atopy 14 patients (70%) had elevated absolute eosinophil count and in 6 patients (30%) there in no such findings.

CHART 5: COMPARISION OF ABSOLUTE EOSINOPHIL COUNT Vs ATOPY



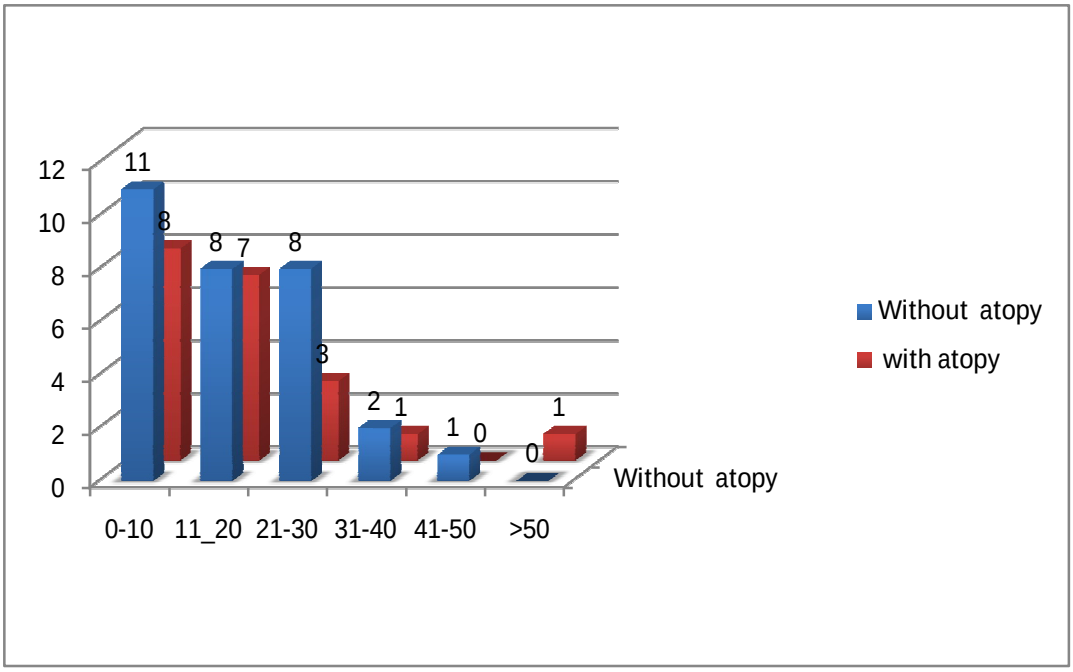
The figure above compares the number of patients from both atopic and non-atopic group with an elevated absolute eosinophil count. This elevation was more in the atopic individuals than the non-atopic individuals.

TABLE 6 - DURATION OF EXPOSURE

Duration	Without Atopy		With Atopy		Total	
	Number	%	Number	%	number	%
0-10	11	36.67%	8	40%	19	38%
11-20	8	26.67%	7	35%	15	30%
21-30	8	26.67%	3	15%	11	22%
31-40	2	6.66%	1	5%	3	6%
41-50	1	3.33%	0	0	1	2%
>50	0	0	1	5%	1	2%

In our study, less than 10 years is the most common duration of exposure, followed by 11 to 30 years. The longest duration of exposure was 52 years and 4 years was the shortest duration of exposure. The mean duration of exposure was 17.64 years.

CHART 6 - DURATION OF EXPOSURE



This bar diagram shows less than 10 years was the most common duration of exposure in both atopics and in non-atopics. The second most common is 11-20 years duration of exposure.

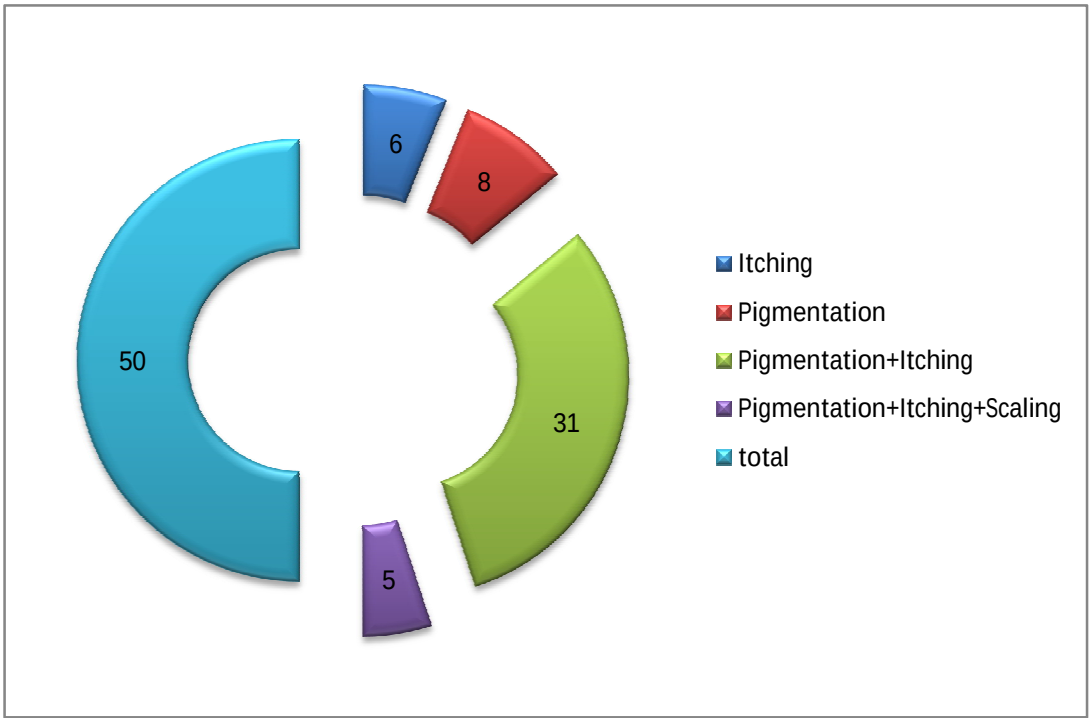
TABLE 7- COMPARISION OF SYMPTOMS IN KUMKUM DERMATITIS

Symptoms	Frequency	Percentage
Itching only	6	12%
Pigmentation only	8	16%
Pigmentation+itching	31	62%
Pigmentation+itching+scaling	5	10%
Total	50	100%

Pigmentation with itching is the most predominant symptom in our study, occurring in 31/50 patients (62%), pigmentation only is the second most common symptom occurring in 8 patients (16%), 6 patients presented

with only itching (12%), pigmentation with itching and scaling is seen in 5 patients (10%).

CHART 7- COMPARISION OF SYMPTOMS IN KUMKUM DERMATITIS



Pigmentation is quite common symptom in majority(31) cases is well understood from this chart. They can present either as only pigmentation or can be associated with scaling. Itching is the only presentation in 6 cases.

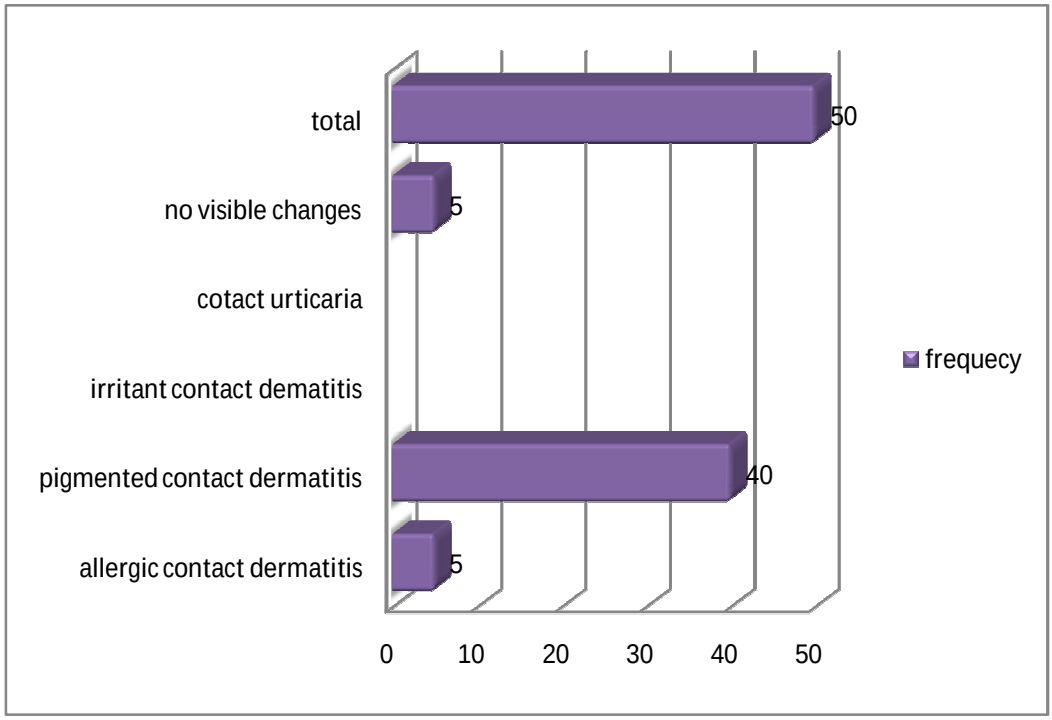
TABLE 8 – CLINICAL PRESENTATION OF KUMKUM DERMATITIS

Clinical presentation	Frequency	Percentage
Allergic contact dermatitis	5	10%
Pigmented contact Dermatitis	40	80%
Irritant contact dermatitis	-	-
Contact urticaria	-	-
No visible changes	5	10%

Among 50 patients, 40 patients (80%) had pigmented contact dermatitis mostly hyperpigmentation. This was followed by allergic

contact dermatitis in 5 patients (10%) and no visible skin changes in 5 patients (10%).

CHART 8 – CLINICAL PRESENTATION OF KUMKUM DERMATITIS



This bar chart denotes, higher number of cases of pigmented contact dermatitis to kumkum making it as the most common presentation. Allergic dermatitis comes next in line. No cases of contact urticaria and irritant contact dermatitis was noted.

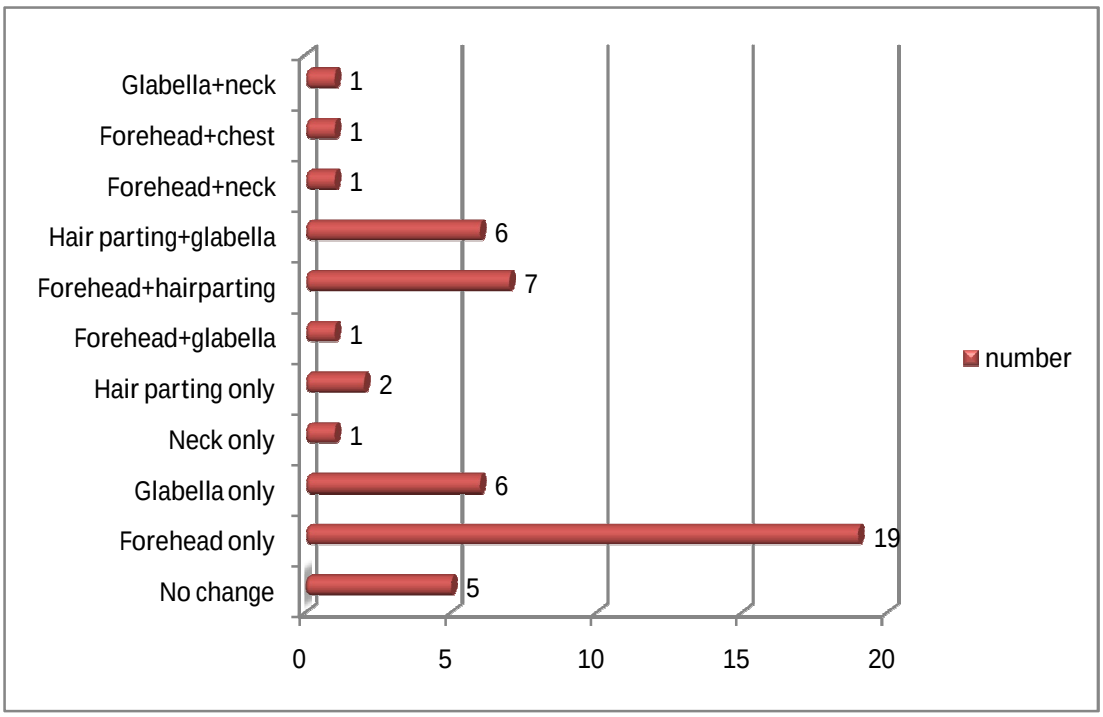
TABLE 9- CLINICAL PATTERN OF KUMKUM DERMATITIS

Clinical pattern	Number	Percentage
No change	5	10%
Forehead only	19	38%
Glabella only	6	12%
Neck only	1	2%
Hair parting only	2	4%
Forehead+glabella	1	2%
Forehead+hairparting	7	14%
Hair parting+glabella	6	12%
Forehead+neck	1	2%
Forehead+chest	1	2%
Glabella+neck	1	2%

Among 50 patients, 19 patients (38%) presented with only forehead involvement. Forehead & hairparting involvement in 7 patients (14%), glabella only in 6 patients (12%), hairparting & glabella in 6

patients (12 %), 5 patients (10%) had no visible skin lesions but came with complaints of itching. Involvement of hair parting area only noted in 2 patients (10%).

CHART 9- CLINICAL PATTERN OF KUMKUM DERMATITIS



The chart shows forehead involvement as the frequent site of kumkum dermatitis.

TABLE 10 – PATCH TEST RESULT

Patch test	Number	Percentage
Positive	28	56%
Negative	22	44%
Total	50	100%

Out of 50 patients who were subjected to patch testing , 28 patients showed patch test positivity (56%) and 22 patients were negative for patch test (44%).

CHART 10 : PATCH TEST RESULT

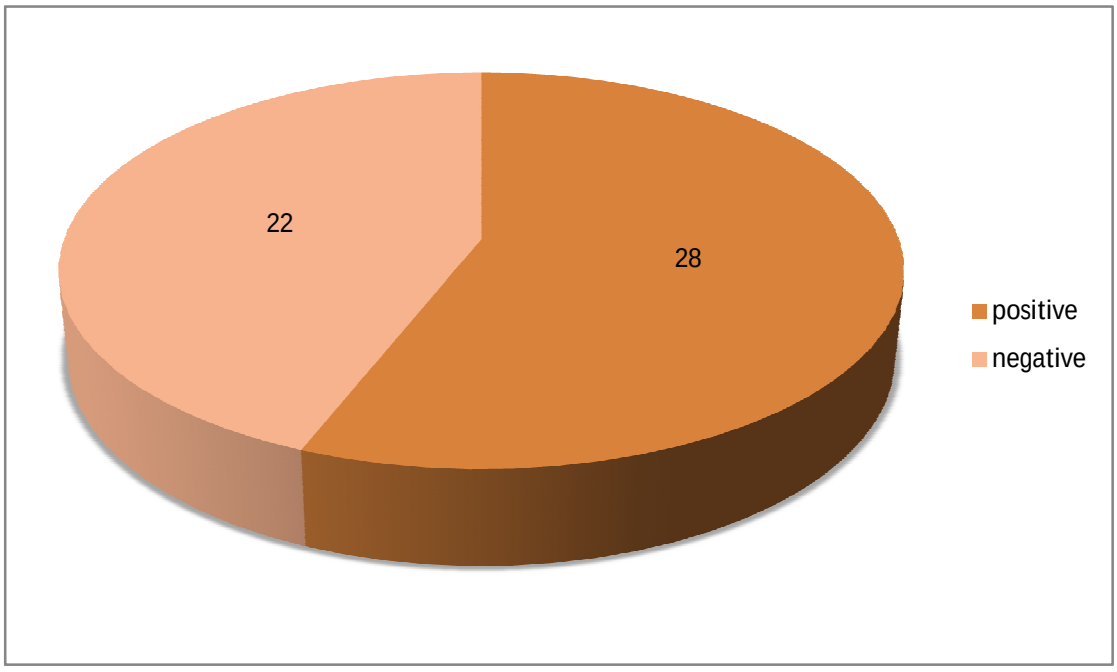
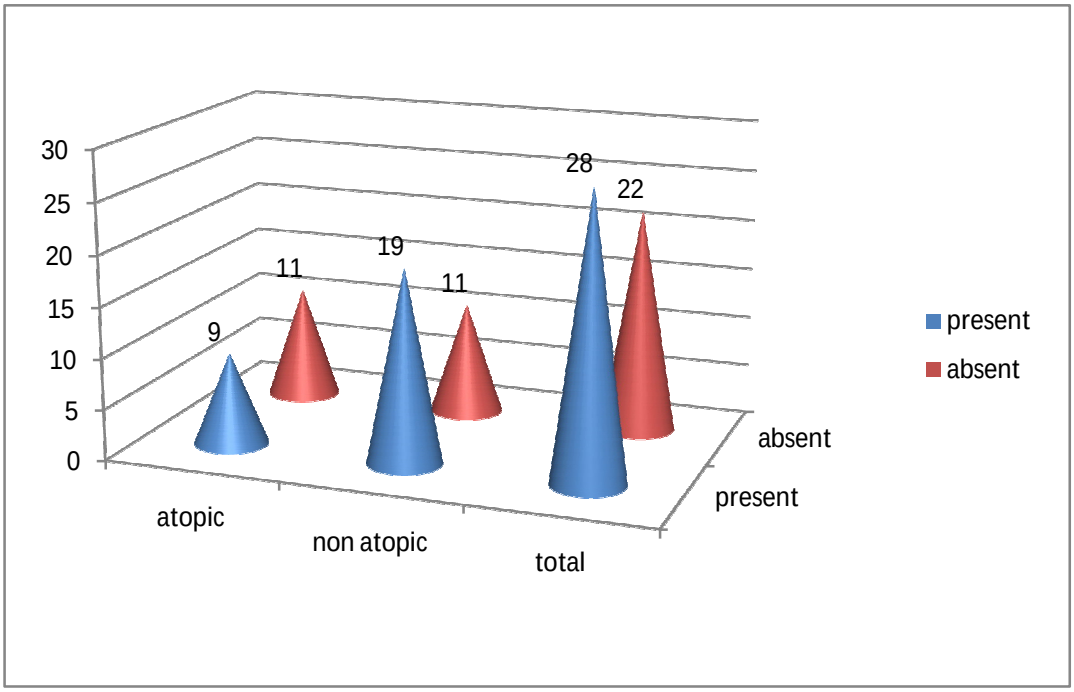


TABLE – 11 COMPARISION OF PATCH TEST RESULT WITH ATOPY

Patch test	Atopy		No atopy		Total	
	Number	%	Number	%	Number	%
Present	9	45%	19	63.3%	28	56%
Absent	11	55%	11	36.7%	22	44%

Among the atopics 45% had positive patch test whereas among the nonatopics, 63.3% had positive patch test. Thus atopy did not significantly influence the propensity for developing contact dermatitis. Thus even patients with history of non atopy also should be investigated for eosinophil and absolute eosinophil count.

CHART – 11 COMPARISION OF PATCH TEST RESULT WITH ATOPY



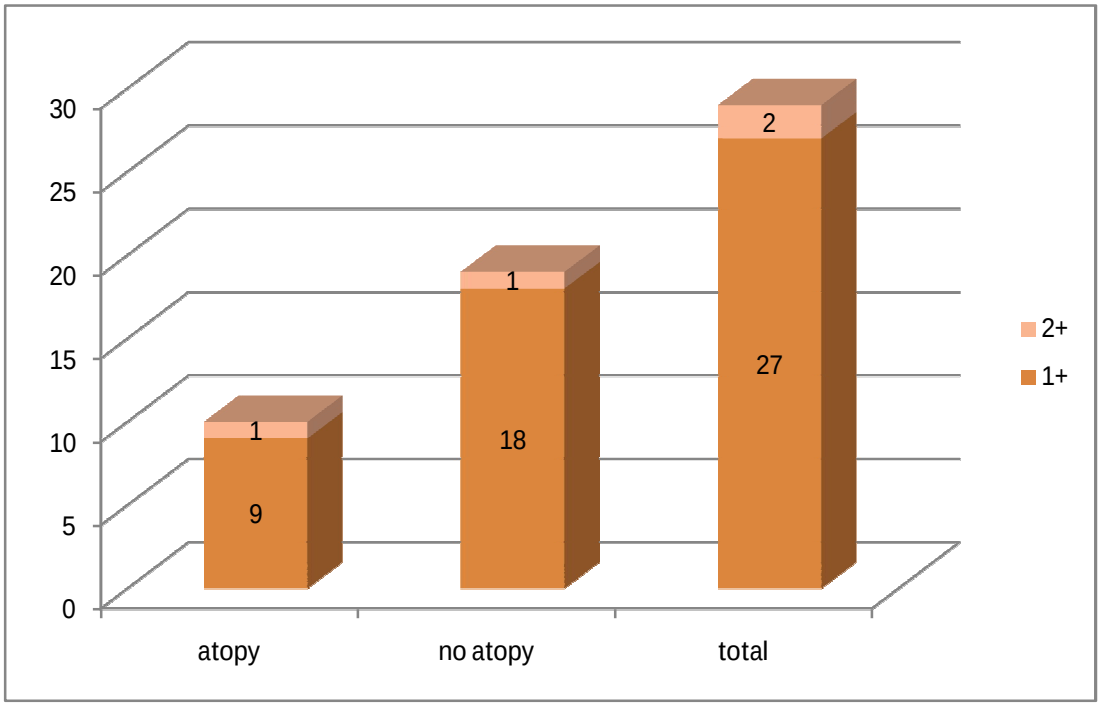
This picture enumerate the association of atopy with patch testing. 19 non-atopic patients shows positive patch test reaction. This emphasis that contact dermatitis occur in both atopic and non atopic individuals. History of atopy act as a confounding factor.

TABLE 12 – GRADING OF PATCH TEST

Grading	Atopy		No atopy		Total	
	No	%	No	%	No	%
1+	9	90%	18	94.7%	27	93.1%
2+	1	10%	1	5.3%	2	6.9%

As per grading the patch test reading , among 28 patients who showed positive patch test reaction, grade 1+ (erythema ad papules-non vesicular) was seen in a total of 27 patients (93.1%). This includes 9 atopics (90%) and 18 non-atopics (94.7%). Grade 2+ (erythema, papules and vesicules-vesicular) was seen in total of 2 patients (6.9%). This includes 1 patient with atopic history (10%) and 1 patient (5.3%) without atopic history.

CHART 12 – GRADING OF PATCH TEST



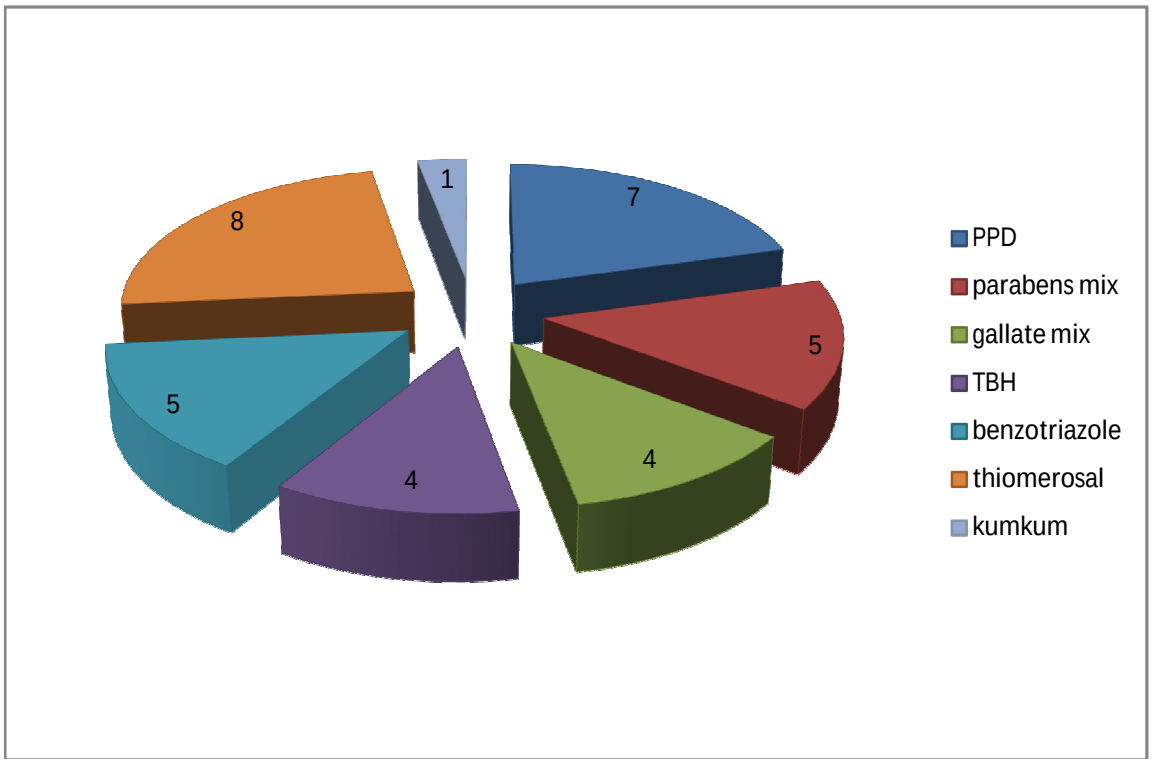
The above bar diagram points out that grade 1+(erythema ad papules-non vesicular) is most common in kumkum dermatitis. This seen in 9 patients of atopic individuals and 18 patients in non atopic individuals. Grade 2+ (erythema, papules and vesicles-vesicular) is seen only in 2 patients (one from the atopic and non-atopic group)

TABLE 13 – PATCH TEST POSITIVITY FOR INDIVIDUAL ALLERGEN

Allergen	Number	Percentage
PPD	7	25%
Parabens mix	5	17%
Gallate mix	4	14%
TBH	4	14%
Benzotriazole	5	17%
Thimerosal	8	28%
Kumkum	1	3%

In our study, the most common allergen that cause contact dermatitis was found to be thimerosal which is positive in 8 patients (28%) followed by PPD positive in 7 patients (25%), Parabens mix and benzotriazole positive in 5 patients (17%), Gallate mix and ter-butyl hydroquinone in 4 patients each (14%) and kumkum positivity in 1 patient (3%).

CHART 13 : PATCH TEST POSITIVITY FOR INDIVIDUAL ALLERGEN



DISCUSSION

Among the total eczematous skin condition attending our Occupational contact Dermatitis outpatient department which includes both endogenous and exogenous eczema, 1116 patients presented with contact dermatitis to various allergen. Out of which 50 patients had contact dermatitis to kumkum.

DEMOGRAPHIC DATAS:

SEX DISTRIBUTION:

In our study, which includes total of 50 cases, 37 cases were females and 13 cases were males. This shows that the incidence of kumkum dermatitis was more common in females than males. The ratio of female : male is 2.8:1. In two studies conducted by Nath AK and Thappa DM the results were consistent with our study. In first study which includes 46 cases the female:male ratio was 1.8:1, whereas in another study conducted in 35 cases the ratio was 1.9:1.

Study	Sex ratio(female:male)
Our study	2.8:1
Nath AK and Thappa DM	1.8:1
Nath AK and Thappa DM	1.9:1

AGE DISTRIBUTION:

The mean age of kumkum dermatitis in our study was 44.32 years as compared to 46.5 years in the study "kumkum-iduced dermatitis: analysis of 46 cases" done by Nath AK and Thappa DM. In another study "Clinical spectrum of dermatoses caused by cosmetics in south India: High prevalence of *kumkum* dermatitis" the mean duration of exposure was calculated as 42 years. Thus, these studies shows contact dermatitis to kumkum develops in their 4^{th} decade of life. This indirectly denotes chronic exposure is needed.

Study	Average age in years
Our study	44.32 years
Nath AK and Thappa DM	46.5 years
Nath AK and Thappa (35 patients)	42 years

DURATION OF EXPOSURE:

Among the patients in our study who exposed to kumkum, the mean duration of exposure is 17.64 years. In our study the shortest duration was

4 years and 52 years was the longest duration of exposure seen in 67 year old female. This clearly shows that prolonged periods of contact with kumkum is needed for the development of kumkum-induced dermatitis. Though many patients presented late their onset of symptoms was much earlier.

ASSOCIATION WITH ATOPY:

In our study 40 % had history of atopy and in 30 % of patients there is no history of atopy. Suman and Reddy in their study on hand eczema reported history of atopy in 36% of their patients.[(114)] Nilendu Sarma et al in his study on occupational contact dermatitis in construction workers in india reported atopy in 37.5%.[115]

Study	Association of atopy
Our study	40%
Nilendu Sarma et al	37.5%
Suman and Reddy	36%

- Goh et al in a two year study conducted from 1991 to 1993 on 864 atopic and 2283 non-atopic patients reported the prevalence of contact dermatitis was similar among atopics and non-atopics. He also noted there is no significant difference in patch test reaction.

Also the percentage of irritant and allergic contact dermatitis was similar in the study group.[116]

- In our study elevated absolute eosinophil count (>440cells/cu.mm) was seen in 70% atopics and 53.3% of non atopics. Antoszczyk et al in his study on nickel allergy in atopic and contact dermatitis reported 60% of the patient with increased eosinophil count.[117]

Absolute eosinophil count (>440 cells/cumm)	Association with atopy
Our study	70%
Antoszczyk et al	60%

CLINICAL PRESENTATION:

In our study the most common presentation was pigmented contact dermatitis consisting of 40 patients (80%) followed by allergic contact dermatitis in 5 patients (10%). Another 5 patients (10%) presented without any visible changes.

- Nath AK et al in his study on kumkum-induced dermatitis had reported pigmented contact dermatitis seen in 35 patients

constituting 76.1% followed by allergic contact dermatitis in 11 patients (23.9%)

- Goh et al reported tree cases of pigmented contact dermatitis to kumkum[118]
- A study conducted by AK Nath and DM Thappa "Clinical spectrum of dermatoses caused by cosmetics in south India: High prevalence of *kumkum* dermatitis" also commented that pigmented contact dermatitis as most common presentation in 40 patients out of 71 cases studied.
- According to an Indian study by Dogra *et al* , the commonest type of cosmetic dermatosis was allergic contact dermatitis seen in 29 out of 49 cases(59.2%), followed by irritant contact dermatitis in15 cases, hyperpigmentation and hypopigmentation in eight and six cases respectively.[119]

Study	Clinical presentation
Our study	Pigmented contact dermatitis-80% Allergic contact dermatitis- 10% No visible change- 10%
Nath AK and Thappa DM	Pigmented dermatitis-76.1% Allergic contact dermatitis-23.9%

AK Nath and DM Thappa (35 patients)	Pigmented dermatitis-56.33%
Dogra et al	Allergic contact dermatitis-59.2% Irritant contact dermatitis-30.6% Hyperpigmentation – 16.3% Hypopigmentation – 12.2%

Though allergic contact dermatitis was reported as commonest in one study done by Dogra et al, the cumulative results of various studies showed that pigmented contact dermatitis as the most common type of contact dermatitis. In our study also pigmented contact dermatitis is the commonest of all other various clinical presentation followed by allergic contact dermatitis. Other types of presentation such as irritant contact dermatitis and contact urticaria were not encountered in our study.

CLINICAL PATTERN:

Dermatitis localized to forehead was the most common clinical pattern in our study accounting for about 19 patients (38%) followed by forehead & hairparting involvement in 7 patients (14%), glabella only in 6 patients (12%), hairparting & glabella in 6 patients (12 %) , 5 patients (10%)had no visible clinical presentation but comes with history of

kumkum dermatitis. Involvement of hair parting area only noted in 2 patients (10%).

- Nath AK et al in his study on 46 patients showed forehead as the most commonly involved site in 31 patients followed by glabella in 16 patients, hair parting area in 6 patients and neck in 3 patients.

Study	Clinical pattern
Our study	Forehead only – 38% Forehead & hairparting – 14% Glabella only – 12% Hairparting and glabella – 12% No visible changes – 10% Forehead and neck – 2% Forehead and chest – 2% Neck only – 2%
Nath AK et al	Forehead – 67.31% Glabella – 34.78% Hair parting – 13% Neck – 6.5%

Our study shows forehead as the most common site followed by forehead and hairparting area in females as this is site where they frequently keep kumkum. In males forehead is the most common site followed by chest. About 5 patients (10%) who presented without any visible changes, 3 of them showed positive patch test reaction. These may be the earliest presentation and this throws light on the importance of patch testing in allergic contact dermatitis to diagnose the subclinical cases.

PATCH TEST RESULTS:

Among 50 patients, 28 patients (56%) showed positive patch test allergic reaction followed by 22 patients (44 %) showing negative patch test reaction.

- In 28 patients (56%) who showed patch test positivity thimerosal was positive in 8 patients(28%) followed by PPD positive in 7 patients (25%), Parabens mix and benzotriazole positive in 5 patients (17%), Gallate mix and ter-butyl hydroquinone in 4 patients each (14%) and kumkum positivity in 1 patient(3%)
- In study done by Nath AK and Thappa DM in 2007, out of 25 patients thimerosal was positive in 18, followed by gallate mix in 12

cases, Para-phenylenediamine, benzotriazol, tert-butyl hydroquinone and parabens gave positive reaction for one patient each. Patch testing with kumkum was positive in 7 patients.

- Nath AK and Thappa DM in another study “Patch Testing In Cosmetic Dermatoses: A Report From South India” Thimerosal was positive in 27 patients (27/35), gallate mix in 15 patients (15/35), para-phenylenediamine in five patients (5/35), Parabens , benzotriazole, tertiary-butyl hydroquinone was positive in one patient.
- In India, Dogra et al patch tested 200 females with cosmetic dermatitis and found para-phenylenediamine (PPD) to be the commonest (35%) cosmetic allergen, followed by balsam of Peru (22.5%), parabens (19.25%).
- Trattner et al also found the most frequent allergens in their cosmetic series to be Kathon CG (35% of patients), thimerosal (26.2%), triethanolamine (8.7%), and octyl gallate (7.5%)

Study	Allergens
Our study	Thimerosal – 28% PPD – 25% Parabens mix – 17% Benzotriazole – 17% Gallate mix – 14% ter-butyl hydroquinone – 14% kumkum – 3%
Nath AK and Thappa DM	Thimerosal – 72% gallate mix – 48% Para-phenylenediamine – 4% Benzotriazol – 4% tert-butyl hydroquinone – 4% Parabens – 4% Kumkum – 7 patients
Nath AK and Thappa DM (35 patients)	Thimerosal – 77.14% gallate mix – 42.8% paraphenylenediamine – 14.28% Parabens – 2.8%

	Benzotriazol – 2.8% tertiary-butyl hydroquinone-2.8%
Dogra et al	paraphenylenediamine - 35% Parabens - 19.25%

Thus, thimerosal is most frequent allergen in our study. This may be related to previous sensitization of thimerosal as preservative in vaccines, eye drops and drugs. The second most common is PPD since many patients are sensitized with PPD in hairdye. But, in our study no patient gives history of allergy to hairdye.

CONCLUSION

1. The incidence of kumkum dermatitis was 4.48% among 33.87% of patients attending our OPD with history of contact dermatitis. This indicates rising trend in the incidence of kumkum induced dermatitis. This may be due to shopping list of commercial kumkum available in the market and no standard manufacturing guidelines were followed in both large scale and small scale industries.
2. Female to male ratio was 2.8:1 with females predominating in kumkum – induced dermatitis. However, there were 13 male cases out of 50 cases. This shows definite significance of kumkum dermatitis in male population.
3. The mean age of distribution of kumkum dermatitis in our study was 44.32 years due to long latency before which the skin lesions appear.
4. The mean duration of exposure required to develop kumkum dermatitis is 17.64 years.
5. In our study, 40% of the study group were atopics and non atopics constitutes 60%.
6. Higher percentage of patients developed contact dermatitis kumkum within 10 year duration in both atopics (40%) and in non atopics (36.67%). This points out there was no significant difference in both groups when the duration of exposure is compared.

7. About 2/3rd of patients had pigmentation with itching as the predominant symptom. In 12% itching is the only symptom without any clinical manifestation. Thus identifying patients in this early stage could prevent further progress of the disease.
8. Pigmented contact dermatitis (PCD) is seen in 1/5th of the patients. Studies shows PCD is more common in dark complexion individuals. Since, majority of our population are wheatish complexion this could be the reason for increased incidence of pigmentation.
9. Comparing the site, forehead is the common site followed by hairparting area.
10. When patch test results are compared, it came positive in 63.3% of non-atopic and 45% of atopic individuals. Thus, history of non atopy does not influence the results of patch test reaction.
11. Interpretation of patch test results indicates grade1+ reaction (erythema and papules-non vesicular) is the commonest. Grade 2+ (erythema, papules and vesicles-vesicular) is the second commonest.
12. Our study shows thimerosal as the commonest allergen. The next in line is para-phenylenediamine. But none of our patients gives history of allergy to hairdye though 4 patients give history of hairdye application.

The treatment of kumkum is divided as

1. Preventive measures
2. Corrective measures
3. Treatment of substitution

PREVENTIVE MEASURES:

Given in patients sensitive to multiple cosmetics or to those suffering from multiple cosmetic intolerance syndrome.

CORRECTIVE MEASURES:

1. Avoidance of kumkum usage
2. Symptomatic treatment for pigmentation and itching with topical corticosteroids and antihistamines respectively. Demelanizing agents like hydroquinone, arbutinin and kojic acid.

TREATMENT OF SUBSTITUTION:

Patients those who are unable to completely stop using kumkum can be substituted with less sensitive products. Some may improve with change in the brand used but will definitely develop dermatitis after certain period of exposure. Patient can be adviced to use kumkum over Vaseline applied skin. Another alternative is to use “santhu”. Castilani’s paint can also be substituted.

Our patients were treated symptomatically with topical corticosteroids and oral antihistamines and they showed good clinical improvement. They are also adviced to avoid using kumkum and suggested other alternatives. Advice to avoid hairdye application in PPD sensitive individuals was given. Other allergens like Parabens mix, Gallate mix, TBH were also used in cosmetics and toiletries patients are warned about other cosmetics induced dermatitis.

This study emphasizes the need for standardization of methods employed in commercial kumkum manufacturing industries. Such practises may prevent the incidence of kumkum-induced dermatitis in near future.

Limitations of this study were other allergens such as kanaga oil, sudan I, Brilliant lake red were not tested as they are not available.This stress the importance of adding these allergens in Indian standard series. As the Indian study on kumkum dermatitis were very few, a large group study must be employed to know in depth of actual prevalence of kumkum dermatitis.

PROFORMA

Name of the patient:

Patient ID number:

Age:

Sex:

Patient phone no:

Address:

Education status:

Occupation:

Chief complaints with duration of symptoms:

History of Presenting complaints:

Onset

Progression

Exacerbating factors

History of contact with kumkum and duration of exposure:

History of Atopy

PAST HISTORY:

Similar illness in the past

Diabetes, hypertension

FAMILY HISTORY:

History of atopy in family members

TREATMENT HISTORY:

GENERAL EXAMINATION:

Vital signs:

PR:

BP:

System examination:

CVS:

RS:

ABDOMEN:

CNS:

DERMATOLOGICAL EXAMINATION:

MORPHOLOGY:

SITE:

INVESTIGATIONS:

Routine blood investigation

Patch test

DIAGNOSIS:

TREATMENT:

PATIENT CONSENT FORM

Title of the study: CLINICO EPIDEMIOLOGIC STUDY OF CONTACT DERMATITIS TO KUMKUM

Name of the Participant:

Name of the Principal (co-investigator): DR.SUBHASHINI S

Name of the Institution: Department of Dermatology,
Rajiv Gandhi Government General Hospital,
Chennai.

Documentation of the informed consent

I _____ have read the information in this form (or it has been read for me). I was free to ask any questions and they have been answered. I am over 18 years of age and exercising my free power of choice, hereby giving my consent to be included as a participant in the study.

1. I have read and understood this consent form and the information provided to
   me.
2. I have had the consent document explained to me.
3. I have been explained about the nature of the study.

4. My rights and responsibilities have been explained to me by the investigator.

5. I agree to co-operate with the investigator and I will inform him/her immediately if I suffer unusual symptoms.

6. I have not participated in any research study at any time .

7. I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in this hospital.

8. I hereby give permission to the investigators to release the information obtained from me as a result of participation in this study to the sponsors, regulatory authorities, Government agencies and IEC. I understand that they are publicly presented.

9. My identity will be kept confidential if my data are publicly presented.

10. I am aware that if I have any question during this study, I should contact at one of the addresses listed above.

Participant's initials:_____

For adult participants:

Name and signature/thumb impression of the participant (or legal representative if participant incompetent)

_____ _____ _____

Name Signature Date

Name and signature of impartial witness (required for illiterate patients):

_____ _____ _____

Name Signature Date

Address and contact number of the impartial witness:

Name and Signature of the investigator or his representative obtaining consent:

_____ _____ _____

Name Signature Date

KEY TO MASTER CHART

SEX:

1. M – Male
2. F – Female

DE – Duration of exposure

ATOPY:

1. P – Present
2. N –negative

AD – ATOPIC DERMATITIS:

1. P – Present
2. N - Negative

SYMPTOMS

1. PIG - pigmentation
2. ITCH- Itching
3. SC-Scaling

CP – CLINICAL PRESENTATION:

1. ACD – Allergic contact dermatitis
2. ICD – Irritant contact Dermatitis
3. PCD – Pigmented contact dermatitis
4. NO - No visible change

PD - CLINICAL PATTERN OF DISTRIBUTION

1. FH - Forehead
2. HP – Hair parting
3. GL - Glabella
4. N - Neck
5. CH - Chest
6. NO- no visible changes

AEC – Absolute eosinophil count

PATCH TEST

1. P – Positive
2. N – Negative
3. DT – doubtful reaction
4. PPD- para -phenylene diamine
5. PM-parabens mix
6. GM-gallate mix
7. TBH- tert buty hydroquinone
8. BENZ-benzotriazole
9. THIO-thiomersal
10. KUMKUM

ABBREVIATIONS

ACD – Allergic contact dermatitis

AEC – Absolute eosinoplil count

DNCB – Dinitrochlorobenzene

GM-CSF – Granulocyte monocyte colony stimulating factor

IL-1 – Interleukin 1

ICAM-1 – Inter cellular adhesion molecule 1

ICD – Irritant contact dermatitis

LFA – Lympocyte function associated antigen

MHC – Major histocompatibility complex

OPD – outpatient department

PPD – para-phenylenediamine

TNF α – Tumor necrosis factor α

UVA – Ultraviolet A